CLINICAL APPROACHES: A TRAINING MANUAL

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FOUNDATIONAL GUIDELINES

DOSING

Dosing information in these approaches is for an adult weighing 120–150 lb (54–68 kg), and should be adjusted accordingly. For example, an individual weighing 60–75 pounds should take half of the recommended dose.

WEIGHT (lb)	WEIGHT (kg)	DOSE
241+ lb	109+ kg	2 (x label)
211-240 lb	96-108 kg	1¾ (x label)
181-210 lb	82-95 kg	1½ (x label)
151–180 lb	69-81 kg	1¼ (x label)
120-150 lb	54-68 kg	1 (as per label)
90-119 lb	41-54 kg	¾ (of label)
60-89 lb	27-40 kg	½ (of label)
30-59 lb	13-26 kg	¼ (of label)

Shake the liquid products well before each use. Dispense drops by holding the dropper at a 45-degree angle to ensure the proper dosage.

Mix the drops together in a cup made of glass, porcelain, or paper, and add at least 4 oz (120 ml) of water; let sit for at least 1 minute before drinking. Avoid using Styrofoam, plastic, or metal cups; also avoid using distilled, sparkling, or reverse-osmosis water. While the products may be dispensed directly into the mouth, they are most effective when taken with water.

HYDRATION

Adults are urged to drink 2–3 liters or quarts of water per day (adjust as needed, based on weight). Black and green teas, coffee, sodas, and alcoholic drinks are dehydrating. Vegetable and some fruit juices (lemon and lime) are hydrating. Most herbal teas are hydrating but can become dehydrating if too much sugar is added. Use NutraMedix STEVIA as a sweetener instead of sugar.

Drinking 2–3 ounces (60–90 ml) of pure water every 10–15 minutes during waking hours causes most of the water to enter the cells, hydrate the cells, and mobilize toxins out of the cells. Drinking large quantities of water, even a few times per day, does not efficiently hydrate the body, nor does it mobilize toxins out of the body.

STRESS AND DIET

Stress-reduction techniques are highly recommended, such as deep breathing while visualizing a relaxing vacation spot with all senses for 4 minutes before each meal and bedtime.

Patients should be resting in bed (even if not sleeping) from 11 p.m. to 6 or 7 a.m. the next morning, in a pitch-dark bedroom with minimal electromagnetic pollution, to support a normal circadian rhythm and facilitate healing.

Eating more raw, organic, non-GMO food is recommended. Avoid processed foods, fried foods, hydrogenated oils, sugars, excessive starches, and fruits, except for lemons and limes. Avoid common food allergens such as dairy, wheat, corn, soy, peanuts, and black or white pepper. Patients who avoid these foods usually report improved health more quickly.

HERXHEIMER-LIKE REACTION/HEALING CRISIS

If a Herxheimer-like reaction is suspected (feeling worse in any way than before), take BURBUR-PINELLA: 20 drops in 2 oz (60 ml) of clean water every 10 minutes for up to 2 hours. The easiest way to do this is to add four dropperfuls of BURBUR-PINELLA to a bottle of water and sip it over a 2-hour period.

If the symptoms still exist by the time of the next scheduled dose of microbial support, skip that dose and resume with the following scheduled dose. If this happens more than once, increase the dosage more slowly, building up to the full dose as tolerated. For additional Herxheimer- like-reaction support, rub ½ tsp (1.25 ml) Liposomal glutathione on the lower legs every 15 minutes.

IMPORTANT!

NutraMedix liquid products contain 20–24% food-grade ethanol for two main reasons.

First, the blend of water and ethanol is key to extract the different desired components. Some compounds are water soluble while others are ethanol soluble, which allows for a more complete, full-spectrum extract.

Second, the ethanol helps transport the nutrients into the cells. The blend of ethanol and water supports efficient absorption on a cellular level.

CLINICAL APPROACHES

ARTERY SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops twice per day (start with one drop) †				
TAKUNA	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
ADRENAL	20 drops twice per day				
AMANTILLA (Valerian)	15 drops twice per day				
PARSLEY	10 drops twice per day				

† Increase as tolerated to reach the recommended dose.

30+ minutes	after meals	Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

every ot	her night	Morning	Afternoon	Evening	Bedtime
SEALANTRO	40 drops every other night (start with one drop) ‡				

‡ Add one drop per week until reaching the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- Follow the foundational nutritional and lifestyle guidelines at the beginning of the protocol section.
- **Walk 15–30 minutes** several times per week, indoors or outdoors, with a healthy partner and a cell phone for safety.
- **Include Proteolytic enzymes** (5 bromelain or 4 Carnivora or 3 Serazyme or 3 Lumbrokinase) with water and each dose of CUMANDA or BANDEROL. (If there is an allergic tendency, rotate between at least two of these enzymes.)
- **Chromium polynicotinate:** 200-400 mg twice per day (breakfast and supper)
- **Tocotrienols with vitamin E:** dosing according to the label (breakfast and/or supper)
- **EPA/DHA Fish Oil** (with at least 360 mg of EPA): twice per day (lunch and bedtime)
- **Wild Blueberry:** 1 capsule twice per day (lunch and bedtime)
- **L-Lysine:** 2000 mg and **L-Proline:** 2000 mg, twice per day (lunch and bedtime)
- **Coenzyme Q10** (rice-emulsified, without soy): at least 100 mg per day (supper)
- Acetyl-L-Carnitine: 500 mg per day (breakfast); NutraMedix Methyl Complete: 2 capsules per day (lunch)

BLOOD-PRESSURE SUPPORT

I. DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	before meals	Morning	Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops twice per day				
BURBUR-PINELLA	20 drops four times per day				
AMANTILLA (Valerian)	15 drops four times per day				

† If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

30+ minutes	after meals	Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Rationale:

- GLUCOMEDIX may help with metabolic support (blood pressure, blood glucose, and lipids).
- BURBUR-PINELLA supports detoxification.
- AMANTILLA supports healthy stress management.
- MAGNESIUM supports smooth muscle relaxation in artery walls.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- Follow the foundational nutritional and lifestyle guidelines at the beginning of the protocol section.
- Walk 15–30 minutes several times per week, indoors or outdoors, with a healthy partner and cell phone for safety.
- EPA/DHA Fish Oil (with at least 360 mg of EPA): twice per day
- **Coenzyme Q10** (rice-emulsified, without soy): at least 100 mg per day (supper)
- NutraMedix **Vitamin C**: 1,000 mg per day

NOTES	

CARDIOVASCULAR SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Part 1 (days 1-90)					
30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
VITALMEDIX	30 drops twice per day				
GLUCOMEDIX †	30 drops once per day				
SERRAPEPTASE	2 capsules twice per day				
30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
ANTARCTIC KRILL	2 softgels twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

† If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

Part 2 (days 15–90)					
30+ minutes after meals Morning Afternoon Evening Bedtime					Bedtime
VITAMIN C	2 capsules twice per day				

Notes:

- This approach may be continued past 90 days for ongoing support.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- Follow the foundational nutritional and lifestyle guidelines at the beginning of the protocol section.
- Walk 15–30 minutes several times per week, indoors or outdoors, with a healthy partner and cell phone for safety.
- **Tocotrienols with vitamin E:** twice per day (breakfast and supper)
- **EPA/DHA Fish Oil** (with at least 360 mg of EPA): twice per day (lunch and bedtime)
- **Coenzyme Q10** (rice-emulsified, without soy): at least 100 mg per day (supper)
- **Acetyl-L-Carnitine:** 500 mg per day (breakfast)
- NutraMedix **Methyl Complete:** 2 capsules per day (lunch)
- Can use NutraMedix **STEVIA** as a sweetener.

CONSTIPATION SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2–3 capsules twice per day				
VITAMIN C	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- Drink something warm in the morning.
- Stay active and exercise regularly.
- Eat more vegetables.

- Eliminate junk food, grains, cow dairy, and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.

GLUTEN-INTOLERANCE SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

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30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
NONI	30 drops three times per day				
BANDEROL	30 drops twice per day (start with one drop) †				
SAMENTO	20 drops twice per day (start with one drop) †				
ADRENAL	20 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
AMANTILLA (Valerian)	15 drops once per day				
EZOV (Hyssop)	10 drops once per day (start with one drop) ‡				

[†] Increase as tolerated to reach the recommended dose.

[‡] Add one drop every 3–4 days until reaching the recommended dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

every other night		Morning	Afternoon	Evening	Bedtime
SEALANTRO	40 drops every other night §				

§ Start with one drop per serving; add one drop per week until reaching the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- Avoid all grains with gluten, such as wheat (including spelt, kamut, triticale); barley; rye; and oats.
- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- Avoid common food allergens such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or
 peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.
- Take a broad-spectrum probiotic such as BifidoBiotics from Allergy Research Group or Dr. Ohira's Probiotics from
 Essential Formulas every bedtime, along with a prebiotic fiber such as FOS (fructooligosaccharides), psyllium, or
 slippery elm.

This approach is not a substitute for conventional medical care and should be used in conjunction with, not instead of, standard treatment.

GUT SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Phase 1 (Days 1–2)		Morning	Afternoon	Evening	Bedtime
BURBUR-PINELLA	20 drops twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Phase 2 (Days 3-9)	(Add to Phase 1)	Morning	Afternoon	Evening	Bedtime
+ SAMENTO	30 drops twice per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Phase 3 (Days 10-45)	(Add to Phases 1 & 2)	Morning	Afternoon	Evening	Bedtime
+ ENULA	30 drops twice per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Phase 4 (Days	46-90) (A	Add to Phases 1, 2, & 3)	Morning	Afternoon	Evening	Bedtime
+ CURCUMIN	2	2 capsules twice per day				
+ VITAMIN C	2	2 capsules twice per day				

Notes:

- This approach can be continued past 90 days for ongoing support.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as dairy and gluten, as well as caffeine and alcohol.
- Reduce dietary fat, both animal and vegetable.
- Increase dietary soluble fiber; decrease dietary insoluble fiber.
- **Consider soluble fiber supplements** (acacia gum, guar gum, rice soluble fiber, slippery-elm bark, psyllium).

IRRITABLE-BOWEL SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

For stress or fungal cause:		Morning	Afternoon	Evening	Bedtime
AMANTILLA (Valerian)	15 drops four times per day				

For nonfungal microbial cause:		Morning	Afternoon	Evening	Bedtime
MORA	30 drops twice per day				
BLACK WALNUT HULL † (tincture)	30 drops twice per day				

† Not a NutraMedix product

For constipation prevention: ‡		Morning	Afternoon	Evening	Bedtime
VITAMIN C	2 capsules twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

‡ For stronger support, see **Constipation Support**

For diarrhea:		Morning	Afternoon	Evening	Bedtime
ACACIA GUM † (organic powder)	1 teaspoon (5 mg) two to four times per day		(•)		(•)

† Not a NutraMedix product

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- Consume hot peppermint leaf tea or oral peppermint oil.
- Drink hot tea made from crushed fennel seeds.
- Place an **infrared heating pad** on the abdomen.
- Practice **stress-reduction techniques** before meals, at bedtime, and when stressed.
- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as dairy and gluten, as well as caffeine and alcohol.
- Reduce dietary fat, both animal and vegetable.
- Increase dietary soluble fiber; decrease dietary insoluble fiber.
- **Consider a soluble fiber supplement** (acacia gum, guar gum, rice soluble fiber, slippery-elm bark, or psyllium).
- If symptoms do not improve with dietary measures, the cause may be fungal. Consider mold remediation, HEPA charcoal filters, and antifungal treatment for sinuses, gut, and body, if indicated.

LEAKY-GUT SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
ENULA	30 drops three times per day (start with one drop) †				
CUMANDA	30 drops three times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Notes:

- Once reaching the full dose of both herbs, continue this approach for 8 more weeks.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Food-grade Diatomaceous Earth** (DE) 1 teaspoon (5 mg) in 4 ounces (120 ml) of water, with breakfast on Monday through Friday, for the first 6 weeks of this approach. (DE works best when pulsed, with two days off per week.)
- Avoid sugar and starch for 1–2 months.
- Can use NutraMedix **STEVIA** as a sweetener.
- Follow an organic, vegetarian, ketogenic diet.
- Saccharomyces boulardii: one capsule twice per day after meals .

BLOOD-SUGAR SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minut	30+ minutes before meals		Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops three times per day				
TAKUNA	30 drops twice per day				
ADRENAL	20 drops twice per day				
BURBUR-PINELLA	20 drops three times per day				
EZOV (Hyssop)	10 drops once per day (start with one drop) ‡				

[†] If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

[‡] Increase as tolerated to reach the recommeded dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

every other night		Morning	Afternoon	Evening	Bedtime
ALGAS (Asparagus)	20 drops every other night (start with one drop) §				

§ Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix STEVIA as a sweetener.
- Eat low-glycemic foods.
- Chromium polynicotinate: 200 mcg twice per day

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ANAPLASMA and ERLICHIA

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15-26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 3 Days 29–40	(rest on days 41, 42)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				

[†] Increase as tolerated to reach the recommended dose.

Notes:

- Treatment consists of three 14-day cycles (two weeks per cycle), which should be repeated to fill 5-6 months.
- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- **Each cycle uses a different primary herb**: BANDEROL for cycle 1 (days 1–14), CUMANDA for cycle 2 (days 15–28), and TANGARANA for cycle 3 (days 29-42).
- All cycles have identical support herbs: SAMENTO and BURBUR-PINELLA.
- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

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BARTONELLA

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1-12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
HOUTTUYNIA	30 drops three times per day (start with one drop) †				
SAMENTO	30 drops three times per day (start with one drop) †				
BURBUR-PINELLA	20 drops three times per day				
SERRAPEPTASE	2 caps three times per day				

[†] Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15–26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops three times per day (start with one drop) †				
SAMENTO	30 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				
SERRAPEPTASE	2 caps three times per day				

[†] Increase as tolerated to reach the recommended dose.

Cycle 3 Days 29-40	(rest on days 41, 42)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops three times per day (start with one drop) †				
SAMENTO	30 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				
SERRAPEPTASE	2 caps three times per day				

[†] Increase as tolerated to reach the recommended dose.

Notes:

- Treatment consists of three 14-day cycles (two weeks per cycle), which should be repeated to fill 3 months.
- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- Each cycle uses a different primary herb: HOUTTUYNIA for cycle 1 (days 1-14), CUMANDA for cycle 2 (days 15–28), and TANGARANA for cycle 3 (days 29–42).
- All cycles have identical support herbs: SAMENTO, BURBUR-PINELLA, and SERRAPEPTASE.
- For additional support, add NutraMedix **NUTRA-BRT, 30 drops** three times per day, to each cycle.
- NutraMedix **STEVIA** may also be helpful for Bartonella.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA 15 drops**, every 15 minutes for 1–2 hours.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

BLASTOCYSTIS HOMINIS

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop) †				
ENULA	30 drops twice per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15–26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops four times per day (start with one drop) †				
ENULA	30 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Notes:

- Treatment consists of two 14-day cycles (2 weeks per cycle), which should be repeated to fill 5-6 months.
- Herbs should be taken daily until the recommended dosage is reached.
- Once at the recommended dosage, change to a 14-day cycling approach: Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- Each cycle uses a different primary herb: CUMANDA for cycle 1 (days 1–14) and TANGARANA for cycle 2 (days 15-28).
- Both cycles have the same support herb: ENULA.
- Herxheimer-like reactions are not uncommon and can be severe if a patient has Borrelia or Bartonella in addition to worms.
- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- Food-grade Diatomaceous Earth (DE): 1 teaspoon (5 mg) in water, twice per day at the beginning of meals (breakfast and supper).
- **DE** should be administered in 14-day cycles (12 days on and 2 days off), concurrent with the drops.

NOTES		

BRUCELLA

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops three times per day (start with one drop) †				_
MORA	30 drops three times per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15-26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops three times per day (start with one drop) †				
ENULA	30 drops three times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Notes:

- Treatment consists of two 14-day cycles (2 weeks per cycle), which should be repeated to fill 4 months.
- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

■ NOTES

CHLAMYDIA PNEUMONIAE

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops twice per day (start with one drop) †				
SAMENTO	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15–26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops twice per day (start with one drop) †				
SAMENTO	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 3 Days 29–40	(rest on days 41, 42)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops twice per day (start with one drop) †				
SAMENTO	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

† Increase as tolerated to reach the recommended dose.

Notes:

- **Chlamydia pneumoniae is a common cause of respiratory infections** and is different from the STD.
- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- **Each cycle uses a different primary herb**: BANDEROL for cycle 1 (days 1–14), CUMANDA for cycle 2 (days 15–28), and TANGARANA for cycle 3 (days 29-42).
- All cycles have identical support herbs: SAMENTO, BURBUR-PINELLA, and SERRAPEPTASE.
- Follow this approach for 3 months, repeating cycles as needed.
- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

This approach is not a substitute for conventional medical care and should be used in conjunction with, not instead of, standard treatment.

CLOSTRIDIUM DIFFICILE (C DIFF)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)

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mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops three times per day (start with one drop) †				
MORA	30 drops three times per day				_

† Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Liposomal glutathione:** 1/4 teaspoon (1.25 ml) on the lower legs every 15 minutes for a Herxheimer-like reaction, if further support is needed
- **MegaSporeBiotic** (Microbiome Labs) or other spore-based probiotic, preferably with mutiple strains: per label instructions
- Mega IgG2000 (Microbiome Labs): per label instructions

■ NOTES

This approach is not a substitute for conventional medical care and should be used in conjunction with, not instead of, standard treatment.

COXIELLA BRUNETTI (Q FEVER)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15-26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 3 Days 29–40	(rest on days 41, 42)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops four times per day (start with one drop) †				
SAMENTO	30 days twice per day				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Notes:

- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- **Each cycle uses a different primary herb**: BANDEROL for cycle 1 (days 1–14), CUMANDA for cycle 2 (days 15–28), and TANGARANA for cycle 3 (days 29-42).
- All cycles have identical support herbs: SAMENTO and BURBUR-PINELLA.
- Follow this approach for 5-6 months, repeating cycles as needed.
- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

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DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
TAKUNA †	30 drops four times per day				
SAMENTO	30 drops four times per day (start with one drop) ‡				
BURBUR-PINELLA	20 drops four times per day				

[†] For maximum support, use **TAKUNA** at **30 drops** per hour.

[‡] Increase as tolerated to reach the recommended dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
ELDERBERRY	2 capsules four times per day				

Notes:

• If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.

i ALSO RECOMMENDED

• For fever, the individual should take off most of their clothes, wipe their skin with lukewarm water, and allow the water to evaporate (use a fan if needed).

■ NOTES

EPSTEIN BARR (MONO)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
DANDELION	30 drops three times per day				

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MONOLAURIN†	3 capsules (600 mg each) three times per day				
VITAMIN C	1 capsule three times per day‡				
HISTAQUEL † §	2 capsules twice per day				
CYSTOQUEL † §	3 capsules once per day				
BINDER PLUS	2 capsules once per day ¶				

- † Not a NutraMedix product
- **‡** To bowel tolerance
- § Researched Nutritionals brand
- ¶ Take at least 2 hours before or after drops, supplements, and medications.

Notes:

- Provides viral, toxin, mast cell, and immune support.
- Follow this approach for 2–4 months post resolution, while slowly weaning off.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

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HELICOBACTER PYLORI (H PYLORI)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals and bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops three times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 15–26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops four times per day (start with one drop) †				
SAMENTO	30 drops three times per day				

[†] Increase as tolerated to reach the recommended dose.

Notes:

- Continue treatment for a total of 6 cycles.
- Cycle 1 will last longer than 1 week while building up to a full dose; once a full dose is achieved, continue for 5 additional days followed by 2 rest days.
- Cycle 2 will last for 1 week, consisting of 5 days of herbal treatment followed by 2 days off.
- If a stress reaction occurs, add **AMANTILLA: 15 drops** every 15 minutes until stress abates.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- After reaching full dose of both herbs, add Jarrow **Mastic Gum:** 2 capsules, twice per day at the beginning of meals; as with the herbs in cycles 2–6, take for 5 days and then rest for 2 days.
- **Practice stress reduction techniques** before each meal and bedtime.
- NutraMedix **AVEA:** 15 drops two to four times per day
- NutraMedix **CHANCA PIEDRA:** 30 drops two to four times per day (start with one drop; increase as tolerated to reach the recommended dose)

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HEPATITIS

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
TAKUNA	30 drops four times per day				
PARSLEY	10 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				

Notes:

- Continue this approach for 3 months.
- If Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- Drink 3 to 4 liters (quarts) of water per day (clean mineralized, not distilled or reverse osmosis).
- **R-Lipoic Acid:** 200 mg twice per day
- Trimethylglycine: 2,000 mg twice per day with food

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HERPES SIMPLEX

I. DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	Morning	Afternoon	Evening	Bedtime	
TAKUNA	30 drops four times per day				
PARSLEY	10 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				

Notes:

- Continue this approach for 3 months.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **R-Lipoic Acid:** 200 mg twice per day
- Trimethylglycine: 2,000 mg twice per day with food

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INFLUENZA

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

TAKUNA	30 drops	Day 1	Every hour †			
	30 drops	Day 2	Every 2 hours †			
	30 drops	Day 3	Every 4 hours †			
	30 drops	Day 4	Every 8 hours †			
		Morning	Afternoon	Evening	Bedtime	
VITAMIN D3 & K2	2 capsules on	nce per day ‡				
ELDERBERRY	1 capsule twice per day					

[†] While awake

‡ Do not take Vitamin D3 & K2 if taking warfarin

If there is yellow-green phlegm, add the following:		Morning	Afternoon	Evening	Bedtime
BARBERRY (Oregon grape)	30 drops four times per day				

Notes:

- **TAKUNA** is taken for 4 days; dosing decreases as symptoms abate.
- BARBERRY is used only if there is yellow/green phlegm, and should be taken at least 15 minutes apart from TAKUNA.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- Larix (Eclectic Institute): 1 teaspoon (5 mg) every hour
- For fever, use a lukewarm washcloth to apply water to the skin, then let it evaporate to lower core body

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MORGELLON

DOSING - PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime; caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops twice per day (start with one) †				
ENULA	30 drops twice per day (start with one) †				
MORA	30 drops twice per day				
SERRAPEPTASE	2 capsules three times per day ‡				

[†] Start with one drop per serving; increase as tolerated to reach the recommended dose.

[‡] Take with water only (not other liquids).

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
VITAMIN C	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Bromelain:** 1,000 mg at bedtime
- MSM: 3,000 mg twice per day
- Allicillin: 4 softgels twice per day, immediately before breakfast and supper
- Avoid sugar and starch for 1-2 months.
- Can use NutraMedix **STEVIA** as a sweetener.

NOTES		

MYCOPLASMA PNEUMONIAE

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1-5	(rest on days 6, 7)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops three times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 8-12	(rest on days 13, 14)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops three times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Notes:

- This approach consists of two 7-day cycles (1 week per cycle).
- Herbs should be taken for days 1-5 of each cycle with rest days (no herbs) on days 6 and 7.
- Alternate cycles for 2 months.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

■ NOTES

PARASITE SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



▲ drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1-5	(rest on days 6, 7)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops three times per day (start with one drop) †				
MORA	30 drops three times per day				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 8–12	(rest on days 13, 14)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops three times per day (start with one drop) †				
ENULA	30 drops three times per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

[†] Increase as tolerated to reach the recommended dose.

Notes:

- Herbs should be taken for days 1-5 of each cycle, with rest days (no herbs) on days 6 and 7.
- Each cycle uses different primary herbs: TANGARANA and MORA for cycle 1 (days 1-7) and CUMANDA and ENULA for cycle 2 (days 8-14).
- **Both cycles have identical support herbs**: BURBUR-PINELLA and SERRAPEPTASE.
- Alternate cycles for 3 months.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

Food-grade Diatomaceous Earth (DE): 1 teaspoon (5 mg) twice per day at the beginning of a meal; take for the first 6 weeks of this approach in conjunction with the same schedule (5 days on, 2 days off).

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STAPHYLOCOCCUS AUREUS

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop)				
ENULA	30 drops four times per day (start with one drop)				

† Increase as tolerated to reach the recommended dose.

Notes:

- Continue treatment for 6 months.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Liposomal Glutathione**: 1/4 teaspoon (1.25 ml) on the lower legs every 15 minutes
- NutraMedix **AVEA** (Turmeric root): 15 drops two to four times per day
- NutraMedix **NONI**: 30 drops two to four times per day
- NutraMedix **TEASEL**: 30 drops two to four times a day (start with one drop; increase as tolerated to reach the recommended dose)

■ NOTES

STREPTOCOCCUS PYOGENES

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BARBERRY (Oregon grape)	30 drops three times per day				
PARSLEY	10 drops three times per day				

Notes:

- **If symptoms persist after 1–2 weeks**, replace **BARBERRY** with **CUMANDA** or **BANDEROL**; start with one drop per serving and increase as tolerated to reach 30 drops per serving.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Gargle with warm salt water for sore throat** (1/4 teaspoon or 5 mg of salt in 1 cup/120 ml of warm water).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.
- NutraMedix **NONI:** 30 drops two to four times per day
- NutraMedix **AVEA** (Turmeric root): 15 drops two to four times per day

■ NOTES

TOXOPLASMA GONDII

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops four times per day (start with one drop) †				
ENULA	30 drops four times per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

Notes:

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- Once a full dose of both herbs is reached, take the herbs for 5 days, then stop for 2 days.
- Repeat the 7-day cycle (5 days on, 2 days off) for 6 months.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Cryptolepis tincture:** 60 drops twice per day on the same schedule as CUMANDA and ENULA; start with a low dose and build up
- **Liposomal glutathione: 1/4 teaspoon** (1.25 ml) on the lower legs every 15 minutes until symptoms abate, if additional support is needed for a Herxheimer-like reaction

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VARICELLA ZOSTER (SHINGLES)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

TAKUNA	Phase 1: Initial treatment	30 drops ever	y 1 hour †		
	Phase 2 : After symptoms start improving (48 hours)	30 drops ever	y 2 hours †		
	Phase 3 : 2 days (48 hours)	30 drops ever	y 4 hours †		
	Phase 4 : 2 days (48 hours)	30 drops ever	y 8 hours †		
		Morning	Afternoon	Evening	Bedtime
BURBUR-PINELLA	20 drops four times per day				

† While awake

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- Monolaurin (Cardiovascular Research): 1,800 mg three times per day
- Reishi or other mushroom blend: dosing as per the label

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VIRAL SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

For long-term support, continue this approach for 3 months

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
TAKUNA	30 drops three times per day				
SAMENTO	30 drops three times per day (start with one drop) †				
BURBUR-PINELLA	20 drops three times per day				
SERRAPEPTASE	2 capsules twice per day				

† Increase as tolerated to reach the recommended dose.

For intensive, short-term support, substitute the below dosing for **TAKUNA**:

TAKUNA	Day 1	30 drops every 1 hour ‡
	Day 2	30 drops every 2 hours ‡
	Day 3	30 drops every 4 hours ‡
	Day 4+	return to regular dosing (30 drops three times per day)

While awake

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

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YERSINIA

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1-5	(rest on days 6, 7)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops three times per day (start with one) †				
SAMENTO	20 drops three times per day (start with one) †				
BURBUR-PINELLA	20 drops three times per day				

† Increase as tolerated to reach the recommended dose.

Cycle 2 Days 8–12	(rest on days 13, 14)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops three times per day (start with one) †				
SAMENTO	20 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				

† Increase as tolerated to reach the recommended dose.

Notes:

- This approach consists of two 7-day cycles (1 week per cycle).
- Herbs should be taken for days 1-5 of each cycle with rest days (no herbs) on days 6 and 7.
- Each cycle uses a different primary herb: CUMANDA for cycle 1 (days 1-7) and TANGARANA for cycle 2 (days
- **Both cycles have the same support herbs**: SAMENTO and BURBUR-PINELLA.
- Alternate cycles for 60 days.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

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GOUT SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)

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mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA or TANGARANA	30 drops three times per day (start with one drop) †				
PARSLEY	10 drops three times per day				_

† Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Eat a vegetarian ketogenic diet** (plenty of nuts, seeds, nut butters, seed butters, avocados, coconut oil, healthy oils on salad, and vegetables).
- **Avoid** organ meats, dairy, alcohol, and vinegar.
- **Avoid** grains, starches, sugars, or fruits (other than lemons and limes).
- Can use NutraMedix **STEVIA** as a sweetener.

■ NOTES

JOINT SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	Morning	Afternoon	Evening	Bedtime	
BARBERRY (Oregon grape)	30 drops twice per day				
TAKUNA	30 drops twice per day				
MOODMEDIX	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
ANTARCTIC KRILL	2 capsules twice per day				
CURCUMIN	2 capsules twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts and peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.
- Avoid all grains with gluten, such as wheat (including spelt, kamut, triticale); barley; rye; and oat.
- **Avoid foods in the nightshade family** (potatoes, tomatoes, peppers, eggplant, tobacco), as as they contain alkaloids that may worsen inflammation.
- **Avoid coffee**, as it may worsen inflammation.
- **Deep Ocean Trace Minerals:** 1-2 capsules per day, after a meal

ATTENTION / FOCUS SUPPORT (Adult)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

The given dosing is for a 120-150 lb adult. Adjust by weight as necessary.

WEIGHT (lbs)	90-120	120-150	150-180	180-210	210-240	240+
DOSE	3/4	1	1 1/4	1 ½	1 3/4	2

30+ minutes	Morning	Afternoon	Evening	Bedtime	
SAMENTO	30 drops three times per day (start with one drop) †				
STEVIA	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops four times per day				
AMANTILLA (Valerian)	15 drops four times per day				

† Increase as tolerated to reach the recommended dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
DEEP OCEAN TRACE MINERALS	2 capsules once per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- NutraMedix **ANTARCTIC KRILL:** 2 capsules twice per day after meals
- Acetyl-L-Carnitine: 1,000 mg twice per day with food (breakfast and lunch) for 6 months
- Focus Factor: dosing according to the label
- Nature's Way Bitter Orange: 1-2 tablets per day
- **ION Biome:** 1 teaspoon (5 ml) before meals
- Broccoli Seed Extract: 200 mg per day
- Bacopa monnieri: 50-500 mg per day

ATTENTION / FOCUS SUPPORT (Child)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Dosing is by weight. Please consult the Attention/Focus (Adults) page for individuals over 120 lbs.

SIZE	Small	Medium	Large	
WEIGHT	30-60 lbs	60-90 lbs	90-120 lbs	

30+ minutes before meals				Morning	Afternoon	Evening	Bedtime
SAMENTO	drops thr	drops three times per day					
(start with one drop) †	S: 7	M: 15	L: 22				
STEVIA	drops twice per day						
(start with one drop) †	S: 7	M: 15	L: 22				
BURBUR-PINELLA	drops for	drops four times per day					
	S: 5	M: 10	L: 15				
AMANTILLA (Valerian)	drops four times per day						
	S: 5	M: 10	L: 15				

[†] Increase as tolerated to reach the recommended dose.

30+ minutes after meals				Morning	Afternoon	Evening	Bedtime
DEEP OCEAN capsule(s) once per day							
TRACE MINERALS	S: 1	M: 1	L: 2				
MAGNESIUM MALATE	capsule(s) twice per	day				
*Avoid in kidney failure	S: 1	M: 1–2	L: 2				
VITAMIN C	capsule(s) twice per day						
	S: 1	M: 1–2	L: 2				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- NutraMedix ANTARCTIC KRILL: 1 capsule one to two times per day after meals, depending on weight
- Acetyl-L-Carnitine: 250-750 mg twice per day with food (breakfast and lunch) for 6 months
- Focus Factor: dosing according to the label
- Nature's Way Bitter Orange: 1 tablet per day
- **ION Biome:** 1 teaspoon (5 ml) before meals
- Broccoli Seed Extract: 75–150 mg per day
- **Bacopa monnieri:** 100–250 mg per day

BRAIN SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	Morning	Afternoon	Evening	Bedtime	
VITALMEDIX 30 drops twice per day					
BURBUR-PINELLA	20 drops twice per day				

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
ANTARCTIC KRILL	2 softgels twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

every other night		Morning	Afternoon	Evening	Bedtime
ALGAS (Asparagus)	20 drops every other night †				

[†] Increase as tolerated to reach the recommended dose.

Notes:

NOTES

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- Follow the foundational nutritional and lifestyle guidelines at the beginning of the protocol section.
- **Exercise** several times per week, indoors or outdoors.
- Sleep for 7–9 hours per night.

HEADACHE / MIGRAINE SUPPORT

I DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

CONDURA	30 drops	Step 1: Add drops (CONDURA, BURBUR-PINELLA, and PARSLEY) to 120 ml (4 oz) of water.
BURBUR-PINELLA	10 drops	Step 2 : Ópen MAGNESIUM MALATE capsule and add the powder to the water. Stir, let rest one minute, and drink.
PARSLEY	30 drops	Step 3: Rub additional CONDURA on the painful location (forehead, temples, back of neck, etc.).
MAGNESIUM MALATE *Avoid in kidney failure	1 capsule	Step 4 : Repeat every 10–15 minutes until the pain subsides.

i ALSO RECOMMENDED

- Drink 3 to 4 liters (quarts) of water per day (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.

■ NOTES

NEUROLOGICAL SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)

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mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BURBUR-PINELLA	20 drops three times per day				
PARSLEY	10 drops three times per day				
ANTARCTIC KRILL	1–2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Liposomal glutathione:** 1/4 teaspoon (1.25 ml) rubbed on the lower legs every 15 minutes for 2 hours
- NutraMedix **BINDER PLUS:** 2 capsules at bedtime for ongoing support, at least 2 hours before or after drops, supplements, and medications
- Lymphatic drainage can also reduce Herxheimer-like reactions.

■ NOTES

MOOD SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
MOODMEDIX	10 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				
AMANTILLA (Valerian)	15 drops three times per day †				

† If needed for stress support

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Lithium orotate:** 120 mg twice per day
- Use full-spectrum light bulbs.
- Sit in the sunlight for 30 minutes two to three times per day if weather permits; otherwise, aim for six hours per day of full-spectrum light bulb exposure.
- Sleep for 7-9 hours per night.
- If having thoughts of self-harm, seek immediate medical attention.

NOTES

RELAXATION SUPPORT

I DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
RELAXMEDIX	15 drops four times per day				
VITALMEDIX	30 drops once per day				
ADRENAL	20 drops twice per day				

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Once sleeping well, add to the above:		Morning	Afternoon	Evening	Bedtime
EZOV (Hyssop)	10 drops once per day (start with one drop) †				

[†] Add one drop every 3-4 days until reaching the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Eat a vegetarian ketogenic diet** (plenty of nuts, seeds, nut butters, seed butters, avocados, coconut oil, healthy oils on salad, and vegetables).
- Can use NutraMedix **STEVIA** as a sweetener.
- Exercise earlier in the day.
- Have a bedtime routine to help wind down.

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SLEEP SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
AMANTILLA (Valerian)†	30 drops 30 minutes before bed				
BABUNA (Chamomile)†	30 drops 30 minutes before bed				
MELATONIN	5–10 drops 30 minutes before bed ‡				

[†] If waking during the night, can take AMANTILLA and BABUNA every 15 minutes until falling back to sleep.

[‡] Start with 5 drops; can increase up to 10 drops if needed.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

ALSO RECOMMENDED

- 5-hydroxytryptophan (5-HTP): 100 mg at bedtime; do not use 5-HTP if taking antidepressants.
- Eliminate nighttime light exposure, as it decreases natural melatonin production.
- **Keep the bedroom pitch black during sleeping hours**; use blackout shades as well as a towel under the door if light comes in from the hallway.
- **Keep a faint red flashlight** to find your way to the bathroom at night, if necessary.
- If you prefer to have a bathroom night-light, use a red one and keep the bathroom door closed.

■ NOTES

STRESS SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
AMANTILLA (Valerian) 15 drops four times per day					
ADRENAL	20 drops twice per day				

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Notes:

- For stronger support, use **AMANTILLA: 15 drops** every 15 minutes until symptoms subside.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

- NutraMedix Methyl Complete (B vitamins): 2 capsules once per day, in the morning with food
- Chromium polynicotinate: 200 mg twice per day

■ NOTES

BRONCHIAL SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BARBERRY† (Oregon grape)	30 drops three times per day				
SAMENTO	20 drops three times per day (start with one drop) ‡				
ADRENAL	20 drops twice per day				
BURBUR-PINELLA	10 drops three times per day				

† If symptoms persist after one to two weeks, replace BARBERRY with CUMANDA or BANDEROL at the same dosage.

‡ Increase as tolerated to reach the recommended dose.

Notes:

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- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- Drink 3 to 4 liters (quarts) of water per day (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix **STEVIA** as a sweetener.
- Add **Sinus Support** if indicated.

LUNG SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	30+ minutes before meals		Afternoon	Evening	Bedtime
BARBERRY (Oregon grape)	30 drops three times per day				
BURBUR-PINELLA	20 drops three times per day				
SAMENTO	20 drops twice per day (start with one drop) †				
ADRENAL	20 drops twice per day				
CUMANDA	15 drops twice per day (start with one drop) †				

† Increase as tolerated to reach the recommended dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar.
- Can use NutraMedix STEVIA as a sweetener.
- If symptoms persist, avoid all grains with gluten, such as wheat (including spelt, kamut, triticale); barley; rye; and
- Take a broad-spectrum probiotic such as BifidoBiotics from Allergy Research Group or Dr. Ohira's Probiotics from Essential Formulas.

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SINUS SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BARBERRY	30 drops three times per day				
STEVIA	30 drops three times per day (start with one drop) †				
BURBUR-PINELLA	20 drops three times per day				
ADRENAL	20 drops twice per day				

† Add one drop per week until reaching the recommended dose.

Notes:

- If symptoms persist after 1-2 weeks, replace BARBERRY with CUMANDA or BANDEROL; start with one drop per serving and increase as tolerated to reach the recommended dose.
- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Use a broad-spectrum probiotic**, such as BifidoBiotics from Allergy Research Group or Dr. Ohira's Probiotics from Essential Formulas, taken with a prebiotic fiber such as FOS, psyllium, or slippery elm, every night at bedtime.
- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar—can use NutraMedix STEVIA as a sweetener.
- Keep animals out of the bedroom.
- Use pillow and mattress covers designed for allergies to protect from dust mites.
- Consider replacing carpet with wood flooring.

3	NOTES		

ACNE SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops three times per day				
BARBERRY (Oregon grape)	30 drops three times per day				

† If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

Notes:

NOTES

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- Eat a mostly plant-based, ketogenic diet.
- Avoid grains, potatoes, or other starches.
- Avoid margarine, hydrogenated fats, and fried foods.
- Avoid fruits other than lemons and limes.
- Avoid sugars, artificial sweeteners, honey, syrup, agave, and sugar alcohols such as erythritol.
- Can use NutraMedix STEVIA as a sweetener.
- **SSKI** (Saturated Solution of Potassium Iodide): Apply 1–2 drops to each pimple once daily at night.
- Nutramedix **AVEA** (Turmeric root): 15 drops twice per day or **CURCUMIN**: 2 capsules once per day, after a meal.

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PSORIASIS SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtimecaps 30+ minutes after meals (except Serrapeptase)

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mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				
ADRENAL	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Avoid common food allergens** such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); black or white pepper; and sugar, starch, and fruits (except for lemons and limes).
- Use NutraMedix **STEVIA** as a sweetener.
- **Consider replacing dental amalgams** with composites by a biological dentist; build up eiher Chlorella or Spirulina to 1,500 mg per day before amalgams are removed.
- **After amalgam removal**—NutraMedix **SEALANTRO:** 40 drops every other night and either **Chlorella** or **Spirulina:** 1,500 mg per day, for 3–4 months

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PROSTATE SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops twice per day (start with one drop) †				
BURBUR-PINELLA	20 drops twice per day				

† Increase as tolerated to reach the recommended dose.

every other night		Morning	Afternoon	Evening	Bedtime
SEALANTRO	40 drops every other night (start with one drop) ‡				

‡ Add one drop per week until reaching the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Saw Palmetto:** 2 capsules twice per day
- Use **Saw Palmetto and Pygeum combination**, 2 capsules twice per day, for stronger support.
- Take a broad-spectrum probiotic such as BifidoBiotics from Allergy Research Group or Dr. Ohira's Probiotics from Essential Formulas every bedtime with a prebiotic fiber such as FOS or psyllium or slippery elm.
- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- Avoid common food allergens such as cow milk and cheese; corn (including oil, starch, and corn syrup); peanuts or peanut oil; soy (a common filler in fast food); and black or white pepper.
- **Avoid all sugars and starches,** including fruits and their juices (except for lemons and limes), honey and maple syrup, all grains, all dried beans, and all root vegetables (including potatoes and carrots) for at least two months while using this approach.
- Can use NutraMedix **STEVIA** as a sweetener.

3	NOTES		

STONE SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER



drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minu	ites before meals	Morning	Afternoon	Evening	Bedtime
CHANCA PIEDRA	30 drops four times per day (start with one drop) †				
CUMANDA	30 drops twice per day (start with one drop) †				
BANDEROL	30 drops twice per day (start with one drop) †				
PARSLEY	10 drops twice per day				

† Increase as tolerated to reach the recommended dose.

30+ minutes	after meals	Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water daily** (clean mineralized, not distilled or reverse osmosis).
- **Orthophosphoric Acid:** 15 drops three times per day for 5 days, before meals; after swallowing, rinse mouth thoroughly to protect tooth enamel.
- **Minimize high-oxalate foods** such as spinach, rhubarb, almonds, and miso (if stones are calcium oxalate).
- Follow a ketogenic diet for 8-10 weeks.
- Treat mold toxicity if present.

NOTES	

URINARY SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	before meals	Morning	Afternoon	Evening	Bedtime
BARBERRY (Oregon grape)	30 drops four times per day				

Notes:

- Continue this approach for 7-8 days.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- Avoid caffeine.
- **D-Mannose:** 1 teaspoon (5 mg) twice per day in water
- Avoid all sugars, sugar alcohols such as erythritol, and artificial sweeteners.
- Can use NutraMedix STEVIA as a sweetener.

■ NOTES

DETOX SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes	before meals	Morning	Afternoon	Evening	Bedtime
VITALMEDIX	30 drops once per day				
BURBUR-PINELLA	20 drops twice per day				
EZOV (Hyssop)	10 drops once per day (start with one drop) †				

† Add one drop every 3–4 days until reaching the recommended dose.

30+ minutes	after meals	Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				

every ot	her night	Morning	Afternoon	Evening	Bedtime
ALGAS (Asparagus)	20 drops every other night (Start with one drop) ‡				

‡ Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add BURBUR-PINELLA: 15 drops every 15 minutes for 1-2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

Those with known SNPs (small mutations) in sulfation pathways should add NutraMedix SPARGA: 15 drops twice per day, as well as **Molybdenum:** 400 mcg every other day.

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ELECTROMAGNETIC FIELD SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
DANDELION	30 drops twice per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- Turn off Wi-Fi in your home, preferably permanently, but at least every night while sleeping.
- Use a wired rather than wireless burglar-alarm system.
- Use a wired rather than wireless baby monitors.
- **Cell phone hygiene**: Cell phones can transmit harmful energies, even when they're turned off, unless they're in airplane mode. Keep your phone on airplane mode, especially at night; turn off airplane mode only to check messages or return urgent calls or texts. Do not chat with your cell phone against your head; get a SafeSleeve phone case; and charge your cell phone at least 20 feet from your bed.
- **Get rid of plug-in alarm clocks or other electrical devices near your bed**; use wind-up or battery-powered clocks instead.
- Turn off the electric breakers controlling power to your bedroom and to adjacent rooms at bedtime; a Gauss meter can be used to determine which breakers to turn off.
- Make an effort to replace utility Smart Meters (electric, water, gas) with the old analog meters, especially if the meter is less than 30 feet from your bed (even if it's in another room).
- **Sleep only in a pitch-dark bedroom** (you should not be able to see your hand held in front of your face during the night); if you get up in the night, use only a faint red light.
- Consider sleeping under a Faraday cage (a German metallized cloth canopy) if your house is less than 330 meters or yards from a cell tower or if you can see nearby wireless networks on your computer, with the same material underneath the bed unless the room is on the ground floor.

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HEALTHY AGING SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops three times per day				
BURBUR-PINELLA	30 drops three times per day				
ADRENAL	20 drops twice per day				

† If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

every other night		Morning	Afternoon	Evening	Bedtime
ALGAS (Asparagus)	20 drops every other night (start with one drop) ‡				

[#] Increase as tolerated to reach the recommended dose.

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Bacopa monnieri:** 50–500 mg per day
- Daily foot soaks in 2–3 gallons (8–11 liters) of very warm water and 1/4 cup (60 grams) of Epsom salts

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HEALTHY WEIGHT SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops three times per day				
ADRENAL	20 drops twice per day				
EZOV (Hyssop)	10 drops once per day (start with one drop) ‡				

[†] If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

[‡] Add one drop every 3-4 days until reaching the recommended dose.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
DEEP OCEAN TRACE MINERALS	2 capsules once per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

Notes:

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- When feeling stressed, add AMANTILLA: 15 drops before meals.
- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- Follow a plant-based ketogenic diet.
- **Avoid starches,** including grains and potatoes.
- **Avoid fruits** except for lemons and limes.
- **Avoid sugar**, honey, syrup, erythritol or other sugar alcohols, and artificial sweeteners.
- Can use NutraMedix **STEVIA** as a sweetener.

HERXHEIMER-LIKE REACTION SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)

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mix drops with at least 120 ml (4 oz) of water

BURBUR-PINELLA	20 drops	Mix BURBUR-PINELLA and PARSLEY with 2–4 ounces (60–120 ml) of water and consume.
PARSLEY	10 drops	

Notes:

- Take these remedies in 2-4 ounces (60-120 ml) of water every 10-15 minutes for 1-2 hours until reaction subsides.
- If this is not sufficient to resolve the Herxheimer-like reaction, rub 1/4 teaspoon (1.25 ml) of **Liposomal glutathione** on the lower legs every 15 minutes for 2 hours.

i) ALSO RECOMMENDED

- Take NutraMedix BINDER PLUS: 2 capsules at bedtime for ongoing support, at least two hours before or after drops, supplements, and medications.
- **Lymphatic drainage** may also help reduce Herxheimer-like reactions.

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This approach is not a substitute for conventional medical care and should be used in conjunction with, not instead of, standard treatment.

LIVER SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
BURBUR-PINELLA	20 drops four times per day				

Notes:

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

i ALSO RECOMMENDED

- **N-acetylcysteine (NAC):** 600 mg twice per day
- Stabilized R-Lipoic Acid: 300 mg twice per day
- Infrared sauna therapy: 5–10 minutes every other day; slowly increase to 30–40 minutes per session.

■ NOTES

METABOLIC SUPPORT

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

30+ minutes before meals		Morning	Afternoon	Evening	Bedtime
GLUCOMEDIX †	30 drops three times per day				
VITALMEDIX	30 drops once per day				

† If you are on blood glucose-lowering medication, consult your physician before taking GlucoMedix.

30+ minutes after meals		Morning	Afternoon	Evening	Bedtime
ANTARCTIC KRILL	2 softgels twice per day				
MAGNESIUM MALATE *Avoid in kidney failure	2 capsules twice per day				
VITAMIN C	2 capsules twice per day				

Notes:

NOTES

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

- **Drink 3 to 4 liters (quarts) of water per day** (clean mineralized, not distilled or reverse osmosis).
- **Eat a vegetarian ketogenic diet** (plenty of nuts, seeds, nut butters, seed butters, avocados, coconut oil, healthy oils on salad, and vegetables).
- **Avoid** organ meats, dairy, alcohol, and vinegar.
- **Avoid** grains, starches, sugars, and fruits (other than lemons and limes).
- Can use NutraMedix **STEVIA** as a sweetener.

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MOLD SUPPORT (page 1 of 2)

DOSING—PRODUCTS CAN BE TAKEN TOGETHER

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drops 30+ minutes before meals or bedtime caps 30+ minutes after meals (except Serrapeptase)



mix drops with at least 120 ml (4 oz) of water

Cycle 1 Days 1–12	(rest on days 13,14)	Morning	Afternoon	Evening	Bedtime
BANDEROL	30 drops twice per day †				
STEVIA	30 drops twice per day †				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				
BINDER PLUS	2 capsules twice per day ‡				

[†] Increase as tolerated to reach the recommended dose.

[‡] Take at least 2 hours before or after drops, supplements, and medications.

Cycle 2 Days 15–26	(rest on days 27, 28)	Morning	Afternoon	Evening	Bedtime
CUMANDA	30 drops twice per day †				
STEVIA	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				
BINDER PLUS	2 capsules twice per day ‡				

Cycle 3 Days 29–40	(rest on days 41, 42)	Morning	Afternoon	Evening	Bedtime
TANGARANA	30 drops twice per day †				
STEVIA	30 drops twice per day				
BURBUR-PINELLA	20 drops twice per day				
SERRAPEPTASE	2 capsules twice per day				
BINDER PLUS	2 capsules twice per day ‡				

Notes:

- The approach consists of three 14-day cycles (2 weeks per cycle).
- Herbs should be taken for days 1-12 of each cycle, with rest days (no herbs) on days 13 and 14.
- **Each cycle uses a different primary herb**: BANDEROL for cycle 1 (days 1–14), CUMANDA for cycle 2 (days 15–28), and TANGARANA for cycle 3 (days 29–42); all cycles have identical support herbs.
- For more intensive support, add to each cycle (1) SAMENTO: 30 drops twice per day (start with one drop and build up) and (2) MAGNESIUM MALATE: 2 capsules twice per day (*Avoid MAGNESIUM MALATE in kidney failure)
- Follow this approach for 3 months (repeat cycles 1-3); lifestyle and environmental measures are also crucial.

MOLD SUPPORT (page 2 of 2)

Notes:

NOTES

- If a Herxheimer-like reaction occurs, add **BURBUR-PINELLA: 15 drops** every 15 minutes for 1–2 hours until the reaction subsides.
- If a Herxheimer-like reaction does not resolve within 2 hours, stop treatment for the rest of the day, skip the following day, and then resume treatment at the previous well-tolerated dose.

ALSO RECOMMENDED

Lifestyle and environmental measures are crucial to success, and the following steps must be completed <u>in this</u> order for treatment to be effective:

- Resolve all water leaks/damage in the home and workplace; remove and remediate with new building materials—this needs to be done first.
- **Follow a ketogenic diet**—avoid all sugars, starches, and fruits, except for lemons and limes.
- Can use NutraMedix **STEVIA** as a sweetener.
- **Follow a low-mold diet**—avoid grains, dried beans, root vegetables such as potatoes and carrots, alcohol, and vinegar for at least two months while using this approach; nuts are permitted if mold-free.
- Take a comprehensive **probiotic**, such as BifidoBiotics from Allergy Research Group or Dr. Ohira's Probiotics from Essential Formulas, taken with a **prebiotic** fiber such as FOS, psyllium, or slippery elm, every night at bedtime.

WHITE PAPERS



APPLICATIONS

- Stress Management and Adrenal Support
- Antioxidant Support
- Neurological Support
- Athletic Support



INTRODUCTION

NutraMedix Adrenal consists of adaptogenic herbs Astragalus root (*Astragalus mongholicus*), Rhodiola root (*Rhodiola rosea*), American Ginseng root (*Panax quinquefolius*), and Schisandra berry (*Schisandra chinensis*). Adaptogens help to support a healthy stress response by facilitating adaptation to physical and mental stress, enhancing the ability to adjust and thrive in uncertain circumstances.* In traditional Chinese health practices, adaptogens are generally known as gi tonics.

Astragalus spp. root has been used for centuries in traditional Chinese health practices where it is known as Huang Qi and considered a qi tonic, nourishing overall wellness and vitality.* The first known written mention of this herb is from the second century *Shen Nong Ben Cao Jing*.² Astragalus belongs to the Fabaceae family, and its constituents include astragaloside along with the flavonoids calycosin, quercetin, ononin, calycosin-7-glucoside, formononetin, and kaempferől.³

Rhodiola root (*Rhodiola rosea*) belongs to the Crassulaceae family and is native to Tibet, Mongolia, and China.⁴ The first known written mention of this herb is from the first century *De Materia Medica* by the Greek physician Dioscorides.⁵ The polyphenol content is approximately 41% and includes rosavin, salidroside and tyrosol.⁴ *R. rosea* is also known as golden root or rose root, and is used in both Asia and Eastern Europe to support physical and mental performance.⁴⁴

American Ginseng root (*Panax quinquefolius*) is native to eastern North America and belongs to the Araliaceae family.⁶ It is used in traditional Chinese medicine where it is known as *xi yang shen* and is considered a qi tonic.^{*} The first known written mention of this herb is from the *Ben Cao Cong Xin* by Wu Yi-Luo in 1751.⁷ Constituents include ginsenosides, polysaccharides, phenolic compounds, polyacetylenes, peptides, and essential oils.^{*6}

Schisandra berry (Schisandra chinensis) has been used for centuries in traditional

Chinese health practices where it is known as wu wei zi, or "five-flavored seed." It belongs to the Schisandraceae family. The first known written mention of this herb is from the second century Shen Nong Ben Cao Jing. Schisandra is considered to be balancing, containing the five different tastes of sweet, salty, pungent, bitter, and sour.*8 Constituents include lignans, flavonoids, phenolic acids, triterpénoids, organic acids, and fatty acids.9

Adrenal is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

STRESS MANAGEMENT AND ADRENAL SUPPORT

To understand how Adrenal may help to support a healthy stress response, we first need to understand how the nervous system responds to everyday stress. The autonomic nervous system consists of two divisions, the sympathetic nervous system (fight or flight) and the parasympathetic nervous system (rest and digest). Ideally, there is a healthful balance between the sympathetic and parasympathetic responses. However, in occasional stressful times, the adrenal response to the sympathetic and parasympathetic responses. glands may work to keep up with secreting the epinephrine and norepinephrine that facilitate the sympathetic response.

Adaptogens may help to support healthy adaptation to both physical and mental everyday stress, aiding in healthy stress management.* A normal stress response avoids overworking the adrenals and helps to maintain levels of epinephrine and norepinephrine already within the normal range.* Through supporting these adaptive mechanisms, adaptogens help with both adrenal support and athletic support, nourishing healthy vitality and facilitating healthy stress management.* Additionally, NutraMedix Adrenal may help to support antioxidant activity and healthy nouriborical function.* healthy neurological function.*

Astragalus spp. have been used for centuries in traditional Chinese health practices to support healthy vitality.*¹¹ Rhodiola (*R. rosea*) may help to support normal physical and mental energy as well as healthy stress management.*^{12,13} Salidroside from *R. rosea* may help to support exercise tolerance,⁴ as well as the normal capacity for mental work (p<0.001).*¹⁴ American ginseng (*P. quinquefolius*) may help to support healthy energy levels.*¹⁵ Schisandra (*S. chinensis*) may help to support healthy physical endurance.*¹⁶

OTHER USES

Antioxidant Support

Salidroside from *R. rosea* may help to maintain malondialdehyde (MDA), catalase, superoxide dismutase (SOD), and glutathione peroxidase levels already within the superoxide dismutase (SUD), and glutathione peroxidase levels already within the normal range.*4 In vitro, *P. quinquefolius* root was found to support antioxidant activity as evidenced by DPPH and superoxide radical scavenging assays.*17 In a mouse study, proteins from *P. quinquefolius* root helped to maintain MDA, SOD, and glutathione peroxidase already within the normal range.*6 Schisandrins A and B from *S. chinensis* may help to support antioxidant activity.*18,19 Schisandrin B may help to maintain ROS, MDA, SOD and glutathione levels already within the normal range, the latter two through Nrf2 pathways.*20

Neurological Support

Astragalus spp. may help to support neurological health.*¹¹ A. mongholicus may help to support a healthy mood.*²¹ Additionally, A. mongholicus may also help to maintain axonal and synaptic health, as seen in mice.*²² Rhodiola (R. rosea) contains rosin and salidroside which may help to support neurological health.*²³ R. rosea may help to maintain MAPK function already within the normal range and help to support a healthy mood.*^{23,24} Additionally, R. rosea may help to support neurological health.*^{25,26} normal working memory and concentration during mental performance.*2

Schisandra (*S. chinensis*) has been used in traditional Chinese medicine to support healthy cognition and may help to maintain neurotransmitters and BDNF already within the normal range.*18,27 In a study with mice under mild and unpredictable everyday stress, Schisandra helped to maintain normal cognition and healthy mood.*27 Schisandrin B may be particularly helpful in neurological support.*19 Schisandrin B may help to maintain IL-1-beta and TNF-alpha already within the normal range.*28 Schisandrin B may also help to maintain IL-6, PEG2,

and NO already within the normal range.*29

Athletic Support

R. rosea and its constituent salidroside may help to support healthy exercise tolerance as well as exercise performance, for both aerobic and anaerobic exercise.*4,30 In a study with mice, proteins from *P. quinquefolius* helped to maintain blood lactate, serum urea nitrogen, and hepatic glycogen already within the normal range.*6 *S. chinensis* may help to maintain normal muscle strength and help to maintain lactate levels already within the normal range.*31,32 Adaptogenic herbs, by nature, are useful in athletic support due to the facilitation of normal adaptation to physical and mental exertion.*

SAFETY AND CAUTIONS

Astragalus root (*Astragalus spp.*) is generally well tolerated, and serious adverse effects are rare. A case of enterocolitis and nausea was reported in one study, though may not have been due to astragalus.³³ There has been one case of elevated CA19-9 levels with liver and kidney cysts in a 38-year-old female, which resolved after discontinuing astragalus.³⁴ Astragalus may theoretically interfere with cyclophosphamide, though animal studies are mixed.^{33,36} It may theoretically interfere with immunosuppressants, due to immunostimulant effects.³⁷ Astragalus may also, due to effects on sodium and water retention, increase levels and adverse effects of lithium.³⁸

Rhodiola root (*R. rosea*) is generally well tolerated. The most common adverse effects are dizziness and dry mouth.³⁹ *R. rosea* may have additive effects with hypoglycemics due to alpha-glucosidase.^{40,41} It may also have additive effects with antihypertensives, due to angiotensin converting enzyme (ACE).⁴¹ *R. rosea* may increase levels of medications that are CYP2C9 substrates, and may have additive effects with losartan.⁴² *R. rosea* may theoretically increase the levels of P-glycoprotein substrates and may interfere with immunosuppressant therapy due to immunostimulatory effects.^{43,44}

American Ginseng root (*P. quinquefolius*) is generally well tolerated. Adverse effects may include headaches.⁴⁵ *P. quinquefolius* should not be used concurrently with warfarin, as it may decrease its therapeutic effects.⁴⁶ It may have additive effects with hypoglycemic medications,⁴⁷ may interfere with MAOIs, and may oppose the effects of immunosuppressants.⁴⁸

Schisandra berry (*S. chinensis*) is eaten as a food and is generally well tolerated.⁴⁹ Adverse effects may include acid indigestion, stomach pain, decreased appetite, allergic skin rashes, and urticaria.⁴⁹ *S. chinensis* may increase metabolism and decrease levels of warfarin, attributed to CYP2C9 metabolism.⁵⁰ It may decrease the bioavailability of talinolol, attributed to inhibition of P-glycoprotein drug transporter.⁵¹ It may increase the bioavailability of tacrolimus.⁵² It may raise levels and increase the effects of midazolam, attributed to CYP3A4 inhibition.⁴⁹ It may induce CYP2C9 enzymes, inhibit CYP3A4 enzymes, and inhibit P-glycoprotein carrier protein.⁴⁹

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.



REFERENCES

²⁷ Yan, T., He, B., et al. (2017). Scientific Reports, 7(1), 6903.

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<sup>1</sup> Panossian, A. (2017). Annals of the New York Academy of Sciences, 1401(1), 49–64.
<sup>2</sup> Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 847-853). Art of Medicine Press.
<sup>3</sup> Li, L., Zheng, S., Brinckmann, J. A., et al. (2017). PloS One, 12(9), e0184791.
4 Chiang, H. M., Chen, H. C., et al. (2015). Journal of Food and Drug Analysis, 23(3), 359-369.
<sup>5</sup> Shikov, A. N., Kosman, V. M., et al. (2020). Molecules (Basel, Switzerland), 25(8), 1826.
<sup>6</sup> Qi, B., Liu, L., et al. (2014). Journal of Ethnopharmacology, 153(2), 430–434.
7 Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 841-842). Art of Medicine Press.
<sup>8</sup> Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 985-988). Art of Medicine Press.
<sup>9</sup> Yang, S., Shan, L., et al. (2017). Molecules (Basel, Switzerland), 22(10), 1778.
<sup>10</sup> Kopustinskiene, D. M., & Bernatoniene, J. (2021). Antioxidants (Basel, Switzerland), 10(4), 620.
11 Jalsrai, A., Grecksch, G., & Becker, A. (2010). Journal of Ethnopharmacology, 131(3), 544–549.
<sup>12</sup> Ishaque, S., Shamseer, L., et al. (2012). BMC Complementary and Alternative Medicine, 12, 70.
13 Mattioli, L., & Perfumi, M. (2007). Journal of Psychopharmacology (Oxford, England), 21(7), 742-750.
14 Shevtsov, V. A., Zholus, B. I., et al. (2003). Phytomedicine: International journal of phytotherapy and phytopharmacology, 10(2-3), 95–105.
15 Barton, D. L., Soori, G. S., et al. (2010). Supportive Care in Cancer: Official journal of the Multinational Association of Supportive Care in Cancer, 18(2), 179–187.
<sup>16</sup> Nowak, A., Zakłos-Szyda, M., et al. (2019). Nutrients, 17(2), 333.
<sup>17</sup> Kim, K. T., Yoo, K. M., et al. (2007). Journal of Ethnopharmacology, 171(3), 443–450.
<sup>18</sup> Zhang, M., Xu, L., & Yang, H. (2018). International Journal of Molecular Sciences, 19(7), 1970.
<sup>19</sup> Nasser, M. I., Zhu, S., et al. (2020). Oxidative Medicine and Cellular Longevity, 2020, 2172740.
<sup>20</sup> Wu, Y., Li, Z. C., et al. (2019). Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquee, Nutrition et Metabolisme, 44(1), 1–6.
<sup>21</sup> Molodavkin, G. M., Voronina, T. A., & Aldarmaa, J. (2000). Eksperimental naia i Klinicheskaia Farmakologiia, 63(6), 12–14.
<sup>22</sup> Tohda, C., Tamura, T., et al. (2006). British Journal of Pharmacology, 149(5), 532–541.
<sup>23</sup> Lee, Y., Jung, J. C., et al. (2013). Evidence-Based Complementary and Alternative Medicine: eCAM, 2013, 514049.
<sup>24</sup> Cropley, M., Banks, A. P., & Boyle, J. (2015). Phytotherapy Research: PTR, 29(12), 1934–1939.
<sup>25</sup> White, D. J., Camfield, D. A., et al. (2020). Human Psychopharmacology, 35(6), 1–6.
<sup>26</sup> Olsson, E. M., von Schéele, B., & Panossian, A. G. (2009). Planta Medica, 75(2), 105–112.
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28 Lee, T. H., Jung, C. H., & Lee, D. H. (2012). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 50 (12), 4239–4245.

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<sup>29</sup> Zeng, K. W., Zhang, T., et al. (2012). European Journal of Pharmacology, 692(1-3), 29–37.
<sup>30</sup> Ballmann, C. G., Maze, S. B., et al. (2019). Journal of Sports Sciences, 37(9), 998–1003.
<sup>31</sup> Park, J., Han, S., & Park, H. (2020). International Journal of Environmental Research and Public Health, 77(7), 2475.
<sup>32</sup> Cho, Y. H., Lee, S. Y., et al. (2021). The American Journal of Clinical Nutrition, 113(6), 1440–1446.
<sup>33</sup> Matkovic, Z., Zivkovic, V., et al. (2010). Phytotherapy Research: PTR, 24(2), 775–181.
<sup>34</sup> Tong, X., Xiao, D., et al. (2010). Journal of Clinical Pharmacy and Therapeutics, 39(5), 561–563.
<sup>35</sup> Chu, D. T., Wong, W. L., & Mavligit, G. M. (1988). Journal of Enincial & Laboratory Immunology, 25(3), 125–129.
<sup>36</sup> Khoo, K. S., & Ang, P.T. (1995). Singapore Medical Journal, 36(4), 387–390.
<sup>37</sup> Sun, Y., Hersh, E. M., et al. (1983). Journal of Biological Response Modifiers, 2(3), 227–237.
<sup>38</sup> Ma, J., Peng, A., & Lin, S. (1998). Chinese Medical Journal, 11(1), 17–23.
<sup>39</sup> Bystritsky, A., Kerwin, L., & Feusner, J. D. (2008). Journal of Alternative and Complementary Medicine (New York, N.Y.), 14(2), 175–180.
<sup>40</sup> Kim, S. H., Hyun, S. H., & Choung, S. Y. (2006). BioFactors (Oxford, England), 26(3), 209–219.
<sup>41</sup> Kwon, Y. I., Jang, H. D., & Shetty, K. (2006). Asia Pacific Journal of Clinical Nutrition, 15(3), 425–432.
<sup>42</sup> Thu, O. K., Spigset, O., et al. (2016). Planta Medica, 76(4), 331–338.
<sup>44</sup> Hellum, B. H., Tosse, A., et al. (2010). Planta Medica, 76(4), 331–338.
<sup>45</sup> Stavro, P. M., Woo, M., et al. (2006). Hypertension (Dalka, Tex: 1979). 47(4), 791–796.
<sup>46</sup> Yuan, C. S., Wei, G., et al. (2000). Inhanta of Internal Medicine, 141(1), 23–27.
<sup>47</sup> Vulsan, V., Stavro, M. P., et al. (2000). Diabetes Care, 23(9), 1221–1226.
<sup>48</sup> Natural Medicines. (2021, September 18). Schisandra [monograph]. http://naturalmedicines.therapeuticresearch.c
```

Mu, Y., Zhang, J., et al. (2006). The Journal of Pharmacology and Experimental Therapeutics, 316(3), 1369–1377.
 Fan, L., Mao, X. Q., et al. (2009). Xenobiotica: The fate of foreign compounds in biological systems, 39(3), 249–254.

52 Xin, H. W., Wu, X. C., et al. (2007). British Journal of Clinical Pharmacology, 64(4), 469–475.



APPLICATIONS

- Detox Support
- Antioxidant Support



INTRODUCTION

Algas™ is a hydro-ethanolic extract of Pacific cold-water red seaweed (Chondracanthus chamissoi). C. chamissoi, a marine macroalga known commonly as Pacific cold-water red seaweed, belongs to the Gigartinaceae family.¹ It is also known as Sphaerococcus chamissoi, Gigartina chamissoi, and Chondroclonium chamissoi.¹ Nutrient-rich macroalga, also known as seaweed, has been consumed as a dietary staple in Asia for centuries.² Of all of the seaweed groups—Chlorophyta (green), Phaeophyceae (brown), and Rhodophyta (red), red seaweed contains the highest percentage of bioactive compounds, including 53% of the total compounds known in seaweed.*²

C. chamissoi contains sulfated polysaccharides such as carrageenans, including 24.6% xi/theta and 13.5% kappa/iota carrageenans per dry weight. ^{2,4,5} It contains chlorophyll and carotenoid pigments as well as antioxidant mycosporine-like amino acids (MAAs). ^{*2,6} It also contains vitamins, minerals, and essential fatty acids in a beneficial omega 3:6 ratio, in addition to phenolic compounds including polyphenols, flavonoids, and phenolic acids. ^{*2,7,8} It is worth noting that not all carrageenans are equal; only chemically unaltered, native carrageenans, such as found in Pacific cold-water red seaweed, may help with health support. ^{*9}

Algas is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

DETOX SUPPORT

Pre-clinical studies have shown that Pacific cold-water red seaweed (*C. chamissoi*) is an effective biosorbent for metals, which is attributed to cation exchange via carboxylic and sulfonic functional groups.*10-13 Seaweeds naturally concentrate metals from seawater as the structural polysaccharide carrageenan is a cation salt of sodium, potassium, and other metals.^{10,11}

ANTIOXIDANT SUPPORT

Pacific cold-water red seaweed (*C. chamissoi*) may contribute antioxidant support as determined by TRAP, FRAP, and DPPH assays.*^{3,7} Several components of red seaweed may contribute to its antioxidant effects.* Red seaweed contains phenolic compounds such as polyphenols, flavonoids, and phenolic acids, which are known to help with antioxidant support.*^{2,7,8} The compound fucoidan as well as the mycosporine-like amino acids (MAAs) palythine (PI) and shinorine (SH) may also contribute to antioxidant support.*^{2,6}

SAFETY AND CAUTIONS

Pacific cold-water red seaweed (*C. chamissoi*) has been consumed as a food for centuries and is generally well-tolerated.² While carrageenan degraded by acid hydrolysis may have negative effects, this process can only occur under laboratory conditions at very low pH and extremely high temperatures (>80°C or 176°F); acid hydrolysis of carrageenan cannot occur in the human stomach.⁹ Native, undegraded carrageenan such as found in red seaweed is approved by the European Food Safety Authority (EFSA) and is generally recognized as safe (GRAS) in the United States.⁴ Very little data is available regarding the potential for drug interactions or adverse effects.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.

NutraMedix 🦈

SHAKE WELL BEFORE EACH USE:

Put 20-40 drops in 4 oz (120mL) of water and wait one minute before drinking. Take every other day (30 min. before a meal) or as directed by your physician. Do not use if pregnant or nursing. Stop use if adverse reactions develop. Keep out of reach of children. children.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or property any disease. prevent any disĕase.



ALGAS

DETOX SUPPORT†

Dietary Supplement 1 fl oz. (30mL)

Supplement Facts
Serving Size 40 drops
Servings Per Container 15

Amount Per Serving

Chondracanthus chamissoi extract 2.0 mL*

*Daily Value not established

Other ingredients: mineral water, ethanol (20-24%)

NutraMedix 🛣

Jupiter, Florida 33458 USA www.nutramedix.com 561-745-2917

REFERENCES

1 Guiry, M.D. & Guiry, G.M. (2021). AlgaeBase. World-wide electronic publication, National University of Ireland, Galway. http:// www.algaebase.org; searched on 25 July 2021.

2 Carpena, M., Garcia-Perez, P., et al. (2022). Phytochemistry Reviews: Proceedings of the Phytochemical Society of Europe, 1–32.

3 Echave, J., Fraga-Corral, M., et al. (2021). Marine Drugs, 19(9), 500.

4 Álvarez-Viñas, M., Souto, S., et al. (2021). Marine Drugs, 19(8), 437.

5 Wang, P., Zhao, X., et al. (2012). Carbohydrate Polymers, 89(3), 914-919.

6 Sun, Y., Zhang, N., et al. (2020). Marine Drugs, 18(1), 43.

7 Miranda-Delgado, A., Montoya, M. J., et al. (2018). Latin American Journal of Aquatic Research, 46(2), 301-313.

8 Kalasariya, H. S., Yadav, V. K., et al. (2021). Molecules, 26(17), 5313.

9 McKim, J. M., Willoughby, J. A., et al. (2021). Critical Reviews in Food Science and Nutrition, 59(19), 3054-3073.

10 Yipmantin, A., Maldonado, H. J., et al. (2011). Journal of Hazardous Materials, 185(2-3), 922-929.

11 Veroy, R. K., Montano, N., et al. (2009). Botanica Marina, 23, 59-62.

12 Ibrahim W. M. (2011). Journal of Hazardous Materials, 192(3), 1827-1835.

13 Arumugam, N., Chelliapan, S., et al. (2018). International Journal of Environmental Research and Public Health, 15(12), 2851.

APPLICATIONS

- Relax/Sleep Support
- Stress Management Support



INTRODUCTION

Amantilla is a hydro-ethanol extract made from Valerian root (*Valeriana officinalis*), which belongs to the Caprifoliaceae/Valerianaceae family.\(^1\) Various species of Valerian continue to be used for relaxation, sleep support, and stress management in the traditional health practices of China, India, and the Middle East.\(^2\) Valerian root contains monoterpenes such as borneol; sesquiterpenes such as valerenal and valerenic acid; valepotriates such as valtrate; alkaloids such as actinidine; flavonoids such as linarin; minerals such as copper, zinc, and manganese; lignans; amino acids; and small amounts of GABA.\(^1.3.4.5\) Valerian root and its constituent valerenic acid may act as a GABA agonist as well as a partial 5-hydroxytryptamine (5-HT5a) agonist.\(^2.6.8\) It may also act as an adenosine A1 receptor agonist.\(^5\) Activity at these receptors may account for Valerian root's role in the support of healthy relaxation, sleep, and stress management.\(^8\)

Amantilla is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

RELAX / SLEEP SUPPORT

According to a recent systematic review and meta-analysis of human studies, Valerian root (*V. officinalis*) may help to support normal relaxation and healthy sleep during times of occasional sleeplessness.*5 It may also help to support sleep through skeletal muscle relaxation,* and also supports smooth muscle

relaxation.*9 In a mouse study, researchers notably found that Valerian root helped to support skeletal muscle relaxation while maintaining normal endurance and healthy neuromuscular tone, suggesting that Valerian root may assist with sleep support without the side effects typical of other treatments.*8

Valerian root (*V. officinalis*) may help to support both quality and quantity of sleep, with fewer nighttime awakenings.*10 It may also help to support a normal sleep onset.*4 Some of Valerian root's constituents, including the flavonoid linarin and the sesquiterpene valerenic acid, may help to support calm relaxation and healthy sleep.*3 Research suggests that blood levels of Valerian root peak from one to two hours after consumption, and because of this, it is recommended to take Valerian root 30 minutes to 2 hours before bed for optimal support.*11 While single doses may be helpful, studies lasting 14 days or longer showed more consistent support.*4,12 A key benefit of Valerian root for sleep support is that it rarely causes next-day drowsiness when used as recommended.*4

There are several mechanisms by which Valerian root may help with sleep support.* Valerian root is a GABAA receptor agonist, which may help maintain normal central nervous system (CNS) activity; this may facilitate a feeling of calm relaxation.*2,5,7 Both Valerian root and its constituent valerenic acid may act as a partial 5-HT5a agonist to maintain normal serotonergic function, supporting healthy sleep.*5 As 5-HT5a receptors are prevalent in the suprachiasmatic nucleus (SCN) and other areas of the brain involved with the circadian rhythm, this may be another avenue for potential sleep support.*5 Lastly, Valerian root is known to be a partial adenosine A1 agonist, which may help to support and maintain healthy and restorative slow-wave sleep.*5

In a randomized, double-blind, placebo-controlled, crossover study, 15 healthy participants were given either Valerian root extract or a vitamin E placebo. The Valerian group experienced decreased intracortical facilitation (ICF), or decreased brain excitability, which may also help to support healthy sleep.*13 Brain excitability returned to the pre-treatment baseline after 6 hours, explaining why morning drowsiness is rare with Valerian extract at the recommended dosages.*13 In a previous randomized, double-blind, placebo-controlled, crossover study, 14 days of Valerian root showed more consistent support than a single dose, and researchers concluded that Valerian helps maintain healthy slow-wave sleep.*12

STRESS MANAGEMENT SUPPORT

Many of the same receptors that support healthy sleep (GABAA, 5-HT5a, and adenosine A1) are also involved in stress management. Valerian root (*V. officinalis*) may help support healthy stress management during times of occasional stress through agonist or partial agonist action at these receptors.*5 One human trial with healthy participants compared the effects of valerian alone, kava alone, and no treatment on mental stress during cognitive testing. All three groups underwent baseline cognitive testing, then were administered either valerian, kava, or no treatment, for 7 days. All three groups then underwent a subsequent session of cognitive testing. While both the valerian and kava groups experienced a decrease in systolic blood pressure after the intervention, only the valerian group experienced a lower heart rate during mental stress. While neither intervention affected performance, it appeared to mitigate the perception of mental stress by maintaining normal physiological reactivity.*14

In a randomized, double-blind, placebo-controlled study with 64 mildly stressed volunteers, participants received Valerian root extract or a placebo three times daily for four weeks. While both groups showed some improvement in stress levels, only the Valerian group had significantly better alpha and theta coherence in the brain.*15 The study authors concluded that Valerian root may help maintain normal brain connectivity, supporting a sense of healthy calm.*15 There have been similar findings in rodent studies. In a mouse study, valepotriates from Valerian root helped to support normal stress management,5 which a rat study attributed to healthy HPA axis support.*16

SAFETY AND CAUTIONS

Valerian root (*V. officinalis*) is generally well tolerated. Common side effects include drowsiness, dizziness, and occasional gastrointestinal effects, though some individuals have reported vivid dreams.*¹⁷ Because Valerian root may help to support normal relaxation, it may have additive effects when taken with various sedative substances including, but not limited to, alcohol, benzodiazepines, and CNS depressants.*¹⁸⁻²⁰

Because Valerian mildly inhibits glucuronidation, it is possible that it may increase levels of drugs metabolized by UGT1A1 and UGT2B7.21 While rare, there have been isolated case reports of hepatoxicity, particularly in higher doses, with multi-ingredient formulas, or concurrent with alcohol abuse. Valerian is considered safe at recommended doses for shorter periods, and in extended use, it should be tapered gradually, rather than stopped abruptly, to avoid rebound effects.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

Pilerood, S. A. & Prakash, J. (2013). International Journal of Food, Nutrition, and Dietetics, 1(1), 1-8. 2 Gordan, A., Taheri, E., et al. (2019). Journal of Pharmaceutical Research International, 292, 1-10.

3 Fernández, S., Wasowski, C., et al. (2004). Pharmacology, Biochemistry, and Behavior, 77(2), 399–404.

4 Hadley, S., & Petry, J. J. (2003). American Family Physician, 67(8), 1755–1758.
5 Shinjyo, N., Waddell, G., et al. (2020). Journal of Evidence-based Integrative Medicine, 25, 2515690X20967323

6 Dietz, B. M., Mahady, G. B., et al. (2005). Brain Research: Molecular brain research, 138(2), 191–197. 7 Benke, D., Barberis, A., et al. (2009). Neuropharmacology, 56(1), 174–181.

8 Caudal, D., Guinobert, I., et al. (2017). Journal of Traditional and Complementary Medicine, 8(2), 335-340. 9 Occhiuto, F., Pino, A., et al. (2009). The Journal of Pharmacy and Pharmacology, 61(2), 251-256.

10 Abdellah, S. A., Berlin, A., et al. (2019). Journal of Traditional and Complementary Medicine, 10(2), 116–123.

11 Anderson, G. D., Elmer, G. W., et al. (2005). *Phytotherapy Research: PTR*, 19(9), 801–803.

12 Donath, F., Quispe, S., et al. (2000). Pharmacopsychiatry, 33(2), 47-53.

13 Mineo, L., Concerto, C., et al. (2017). *Neuropsychobiology*, *75*(1), 46–51.

14 Cropley, M., Cave, Z., et al. (2002). Phytotherapy Research: PTR, 16(1), 23-27.

15 Roh, D., Jung, J. H., et. (2019). Phytotherapy Research: PTR, 33(4), 939-948.

16 Shi, S. N., Shi, J. L., et al. (2014). Evidence-based Complementary and Alternative Medicine: eCAM, 2014, 325948. 17 Natural Medicines. (2022, August 24). Valerian [monograph]. http://naturalmedicines.therapeuticresearch.com.

18 Chen, D., Klesmer, J., et al. (2002). The American Journal on Addictions, 11(1), 75–77.

19 Donovan, J. L., DeVane, C. L., et al. (2004). Drug Metabolism and Disposition: The biological fate of chemicals, 32(12), 1333–1336.

20 Houghton P. J. (1999). The Journal of Pharmacy and Pharmacology, 51(5), 505–512.

21 Alkharfy, K. M., & Frye, R. F. (2007). Xenobiotica: The fate of foreign compounds in biological systems, 37(2), 113–123.

ANTARCTIC KRILL OIL



APPLICATIONS

- Cardiovascular Support
- Skin Support
- Joint/Muscle Support
- Neurological Support
- Ocular Support



INTRODUCTION

Antarctic Krill Oil is sustainably harvested from Euphausia superba, commonly known as Antarctic krill. Krill are small shrimp-like crustaceans in the Euphausiidae family, harvested from the pristine Southern Ocean surrounding Antarctica. Antarctic krill are at the bottom of the food chain, feeding primarily on phytoplankton. This allows them to provide nutrients such as omega-3s to other marine animals for which they are a primary food source, making them a keystone species. Antarctic krill are one of the most abundant species in the world, having an estimated biomass more than the global population of humans.

NutraMedix Atlantic Krill Oil contains long-chain omega-3 fatty acids (EPA and DHA), phospholipids, choline, and astaxanthin. Omega-3s, designated essential as the body needs but cannot synthesize them, include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA).² Plant sources of omega-3s contain only ALA and include flaxseed, chia seed, walnuts, and canola oil.² While the body can convert ALA to DHA and EPA, conversion is inefficient and the direct consumption of DHA and EPA is preferred.^{2,3} In a randomized, controlled trial with healthy individuals, increased intake of DHA and EPA supported a healthful omega-3 Index (O3-I) while increased intake of ALA did not.³⁴ Dietary sources of the preferred EPA and DHA include cold-water fatty fish such as salmon, herring, sardines, mackerel, and tuna.²

Choline is used to synthesize phospholipids for cell membranes and to produce the neurotransmitter acetylcholine. Choline is produced in limited amounts in the liver, and can be found in foods such as beef liver, egg, soybeans and fish. Astaxanthin is a xanthophyll carotenoid with antioxidant activity and can be found in salmon and shrimp. The astaxanthin in krill oil comes from their diet of phytoplankton, and is a natural-source antioxidant that helps to stabilize the omega-3 fatty acids."

The primary difference between krill oil and fish oil is that krill oil contains

omega-3s in phospholipid form while fish oil contains omega-3s in triglyceride form. Krill oil additionally contains choline and astaxanthin. EPA and DHA in phospholipid form may be more bioavailable than in triglyceride form, due to an increased affinity with the phospholipid bilayer.*9,10 In testing the hypothesis that phospholipid content may support bioavailability, krill oil with a higher phospholipid content was found to be more bioavailable than krill oil with a lower phospholipid content.*11 Krill oil may also be more effective than fish oil in maintaining the omega-3 index (03-l) already within the normal range.*12

NutraMedix Atlantic Krill Oil is 100% traceable from sea to shelf, with each batch labeled with coordinates of origin. It is also certified sustainable by the Marine Stewardship Council (MSC). Starting at the moment of harvest, patented Flexitech™ and Eco-Harvesting® technology eliminates by-catch, reduces environmental impact, and removes unwanted salts and other polar constituents, further concentrating the beneficial components. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers, and our products undergo stringent ID testing, microbial testing, and heavy metal testing. Atlantic Krill Oil has been extensively tested and found to be free of contaminants such as dioxins, dioxin-like PCBs (polychlorinated biphenyls), furans, organochlorine pesticides, polybrominated diphenyl ethers (PDBEs), polycyclic aromatic hydrocarbons (PAHs), fluoride, arsenic, trans-fatty acids, marine algal toxins, and heavy metals.¹³

CARDIOVASCULAR SUPPORT

Krill oil may help with cardiovascular support.*14 While it is widely accepted that optimal omega-3 levels help to support cardiovascular health, levels are often suboptimal. In a cross-sectional study with 200 U.S. and German adult participants ages 18-80, only four of the German participants and none of the U.S. participants had omega-3 index (O3-I) blood values within the optimal range. The O3-I is the percent of erythrocyte fatty acids that are DHA and EPA. It is a predictor of cardiovascular health, and thus, of potential risk. An O3-I ≥8 is most cardioprotective while an O3-I ≥4% is least cardioprotective.

Krill oil may help to maintain blood C-peptide levels, HDL levels, and HOMA scores already within the normal range.*18 It may also help to maintain CRP levels, apolipoprotein A1 levels, 19 triglyceride levels, 20 VLDL levels, and chylomicron levels already within the normal range.*21 In a systematic review and meta-analysis of seven randomized, controlled trials with a total of 662 participants, researchers concluded that krill oil may help to maintain LDL, HDL, and triglyceride levels already within the normal range.*22

SKIN SUPPORT

Oral krill oil may help to maintain uniform skin pigmentation.*23 Oral consumption of EPA, such as found in krill oil, may help to maintain dermal EPA and arachidonic acid levels already within the normal range, which may support healthy photoprotection.*24 In combination, with other ingredients in an oral superoxide dismutase-containing formula, krill oil helped to support normal photoprotection and healthy skin elasticity.*25

OTHER USES

Joint/Muscle Support

Krill oil may support healthy joints, helping to maintain CRP levels and WOMAC scores already within the normal range. It may also help to support knee comfort while sleeping and during standing, and help to maintain normal range of motion (ROM)."

Neurological Support

Krill oil may help with neurological support.* In a double-blind, randomized, controlled, parallel trial with healthy male volunteers ages 61-72, krill oil, sardine oil, and medium-chain triglycerides were compared. The effects of krill oil (omega-3s in phospholipids) were compared to the effects of sardine oil (omega-3s in triglycerides) and to the effects of medium-chain triglycerides (placebo). Compared to placebo, both krill oil and sardine oil supported normal oxyhemoglobin levels in the cerebral cortex during memory and calculation tasks, and krill oil was the most effective at maintaining healthy cognitive

function.*28 Krill oil may also help to support normal processing speed.*29

Ocular Support

Krill oil may help with ocular support.*30 While both fish oil and krill oil may help maintain healthy tear osmolarity, krill oil is superior at maintaining a healthy OSDI score already within the normal range.*30

SAFETY AND CAUTIONS

Krill oil is generally well tolerated and has been used safely in doses up to 4 grams daily for as long as 3 months.²⁰ There is insufficient data available on safety in pregnancy and breastfeeding.³¹ Side effects may include gastrointestinal symptoms such as upset stomach, nausea, heartburn, decreased appetite, bloating, flatulence or diarrhea, though at a lesser incidence than with fish oil.³¹ One patient in one trial developed hypertension after taking krill oil, though this has not been seen elsewhere in the literature. 20

Krill oil may theoretically increase the risk of hypoglycemia when taken with hypoglycemic drugs.³¹ It may also, theoretically, increase the risk of bleeding if used concurrently with anticoagulant or antiplatelet drugs.³¹ Krill oil should be discontinued at least two weeks before elective surgery.³¹ Those allergic to seafood may also be allergic to krill oil, though the likelihood of this is currently unknown.³¹ Krill oil should be avoided, or used with caution, in those with seafood allergy.³¹

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



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1 CCAMLR. (2021). Krill fisheries and sustainability | CCAMLR. Ccamlr.org. Retrieved 11 August 2021, from https://www.ccamlr.org/en/fisheries/krill-fisheries-and-sustainability.
2 ODS. (2021). Office of Dietary Supplements - Omega-3 fatty acids. Ods.od.nih.gov. Retrieved 11 August 2021, from https://ods.od.nih.gov/factsheets/Omega-3 FattyAcids-HealthProfessional/.
3 LPL. (2021). Essential fatty acids. Linus Pauling Institute. Retrieved 11 August 2021, from https://lpi.oregonstate.edu/mic/other-nutrients/essential-fatty-acids.

IPI. (2021). Essential fatty acids. Linus Pauling Institute. Retrieved 11 August 2021, from https://lipi.oregonstate.edu/mic/other-nutrients/essential-fatty-acids.
Köhler, A., Heinrich, J., & von Schacky, C. (2017). Nutrients, 9(6), 629.
ODS. (2021). Office of Dietary Supplements - Choline. Ods.od.nih.gov. Retrieved 11 August 2021, from https://lob.od.od.nih.gov/factsheets/Choline-HealthProfessional/.
Ross, A.C., Caballero, B., et al. (2014). Modern nutrition in health and disease (1th ed., pp. 416-26). Wolters Kluwer/Lippincott Williams & Wilkins.
Ambati, R. R., Phang, S. M., et al. (2014). Marine Drugs, 12(1), 128-152.
LPI. (2021). Inflammation. Linus Pauling Institute. Retrieved 11 August 2021, from https://lpi.oregonstate.edu/mic/health-disease/inflammation.
Ulven, S. M., & Holven, K. B. (2015). Vascular Health and Risk Management, 11, 511-524.
Schuchardt, J. P., Schneider, I., et al. (2011). Lipids in Health and Disease, 10, 145.
Ramprasath, V. R., Eyal, I., et al. (2015). Lipids in Health and Disease, 14, 142.
Ramprasath, V. R., Eyal, I., et al. (2013). Lipids in Health and Disease, 12, 178.
Burri, L. (2018). Krill oil concentrate: The phospholipid factor that sets krill oil apart [Ebook]. Aker BioMarine.
Rundhlad A. Holven, K. B. et al. (2018). Journal of Nutritional Science, 2(e2), 1-11.

     <sup>14</sup> Rundblad, A., Holven, K. B., et al. (2018). Journal of Nutritional Science, 7(e3), 1-11.

    Hundblad, A., Holven, K. B., et al. (2018). Journal of Nutritional Science, 7(e3), 1-11.
    Thuppal, S. V., von Schacky, C., et al. (2017). Nutrients, 9(9), 930.
    von Schacky C. (2014). Nutrients, 6(2), 799–814.
    Harris, W. S. & von Schacky, C. (2004). Preventive Medicine, 39(1), 212-220.
    Blobraico, J. M., Dilello, L. C., et al. (2015). BMJ Open Diabetes Research & Care, 3(1), e000107.
    Gicero, A. F., Rosticci, M., et al. (2016). Archives of Medical Science: AMS, 12(3), 507–512.
    Berge, K., Musa-Veloso, K., et al. (2014). Nutrition Research (New York, NY.), 34(2), 126–133.
    Berge, R. K., Ramsvik, M. S., et al. (2015). Lipids in Health and Disease, 14, 163.
    Horoniu S. et al. & Lipid and Blood Procure Meta-analysis (Ollaboration Group (2017). Nutrion

21 Berge, R. K., Ramsvik, M. S., et al. (2015). Lipids in Health and Disease, 14, 163.
22 Ursoniu, S., et al., & Lipid and Blood Pressure Meta-analysis Collaboration Group (2017). Nutrition Reviews, 75(5), 361–373.
23 Kocakoglu, S., & Akpinar, E. (2020). Journal of Medical-Clinical Research & Reviews, 4,(1), 1-3.
24 Pilkington, S. M., Rhodes, L. E., et al. (2014). Molecular Nutrition & Food Research, 58(3), 580–590.
25 Goldberg, L. D., & Crysler, C. (2014). Clinical, Cosmetic and Investigational Dermatology, 7, 139–144.
26 Deutsch L. (2007). Journal of the American College of Nutrition, 26(1), 39–48.
27 Suzuki, Y., Fukushima, M., et al. (2016). PloS One, 17(10), e0162769.
28 Konagai, C., Yanagimoto, K., et al. (2013). Clinical Interventions in Aging, 8, 1247–1257.
29 van der Wurff, I. S., von Schacky, C., et al. (2016). Nutrients, 8(1), 13.
30 Deinema, L. A., Vingrys, A. J., et al. (2017). Ophthalmology, 124(1), 43–52.
31 Natural Medicines. (2021, August 10). Krill Oil [monograph]. http://naturalmedicines.therapeuticresearch.com
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- Relaxation and Stress-Management Support
- Healthy Sleep Support
- Antioxidant Support
- Healthy Inflammatory-Response Support
- Healthy Mood Support



INTRODUCTION

Babuna is a hydro-ethanol extract made from *Matricaria* recutita flowers. *M. recutita* belongs to the Asteraceae/ Compositae family, and its common name is German chamomile. Synonyms include *Matricaria* chamomilla and *Chamomilla* recutita. M. recutita is native to Asia and Europe, and is included in the pharmacopoeia of 26 countries. Due to its pleasant taste and aroma, it is also used in foods and cosmetics.

Chamomile flower (*M. recutita*) has been used for centuries to support health. The Greek physician Dioscorides recommended it for health support in the first century C.E.*4 Ancient Egyptians, Greeks, and Romans all used chamomile for health support,⁵ and the Anglo-Saxons considered it one of their nine most important herbs.*3 Historically, traditional use has included neurological, gastrointestinal, respiratory, liver, and healthy inflammatory-response support.*6

The word chamomile comes from the Greek chamaimēlon, meaning "apple of the ground" due to the mild apple-like scent of its flowers.² The plant is still in widespread use; more than a million cups of chamomile-flower tea are consumed per day

worldwide.⁷ In addition, chamomile has been approved by the German Commission E for health support.*8

Constituents of chamomile include flavonoids such as apigenin and luteolin, terpenes such as geraniol and menthol, volatile oils such as isopentyl and isobutyl isobutyrate, organic acids such as carboxylic acid and sulfonic acid, coumarins such as umbelliferone and alpha-bisabolol, polysaccharides, amino acids, minerals, gamma-aminobutyric acid (GABA), and other compounds.²

Babuna is made at NutraMedix's U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy-metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

SUPPORT FOR RELAXATION AND STRESS MANAGEMENT

German chamomile flowers (*M. recutita*) may help maintain relaxation and support healthy stress management.*5 The constituents apigenin and luteolin may be particularly helpful in supporting healthy stress management because of their affinity with GABA_A receptors.*9

In a double-blind, randomized trial, 90 healthy college students were assigned to either a chamomile capsule (100 mg) three times per day or a positive control, from day 21 of the menstrual cycle until the onset of menstruation. After two cycles, the chamomile group experienced significantly better premenstrual stressmanagement support than the control group.*9

In another double-blind, controlled trial, 57 participants were randomly assigned to chamomile extract capsules (220 mg) or a placebo. Participants were given one capsule per day for the first week, increasing to two capsules per day for the second week. Depending on response, the dose was increased by one capsule per week, for a maximum of five capsules. The researchers concluded that the chamomile group experienced

significantly improved healthy stress-management support compared to the placebo group.*10

HEALTHY SLEEP SUPPORT

German chamomile flowers (*M. recutita*) may help support healthy sleep quality.* In a single-blind, controlled trial with 73 healthy postpartum women, the participants were randomly assigned to standard care plus single-ingredient chamomile tea, or to standard care alone. The chamomile group consumed 1 cup of chamomile tea daily for 2 weeks. Compared to those in the control group receiving standard care only, those who consumed chamomile tea experienced significantly more support for healthy sleep, according to a standardized scale of sleep quality.*⁵

M. recutita has also been shown to help support healthy sleep quality in the elderly.* In a single-blind study, 60 participants age 60 and older were randomly assigned to either two capsules of chamomile extract per day (200 mg each) or a placebo control, for 28 days. Compared to the control group, participants in the chamomile group experienced significant support for maintaining healthy sleep quality.*¹¹

OTHER USES

ANTIOXIDANT SUPPORT

German chamomile flowers (*M. recutita*) may help with antioxidant support, as evidenced by DPPH free radical scavenging assay,³ with luteolin showing the strongest support.*12 Laboratory studies attribute this to the maintenance of antioxidant enzymes, NRF2 signaling, and CD4+ T cell activation, already within the normal range.*6

In a study with rats, chamomile tea helped support and maintain superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), already within the normal range, compared to a control group.*13 Individual constituents such as luteolin, chalmuzene, and apigenin may help with both antioxidant support and healthy inflammatory-response support.*6

HEALTHY INFLAMMATORY-RESPONSE SUPPORT

German chamomile flowers (*M. recutita*) may help support a healthy inflammatory response through the maintenance of IL-1beta, IL-6, and TNF-alpha-induced NO levels already within the normal range, according to laboratory studies with mouse and human cells.*^{6,8} Chamomile flowers may also help maintain NF-kappaB

already within the normal range, which may help maintain NO production and iNOS expression already within the normal range.*8

In addition, chamomile flowers may help maintain prostaglandin E2 and COX-2 already within the normal range.*7 The constituents luteolin, chalmuzene, apigenin, and alpha bisabolol may help with antioxidant support in addition to supporting a healthy inflammatory response.*6,9

HEALTHY MOOD SUPPORT

German chamomile flowers (*M. recutita*) may help support a healthy mood.* In a single-blind, controlled trial, postpartum participants were randomly assigned to standard care plus chamomile tea or to standard care alone. The chamomile group consumed 1 cup of chamomile tea daily for 2 weeks. Compared to those in the control group receiving standard care only, the chamomile group experienced significantly more support for healthy mood and sleep.*5

In a double-blind, randomized trial, researchers examined the effects of a chamomile capsule (100 mg) taken three times per day for 7 days on premenstrual support for healthy mood and stress management.* The capsules were taken during the week before menstruation, for two consecutive menstrual cycles. Compared to the control group, the chamomile group experienced significant support for stress management and a healthy mood.*9

SAFETY AND CAUTIONS

M. recutita is one of the most commonly used herbs worldwide, and is generally well tolerated.¹⁴ It is generally recognized as safe (GRAS) in the United States.^{7,15} Adverse effects are uncommon, but may include nausea or dizziness.¹⁶ It may also cause allergic reactions in those sensitive to other members of the Asteraceae/Compositae family, such as ragweed.¹⁴ In a clinical trial involving 3,851 participants, 3.1% of those taking chamomile experienced an allergic reaction.¹¹

M. recutita should not be taken concurrently with cyclosporine, as it may increase blood levels of cyclosporine. ¹⁷ It may also inhibit the activity of CYP2C9, CYP2D6, CYP3A4, and CYP1A2. ^{1,18} In addition, *M. recutita* may increase the levels and effects of warfarin, as described in one case report. ¹ In vitro studies show that it can also inhibit CYP3A4 and CYP1A2, which may explain a rise in INR. ¹⁸ Theoretically, *M. recutita*

may have interactions with antidepressant and anxiolytic medications.¹

Safety is not documented in breastfeeding or pregnant women, or in children under age 3, due to insufficient safety research.

*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.

REFERENCES

- ¹Natural Medicines. (2022, June 28). German Chamomile [monograph]. http://naturalmedicines.therapeuticresearch.com
- ² Dai, Y. L., Li, Y., et al. (2022). *Molecules*, 28(1), 133.
- ³ Donia, A. E. R. B., Alam, A., et al. (2016). *Bulletin of Environment, Pharmacology and Life Sciences, 5*(7), 30-33.
- ⁴ Mailänder, L. K., Lorenz, P., et al. (2022). *Molecules*, *27*(23), 8508.
- ⁵ Chang, S. M., & Chen, C. H. (2016). *Journal of Advanced Nursing*, 72(2), 306–315.
- ⁶ De Cicco, P., Ercolano, G., et al. (2023). *Journal of Ethnopharmacology*, 116391.
- ⁷ Srivastava, J. K., Shankar, E., et al. (2010). *Molecular Medicine Reports*, *3*(6), 895–901.
- ⁸ Bhaskaran, N., Shukla, S., et al. (2010). *International Journal of Molecular Medicine*, *26*(6), 935–940.
- ⁹ Sharifi, F., Simbar, M., et al. (2014). *Complementary Therapies in Clinical Practice*, 20(1), 81–88.
- ¹⁰ Amsterdam, J. D., Li, Y., et al. (2009). *Journal of Clinical Psychopharmacology*, *29*(4), 378–382.
- ¹¹ Adib-Hajbaghery, M., & Mousavi, S. N. (2017). *Complementary Therapies in Medicine*, *35*, 109–114.

- ¹² Hwang, S. H., Wang, Z., et al. (2018). *Journal of Diabetes Research*, *2018*, 3276162.
- ¹³ Perestrelo, B. O., Carvalho, P. M., et al. (2022). *Brazilian Oral Research*, *36*, e034.
- ¹⁴ Gardiner P. (2007). *Pediatrics in Review*, *28*(4), e16–e18.
- ¹⁵ Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Chamomile. [Updated 2021 Feb 15]. https://www.ncbi.nlm.nih.gov/books/NBK501808/
- LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Chamomile. [Updated 2022 May 24]. https://www.ncbi.nlm.nih.gov/books/NBK548163/
- ¹⁷ Colombo, D., Lunardon, L., et al. (2014). *Journal of Toxicology*, *2014*, 145325.
- ¹⁸ Tan, C. S. S., & Lee, S. W. H. (2021). *British Journal of Clinical Pharmacology*, *87*(2), 352–374.

NutraMedix 🥗

SHAKE WELL BEFORE EACH USE:

Put 15 drops in 4 oz (120mL) of water and wait one minute before drinking. May be taken several times per day as needed, or 30 drops at bedtime, or as directed by your physician. Stop use if adverse reactions develop. Keep out of reach of children.

†These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.



BABUNA
FROM CHAMOMILE
CALMING/SLEEP SUPPORT †

Dietary Supplement 1 fl oz. (30mL)

Supplement Facts

Serving Size 30 drops Servings Per Container 20

Amount Per Serving

Chamomile flower extract 1.5 mL*

*Daily Value not established

Other ingredients: mineral water, ethanol (20-24%)



E



- Microbial Support
- Inflammatory Response Support



INTRODUCTION

Banderol is a hydro-ethanol extract from the bark of wild Otoba parvifolia, including mineral water and 20-24% alcohol. O. parvifolia is also known as Banderilla tree and belongs to the Myristicaceae family. It is sustainably harvested from the Amazon basin ecosystem, and has been used by indigenous groups in the region for hundreds of years. Traditionally, O. parvifolia bank has been used for microbial support.² The proprietary hydro-ethanolic extraction and enhancement process maximizes the bioavailability of isoflavones and other beneficial constituents.³

Banderol is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herb in its original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

MICROBIAL SUPPORT

O. parvifolia (bark) may help with diverse microbial support for various types and morphological forms.*4,5,6 Banderol (O. parvifolia) may be combined with Samento (*U. tomentosa*) for synergistic microbial support.*7 Independently, both *O. parvifolia* and *U. tomentosa* assist with microbial support.*7 In combination, they exhibit more robust support.*7

INFLAMMATORY RESPONSE SUPPORT

O. parvifolia (bark) may help support a healthy inflammatory response.* O. parvifolia has been studied in mice, in which Banderol's inflammatory response support was found comparable to the positive control.*

SAFETY AND CAUTIONS

A mouse study using 500 times the human dosage of Banderol showed no evidence of side effects or toxicity. O. parvifolia inhibits the uptake transporters OATP1B1 and OATP1B3,² so caution is warranted with medications that are substrates or inhibitors of OATP1B1 and OATP1B3.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.



* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.

- Jaramillo-Vivanco, T. & Balslev, H. (2020). Phytotaxa, 441(12); 143-175.

- Jaramiilo-Vivanco, 1. & basiev, n. (2020). Priyetetasa, 441(12); 143-175.

 Weiss J. (2018). Molecules, 24(1), 137.

 Valderrama J. C. (2000). Phytochemistry, 55(6), 505-511.

 Goc, A., & Rath, M. (2016). Therapeutic Advances in Infectious Disease, 3(3-4), 75-82.

 Weniger, B., Robledo, S., et al. (2001). Journal of Ethnopharmacology, 78(2-3), 193-200.
- 6 Rocha, L. G., Almeida, J. R., et al. (2005). Phytomedicine: International journal of phytotherapy and phytopharmacology, 12(6-7), 514–535.
- Datar, A., Kaur, N., et al. (2010). Townsend Letter, 7, 1-4.
- Allende, A. (2005). NutraMedix Laboratories, LLC.
- Allende, A. (2006). NutraMedix Laboratories, LLC. 10 Shitara, Y. (2011). Drug Metabolism and Pharmacokinetics, 26(3), 220–227.

- Detox Support
- Antioxidant Support
- Prebiotic



INTRODUCTION

Binder Plus consists of a proprietary blend of inulin, bentonite zeolite, aloe vera, activated charcoal, fulvic minerals, and chitosan. These ingredients may help synergistically support healthy detoxification pathways to detoxify the body's natural toxins.*

INULIN

Inulin from *Agave* spp. is a soluble, indigestible fiber that is fermented by colonic bacteria to support normal levels of short-chain fatty acids (SCFAs) and may help to support *bifidobacterium* levels already within the normal range.*1,2 Inulin may help to maintain a healthy gut barrier, support a healthy inflammatory response, and maintain normal immune function.*3

Meta-analyses have suggested that inulin may help to support regularity and maintain normal bowel function; help to support metabolic health by maintaining fasting blood glucose (FBG), hemoglobin A1c (HbA1c), fasting insulin, and insulin resistance already within the normal range; and may support a normal BMI by maintaining C-reactive protein and ghrelin levels already within the normal range.

BENTONITE

Bentonite clay, also known as montmorillonite, has been used in traditional health practices for centuries.^{7,8} Bentonite is a polycationic aluminosilicate clay with the ability to bind to negatively-charged substances, which may help support healthy detoxification and support a healthy mucosal gut barrier.*^{9,10,11} It may also help with microbial support.*⁸

ZEOLITE

Zeolite is also a polycationic aluminosilicate clay with the ability to bind to negatively-charged substances, which may help to support healthy detoxification, facilitating excretion through stool.*12,13,14 Zeolite clinoptilolite, the natural-source form, is the most researched and commonly used.¹⁵ It may also support antioxidant activity,^{15,16} maintain normal immune function,¹³ maintain healthy gastrointestinal barrier function,¹⁴ and support a healthy inflammatory response.*17

ALOE VERA

Aloe vera (leaf) contains polysaccharides and phenolics, ¹⁸ and the most-studied constituents include aloe-emodin, emodin, aloesin, aloin, and acemannan. ^{*19} Both aloe-emodin and acemannan may help with prebiotic support. ^{*19} In addition, Aloe may help with antioxidant support, ^{20,21} support a healthy inflammatory response in intestinal tissue, ^{19,21} maintain normal glucose already within the normal range, ^{22,23} and maintain normal lipids already within the normal range. ^{*24}

ACTIVATED CHARCOAL

Charcoal has been used to support gastrointestinal detoxification for over a century.*25 Activated charcoal has more pores and thus greater absorption.*25 Activated charcoal may help to support healthy detoxification and healthy elimination through the stool.*26 It may also help to maintain a healthy gut microbiome.*27

FULVIC MINERALS

Fulvic minerals come from humic substances made by soil micro-organisms. ^{28,29} Fulvic minerals may help support healthy gastrointestinal function, maintain healthy immune function, and support a healthy inflammatory response. *29 They may also help with antioxidant support. *29

CHITOSAN

Chitosan is a polysaccharide that can be derived from a number of sources, ³⁰ and NutraMedix chitosan is from mushrooms. As with bentonite and zeolite, chitosan is polycationic with the ability to bind with the body's natural toxins that are negatively charged. ³¹ Meta-analyses have shown that chitosan may also help to maintain blood pressure, ^{32,33} blood sugar, body weight, ^{33,35} and lipids, already within the normal range. ^{33,36}

DETOX SUPPORT

Inulin's dietary fiber may help to maintain normal intestinal flora by acting as a prebiotic to support and maintain beneficial flora, including *bifidobacterium* and *lactobacillus*, which may help with healthy detoxification support by maintaining the integrity of the gut barrier.* It may also support a healthy fecal weight, aiding in the elimination of the body's natural toxins.*1

Bentonite is a polycationic aluminosilicate clay with the ability to absorb

the body's natural negatively-charged toxins.*7 It may also help support the elimination of the body's natural toxins through the stool.*7 In animals, it has been shown to support and maintain liver health.*7 Bentonite clay may maintain creatinine levels already within the normal range by absorption and excretion through stool.*7 In addition, it may help to support the transfer of urea from blood vessels to intestines, and then to excretion via stool, helping to maintain renal health.*7 Randomized, controlled trials have shown that bentonite may help to support healthy detoxification,9,10 as well as maintain healthy gut barrier function.*11

Zeolite, similar to bentonite, is a polycationic aluminosilicate clay with the ability to absorb the body's natural negatively-charged toxins, ¹⁴ which are then excreted through the stool. ¹² It may support healthy detoxification through the maintenance of zonulin already within the normal range, supporting intestinal mucosal integrity. ^{*14} Its support of antioxidant activity may be partially responsible for its role in detoxification support. ^{*16}

Aloe Vera leaf may help with detoxification support through antioxidant support, prebiotic support, and maintaining a healthy inflammatory response in intestinal tissue. Activated charcoal, as with bentonite and zeolite, has many pores and may help to bind the body's natural toxins, supporting healthy elimination. It is widely used for detoxification support, and may also help maintain a healthy gut microbiome.

Fulvic Minerals may help with detoxification support, antioxidant support, and healthy inflammatory response support through maintaining CRP levels, NF-kappaB, and COX-2 levels already within the normal range.*40,41 Chitosan may also help with detoxification support.*42 As with bentonite and zeolite, chitosan is polycationic with the ability to bind with the body's natural toxins.*31,43

SAFETY AND CAUTIONS

Inulin has GRAS (Generally Recognized As Safe) status in the United States and is generally well-tolerated.² The most common side effects of inulin are gastrointestinal, including constipation, diarrhea, gas, and cramps.² Theoretically, inulin may have additive effects with hypoglycemic medications.²

Bentonite and zeolite clays are generally well tolerated, in short-term use.⁴⁴ Bentonite clay has been used safely in dosages up to 3 g/day for three months.⁴⁴ Zeolite (clinoptilolite) is considered to be nontoxic and biologically neutral for internal use.¹³ Adverse effects from clay consumption are rare, and generally mild, including vomiting, diarrhea, and/or constipation. Long-term use may lead to more severe adverse effects.⁴⁴ In vitro studies have shown that clays may inhibit the absorption of quinine by 30%, and clinical studies have shown that clays may inhibit the absorption of cimetidine when taken concurrently.⁴⁴

Aloe is generally well tolerated when used in the recommended dosages. 45 While whole aloe leaf contains latex, we use only the gel from the inner leaf. Aloe latex may cause gastrointestinal effects like cramps, abdominal pain, and diarrhea,

and high doses of aloe latex have been known to cause hypersensitivity hepatitis.⁴⁵

Aloe latex should not be taken with digoxin, as it may increase the risk of serious adverse effects when taken with cardiac glycosides. Aloe may have additive effects with hypoglycemic drugs. Theoretically, aloe gel may increase risk of bleeding when taken with anticoagulant or antiplatelet drugs, and may do the same when taken with warfarin. Theoretically, aloe may increase electrolyte disturbance when taken with stimulant laxatives and may increase the risk of hypokalemia when taken with diuretics.⁴⁵

Activated charcoal is generally well tolerated. Short-term use is safe and activated charcoal has been used in dosages up to 1.2 grams three times daily for up to 3 years.²⁵ Common side effects include gastrointestinal symptoms such as abdominal pain, bloating, constipation, and flatulence. Black stools may also occur, due to the color of charcoal.²⁵ Activated charcoal should not be routinely combined with laxatives,⁴⁶ and should not be taken at the same time as oral pharmaceuticals, as it may decrease their efficacy.²⁵ Activated charcoal will inactivate syrup of ipecac, and may decrease the efficacy of oral contraceptives. Alcohol may decrease the effects of activated charcoal.²⁵

Fulvic minerals are generally well-tolerated, though may cause headache, sore throat, or diarrhea. Fulvic acid can shorten prothrombin time, increasing the risk of clotting, and may theoretically decrease the effectiveness of antiplatelet or anticoagulant drugs. It may also decrease the effectiveness of immunosuppressants and increase both TSH levels and T4:T3 ratio. The control of the control

Chitosan is nontoxic and generally well tolerated. It has been safely used in studies in dosages up to 1.35 g/day for up to 3 months.³⁰ Side effects, when they occur, are generally gastrointestinal and may include nausea, flatulence, diarrhea, or constipation.³⁰ Chitosan may increase the risk of bleeding when taken with warfarin, and may reduce the effectiveness of acyclovir.³⁰

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.

NutraMedix 😤

KEEP OUT OF REACH OF CHILDREN

STORAGE: Keep tightly closed in a dry place at room temperature. (59-86°F or 15-30°C)

SUGGESTED USE: Take two capsules once or twice daily or as directed by your physician. Do not use if pregnant or nursing. Stop use if adverse reactions develop.

WARNING:This product can expose you to chemicals including lead, which is known to the state of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

[†]This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.





COMPREHENSIVE TOXIN BINDER †



Dietary Supplement 120 Vegetable Capsules

Supplement Facts Serving Size 2 Capsules Servings Per Container 60

Amount Per Serving % DV
Proprietary Blend 1200 mg *
Zeolite, Activated Charcoal, Inulin, Aloe Vera leaf, Fulvic Minerals, Bentonite Clay, Chitosan from mushrooms

*Daily Value not established

Other ingredients: Vegetable Capsule Vegetable Magnesium Stearate GLUTEN, SUGAR & DAIRY FREE

NutraMedix.

Jupiter, Florida 33458 USA www.niutramedix.com 561-745-2917



REFERENCES

1 Tawfick, M. M., Xie, H., et al. (2022). International Journal of Biological Macromolecules, 208, 948.

2 Natural Medicines. (2022, June 03). Inulin [monograph]. http://naturalmedicines.therapeuticresearch.com

3 Shoaib, M., Shehzad, A., et al. (2016). Carbohydrate Polymers, 147, 444-454.

4 Collado Yurrita, L., San Mauro Martín, I., et al. (2014). Nutricion Hospitalaria, 30(2), 244-252.

5 Wang, L., Yang, H., et al. (2019). Journal of Translational Medicine, 17(1), 410.

6 da Silva Borges, D., Fernandes, R., et al. (2020). Nutrition Reviews, 78(3), 235-248.

7 Moosavi M. (2017). Iranian Journal of Public Health, 46(9), 1176-1183.

8 Williams, L. B., Haydel, S. E., & Ferrell, R. E. (2009). Elements (Quebec, Quebec), 5(2), 99-104.

9 Mitchell, N. J., Kumi, J., et al. (2014). The American Journal of Tropical Medicine and Hygiene, 91(4), 777-785.

10 Pollock, B. H., Elmore, S., et al. (2016). Food Additives & Contaminants, 33(8), 1346-1354.

11 Gao, X., Miao, R., et al. (2018). Medicine, 97(39), e12577.

12 Samekova, K., Firbas, C., et al. (2021). Scientific Reports, 11(1), 14796.

13 Kraljević Pavelić, S., Simović Medica, J., et al. (2018). Frontiers in Pharmacology, 9, 1350.

14 Lamprecht, M., Bogner, S., et al. (2015). Journal of the International Society of Sports Nutrition, 12, 40.

15 Mastinu, A., Kumar, A., et al. (2019). Molecules (Basel, Switzerland), 24(8), 1517.

16 Atitlán-Gil, A., Bretón-de la Loza, M. M., et al. (2017). Revista de Investigacion Clinica: Organo del Hospital de Enfermedades de la Nutricion, 69(3), 146-151.

17 Petkov, V., Schütz, B., et al. (2021). Neuro Endocrinology Letters, 42(1), 1-12.

18 Guo, X., & Mei, N. (2016). Journal of Environmental Science and Health. Part C, Environmental Carcinogenesis & Ecotoxicology

19 Sánchez, M., González-Burgos, E., et al. (2020). Molecules (Basel, Switzerland), 25(6), 1324.

20 Heś, M., Dziedzic, K., et al. (2019). Plant Foods for Human Nutrition (Dordrecht, Netherlands), 74(3), 255-265.

21 Kumar, R., Singh, A. K., et al. (2019). Phytomedicine: International journal of phytotherapy and phytopharmacology, 60, 152996. 22 Dick, W. R., Fletcher, E. A., & Shah, S. A. (2016). Journal of Alternative and Complementary Medicine (New York, N.Y.), 22(6), 450-457.

23 Suksomboon, N., Poolsup, N., & Punthanitisarn, S. (2016). Journal of Clinical Pharmacy and Therapeutics, 41(2), 180-188. 24 Zhang, Y., Liu, W., et al. (2016). Nutrients, 8(7), 388.

25 Natural Medicines. (2022, June 03). Activated charcoal [monograph]. http://naturalmedicines.therapeuticresearch.com

26 Skov, K., Graudal, N. A., & Jürgens, G. (2021). Basic & Clinical Pharmacology & Toxicology, 128(4), 568-578.

27 de Gunzburg, J., Ghozlane, A., et al. (2018). The Journal of Infectious Diseases, 217(4), 628-636.

28 Natural Medicines. (2022, June 03). Fulvic Acid [monograph]. http://naturalmedicines.therapeuticresearch.com

29 Winkler, J., & Ghosh, S. (2018). Journal of Diabetes Research, 2018, 5391014.

30 Natural Medicines. (2022, June 03). Chitosan [monograph]. http://naturalmedicines.therapeuticresearch.com

31 Muxika, A., Etxabide, A., et al. (2017). International Journal of Biological Macromolecules, 105 (Pt 2), 1358-1368.

32 Huang, H., Zou, Y., & Chi, H. (2017). Drug Design, Development and Therapy, 12, 67-75.

33 Moraru, C., Mincea, M. M., et al. (2018). Medicina (Kaunas, Lithuania), 54(6), 109.

34 Guo, W., Yi, L., et al. (2020). Nutrition Journal, 19(1), 130.

35 Huang, H., Liao, D., et al. (2020). Critical Reviews in Food Science and Nutrition, 60(11), 1815-1825.

36 Huang, H., Zou, Y., et al. (2018). Molecular Nutrition & Food Research, 62(8), e1700842.

37 Avau, B., Borra, V., et al. (2018). The Cochrane Database of Systematic Reviews, 12(12), CD013230.

38 Chiew, A. L., Gluud, C., et al. (2018). The Cochrane Database of Systematic Reviews, 2(2), CD003328.

39 Walker, K. F., Chappell, L. C., et al. (2020). The Cochrane Database of Systematic Reviews, 7(7), CD000493. 40 van Rensburg, C. E. (2015). Phytotherapy Research: PTR, 29(6), 791–795.

41 Chien, S. J., Chen, T. C., et al. (2015). BMC Complementary and Alternative Medicine, 15, 61.

42 Yang, X., Hu, X., et al. (2021). Toxicon: Official journal of the International Society on Toxinology, 196, 1-7.

43 Wei, B., He, M., et al. (2019). International Journal of Nanomedicine, 14, 6917-6932.

44 Natural Medicines. (2022, June 03). Clay [monograph]. http://naturalmedicines.therapeuticresearch.com 45 Natural Medicines. (2022, June 03). Aloe [monograph]. http://naturalmedicines.therapeuticresearch.com 46 Zellner, T., Prasa, D., et al. (2019). Deutsches Arzteblatt International, 116(18), 311-317.

BURBUR PINELLA



APPLICATIONS

- Detoxification Support
- Neurological Support
- Microbial Support
- Antioxidant Support
- Gastrointestinal Support



INTRODUCTION

Burbur Pinella is a hydro-ethanol extract from the leaves of Burbur™ (Desmodium molliculum) and the stems of PinellaTM (Pimpinella spp.). D. *molliculum* is in the Fabaceae family, and is native to South America. *D. molliculum* contains polyphenols, flavonoids, and reducing sugar, in addition to alkaloids, flavonol glycosides, saponins, and tannins. The flavonoids include quercetin 3-glucuronide, rutin, and luteolin, among others. Pimpinella spp. belong to the Apiaceae/Umbelliferae family, the most well-known of which is Pimpinella anisum, or aniseed. P. anisum contains volatile oils such as trans-anethole and eugenol; fatty acids such as palmitic and oleic acids; 18% mass of protein; and 4% mass of carbohydrate.² Anethole may have phytoestrogenic effects.*3,4 According to research, the whole plant may consist of up to 57.4% trans-anethole.²

Burbur Pinella is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

DETOXIFICATION SUPPORT

Both D. molliculum and P. anisum may help to promote the body's natural detoxification systems, and may help to support and maintain liver health.*5, Additionally, P. anisum may help to support kidney health, and may help to maintain levels of urea, uric acid, and creatinine that are already within the

NEUROLOGICAL SUPPORT

The constituent eugenol, found in *P. anisum*, may help to support neurological health, and may help to maintain brain electrical discharges already within the normal range.*8 *P. anisum* may also help to maintain neurological health by supporting healthy neuroplasticity.*9

OTHER USES

Microbial Support

D. molliculum ethanol extract may help with microbial and mycelial support.*10,11 P. anisum may help with diverse microbial support, some of which may be attributed to its lignin-carbohydrate complexes.*12,13 These complexes may also help to support a normal macrophage response and maintain healthy, balanced immunity.*13

Antioxidant Support

The aerial parts of *D. molliculum* may contribute antioxidant support to help with everyday oxidative stress.*¹⁴ *Pimpinella spp.* may also help with antioxidant support, as assessed by thiocyanate and DPPH scavenging methods.*^{12,15,16} Of the four oleoresins tested, the methanol and ethanol oleoresins were found to contribute the most antioxidant support.*¹⁶

Gastrointestinal Support

P. anisum may help with gastrointestinal support through maintaining healthy gastric mucosa.*17 It may also help to support a healthy microbiome, help to support normal gastrointestinal motility, and help to maintain healthy gastrointestinal function.*20

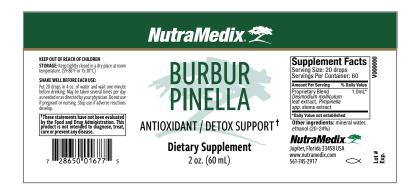
SAFETY AND CAUTIONS

D. molliculum is used in the traditional herbal medicine of South America. D. D. Molliculum is used in the traditional nerbal medicine of South America. D. Molliculum was determined to be non-toxic in a mouse study following the OECD (Organization for Economic Cooperation and Development) 423 test guidelines. In another mouse study, there were no signs of toxicity in mice in doses up to 2000 mg/kg. 22 The average human dose is 40 drops or 2.0 ml dissolved in water, which is approximately 0.000277 mg/kg of body weight. 21 There have been only two case reports of side effects, one involving a severe skin rash in a 72-year-old female, and the other involving mild dizziness and confusion in a 62-year-old female. 23

There have been reports of allergic reactions to *P. anisum*, which may include dermatologic, respiratory, or gastrointestinal symptoms. A *P. anisum* may inhibit implantation and therefore should not be used when attempting to conceive. The constituent anethole may have estrogenic effects. The alcohol extract should be avoided in pregnancy. A *P. anisum* may increase the effects of hypoglycemic drugs or decrease the effects of fluoxetine and impramine. Theoretically, its estrogenic effects may interfere with contraceptives, hormone replacement, or

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Seriki, S. A., Odetola, A. O., & Adebayo O. F. (2019). American Journal of Biomedical Science & Research, 2(4).
- ² Shojaii, A., & Abdollahi Fard, M. (2012). ISRN Pharmaceutics, 2012, 510795.
- ³ Anise. (2021). In *Drugs and lactation Database (LactMed)*. National Library of Medicine (US).
- ⁴ Gardner, Z., & McGuffin, M. (2013). American Herbal Products Association botanical safety handbook (2nd ed., pp. 657-659). CRC Press.
- Gordillo, G., Bonilla, P., et al. (2019). Revista Peruana de Medicina Integrativa, 4(3), 76-82.

 Asadollahpoor, A., Abdollahi, M., & Rahimi, R. (2017). Journal of Research in Medical Sciences: The official journal of Isfahan University of Medical Sciences, 22, 37.
- 7 Amina, B., Nadia, A. H., et al. (2016). *International Journal of Green Pharmacy*, 10(2), 91.
- ⁸ Pourgholami, M. H., Majzoob, S., et al. (1999). *Journal of Ethnopharmacology*, 66, 211-215.
- ⁹ Karimzadeh, F., Hosseini, M., et al. (2012). BMC Complementary and Alternative Medicine, 12(76).
- ¹⁰ Rojas, R., Bustamante, B., et al. (2003). *Journal of Ethnopharmacology*, 88, 199-204.
- ¹¹ Bussman, R. W., Sharon, D., et al. (2008). *Arnaldoa*, 15(1), 127-148.
- ¹² Gülçin, I., Oktay, M., et al. (2003). *Food Chemistry*, *83*, 371-382.
- ¹³ Lee, J. B., Yamagishi, C., et al. (2011). Bioscience, Biotechnology, and Biochemistry, 75(3), 459–465.
- ¹⁴ Lock, O., Castillo, P., et al. (2005). *Acta Horticulturae 675*(675), 103-106. ¹⁵ Delazar, A., Biglari, F., et al. (2006). *Phytochemistry*, *67*(19), 2176–2181.
- ¹⁶ Singh, G., Kapoor, I. P. S., et al. (2008). International Journal of Essential Oil Therapeutics, 2, 122-130.
- ¹⁷ Al Mofleh, I. A., Alhaider, A. A., et al. (2007). World Journal of Gastroenterology, 13(7), 1112–1118.

 ¹⁸ Robles-Zepeda, R. E., Velázquez-Contreras, C. A., et al. (2011). Journal of Medicinal Food, 14(10), 1280–1283.
- Wang, D., Li, Y., Zhong, H., et al. (2019). FEBS Open Bio, 9(9), 1552–1560.
 Mosaffa-Jahromi, M., Lankarani, K. B., et al. (2016). Journal of Ethnopharmacology, 194, 937–946.
- ²¹ Herrara, W., & Simón, G. G. (2005). NutraMedix Laboratories, LLC, Florida, USA.
- ²² Gordillo, G., Bonilla, P., et al. (2019). *Ciencia E Investigación*, 22(1), 31-34.

 ²³ Mendocilla-Risco, M., Bellido-Marin, B., & Serrano-Mestanza, K. (2017). *Revista Peruana de Medicina Integrativa*, 2(2): 108-110.
- ²⁴ Brinker, F. (2001). Herb contraindications & drug interactions (3rd ed., p. 31). Eclectic Medical Publications.
- ²⁵ Zabłocka-Słowińska, K., Jawna, K., et al. (2014). Advances in Člinical and Experimental Medicine: Official organ Wroclaw Medical University, 23(4), 657–663.
- ²⁶ American Botanical Council. Herbalgram.org. (2021). Retrieved 10 June 2021, from https://www.herbalgram.org/resources/commission-e-monographs/approved-herbs/anise-seed/.



Microbial Support



INTRODUCTION

Cumanda is an extract from the bark of Campsiandra angustifolia also known as Campsiandra angustifolia Benth., Campsiandra angustifolia var. angustifolia, and huacapurana.^{1,2} It belongs to the Fabaceae/Leguminosae family and the Caesalpinaceae subfamily, which contains many species of Campsiandra.^{3,4,5,6} Huacapurana is a more general name that can apply to C. comosa and C. laurifolia in addition to C. angustifolia, though C. angustifolia is considered the authentic Peruvian huacapurana.²

C. angustifolia is a medium-sized tree native to Peru and Northern Brazil that is used by local people for food as well as health.2 Constituents found within the bark include proanthocyanidins, flavonoids, gallotannins, and caffeoylquinic acid. Secondary metabolites include steroids, flavonoids, saponins and tannins. In traditional historical use, it has been used for microbial support, healthy inflammatory response support, and gastrointestinal support.*9,10,

Cumanda is made at our U.S. manufacturing facility. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

MICROBIAL SUPPORT

C. angustifolia (bark) may help with single-celled microbial support, and thus, may help to maintain health of erythrocytes and macrophages.*6,12,13 lt may also help with microbial support of varied gram status.*13,14 Additionally, *C. angustifolia* may help with mycelial support.*14

SAFETY AND CAUTIONS

C. angustifolia (bark) has been used traditionally by native South American peoples for some time. Despite this, information on interactions and adverse events is sparse. Currently, there are no known cautions or interactions, though this may change with additional research and new knowledge. Theoretically, C. angustifolia should not be taken concurrently with PDE-5 inhibitors, as it may have additive effects.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- 1 Campsiandra angustifolia Benth. The Plant List. Theplantlist.org. (2021). Retrieved 10 December 2021, from http://www.theplantlist.org/tph.1/record/ild-20132.
- 2 Tropical Plants Database, Ken Fern. tropical.theferns.info. (2021). Retrieved 10 December 2021, from http://tropical.theferns.info/viewtropical.php?id=Campsiandra+angustifolia
- 3 Campsiandra angustifolia Benth.-Encyclopedia of Life. Eol.org. (2021). Retrieved 10 December 2021, from https://eol.org/pages/640211.
- 4 Campsiandra angustifolia. Worldfloraonline.org. (2021). Retrieved 10 December 2021, from http://www.worldfloraonline.org/search?query=campsiandra+angustifolia.
- 5 Farji-Brener, A. G., Durán, S., et al. (2005). Revistà de Biologia Tropical, 53(1-2), 63-71
- Ruiz, L., Ruiz, L., et al. (2011). Journal of Ethnopharmacology, 133(2), 917–921.

 Schmeda-Hirschmann, G., Burgos-Edwards, A., et al. (2019). Journal of Ethnopharmacology, 229, 167–179.

 Schmeda-Hirschmann, G., Burgos-Edwards, A., et al. (2019). Journal of Ethnopharmacology, 229, 167–179.
- Flores, P.C. & Andoa, D. H. (2014). UNAP Repositorio Institucional Digital. https://repositorio.unapiquitos.edu.pe/handle/20.500.12737/4399
- Ganapathy, A. A., Hari Priya, V. M., & Kumaran, A. (2021). Journal of Ethnopharmacology, 267, 113536.
- de Pascoa Júnior, J. G., & de Souza, C. L. L. (2021). Research, Society and Development, 10(14), e163101419965.
- 11 Huaranca Acostupa, R. J., Armas Bardales, J. J., & Vigo Teco, R. M. (2013). Conoc Amaz, 4(2), 77-86 ¹² Kvist, L. P., Christensen, S. B., et al. (2006). *Journal of Ethnopharmacology*, 106(3), 390–402.

 ¹³ Vasquez-Ocmin, P., Cojean, S., et al. (2018). *Journal of Ethnopharmacology*, 210, 372.

 ¹⁴ Roumy, V., Ruiz Macedo, J. C., et al. (2020). *Journal of Ethnopharmacology*, 249, 112411.

- Liver Support
- Metabolic Support
- Antioxidant Support
- Inflammatory Response Support
- Microbial Support
- Mood Support



INTRODUCTION

Dandelion is a hydro-ethanol extract from the leaves of *Taraxacum officinale*. It belongs to the Asteraceae/Compositae family and is native to Europe, though it is widespread throughout the northern hemisphere. The common name of dandelion comes from the French dent de lion, or lion's tooth, due to the serrated edges of the leaves.¹

T. officinale (leaf) contains polysaccharides such as PD1-1;² phenolic compounds such as monocaffeoyltartaric and dicaffeoyltartaric acids, the latter of which is more widely known as chicoric acid; sterols such as beta-sitosterol and stigmasterol; flavonoid glycosides such as quercetin; triterpenoids such as alpha-amyrin; coumarins such as cichoriin and aesculin; and sesquiterpene lactones. The main sesquiterpene lactone in the leaf is taraxinic acid beta-D-glucopyranosyl ester. To officinale contains many amino acids, though primarily L-Asparagine and L-Proline; the only essential amino acid not present in dandelion leaf is L-Methionine.

Dandelion is made at our U.S. manufacturing facility. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

LIVER SUPPORT

Mouse studies have shown that *T. officinale* (leaf) may help with liver support, helping maintain aspartate transaminase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (AKP) already within the normal range. It may also help to maintain hepatic triglyceride levels already within the normal range. Rat studies have shown that *T. officinale* may help to support and maintain liver health. One rat study found that liver support from the ethanol leaf extract was dose-dependent. Much of the liver support may be due to antioxidant support and healthy inflammatory response support, helping to maintain superoxide dismutase (SOD) and glutathione (GSH) already within the normal range, which will be covered in more detail, below.

METABOLIC SUPPORT

T. officinale may help with metabolic and cardiovascular support.*¹³ In a study with rats, dandelion leaf helped to support normal vasodilation.*¹⁴ *T. officinale* may also help to maintain nitric oxide (NO) and endothelial nitric oxide synthase (eNOS) already within the normal range.*¹⁵ The leaf may help with healthy lipid support, maintaining cholesterol and triglyceride levels already within the normal range.*^{14,16,17} In addition, in vitro studies have showed that several constituents from *T. officinale*, particularly chicoric acid, may help to maintain alpha-amylase and alpha-glucosidase levels already within he normal range.*^{3,18} The sesquiterpene lactone taraxacolide-beta-D-glucoside may help to maintain blood sugar levels already within the normal range.*³

ANTIOXIDANT SUPPORT

T. officinale may contribute antioxidant support, as measured in vitro by thiobarbituric acid reactive substances (TBARS) in human plasma, which is attributed to the phenolic compounds.*19 Antioxidant support was also confirmed by cobalt protoporphyrin (CoPP) for the water extract, and by tin protoporphyrin (SnPP) for the ethanol extract,²⁰ as well as by ABTS, DPPH, and FRAP assays.*15 lts antioxidant support may contribute to the maintenance of Nrf2 function already within the normal range,²⁰⁻²² which may assist with neurological support.*21 ln a rat study, rats were given leaf or petal fractions of *T. officinale*. The rats were given the extract for four weeks, which contributed antioxidant support, as quantified by TBARS assay in the spleen and brain.*14 Compared with the root, the leaf extract has significantly higher polyphenol and flavonoid content.*4

INFLAMMATORY RESPONSE SUPPORT

Antioxidant support and healthy inflammatory response support often go together, as shown in the subsequent in vitro studies. *T. officinale* polysaccharides TOP 1 and TOP 2 may help with both antioxidant and anti-inflammatory support by maintaining iNOS and TNF-alpha already within the normal range.*23,24 T. officinale may help maintain IL-1beta and IL-6 already within the normal range.*9,10 *T. officinale* may also help to influence cytokine expression, maintaining NF-kappaB and Nrf2 already within the normal range.*25,26 The sesquiterpene lactone taraxinic acid beta-D-glucopyranosyl ester, found in the leaf extract, may help to maintain Nrf2 function already within the normal range.*4

MICROBIAL SUPPORT

In vitro studies have shown that oligosaccharides from dandelion may help with antimicrobial support,²⁷ including support for organisms of varied gram status and with a variety of morphological forms.*28,29 Dandelion may also help with support for diverse organism types.*29,30

MOOD SUPPORT

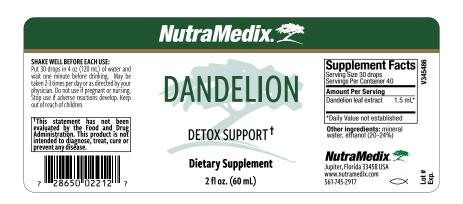
In mouse studies, the water extract of *T. officinale* leaves and roots helped support a dose-dependent healthy mood, attributed to neuroendocrine support and maintenance of BDNF and MKP-1 already within the normal range.*31,32

SAFETY AND CAUTIONS

Dandelion is generally well tolerated, with the most common side effect being gastrointestinal symptoms such as heartburn, stomach discomfort, or diarrhea.1 It may have additive effects with anticoagulant, antiplatelet, and hypoglycemic drugs, may increase levels and reduce excretion of lithium, may increase the risk of hyperkalemia when taken with potassium-sparing diuretics, and may lower blood levels of quinolone antibiotics.1 Dandelion may increase levels of drugs metabolized by CYP1A2 and CYP3A4.^{1,33}

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- 1 Natural Medicines. (2022, May 1). Dandelion [monograph]. http://naturalmedicines.therapeuticresearch.com
- 2 Wang, L., Li, T., et al. (2019). International Journal of Biological Macromolecules, 126, 846-856.
- 3 Wirngo, F. E., Lambert, M. N., & Jeppesen, P. B. (2016). The Review of Diabetic Studies: RDS, 13(2-3), 113–131.
- 4 Esatbeyoglu, T., Obermair, B., et al. (2017). Journal of Medicinal Food, 20(1), 71-78.
- 5 Schütz, K., Kammerer, D. R., et al. (2005). Rapid Communications in Mass Spectrometry: RCM, 19(2), 179–186.
- 6 Williams, C. A., Goldstone, F., & Greenham, J. (1996). Phytochemistry, 42(1), 121–127.
- 7 Qureshi, M. N., Stecher, G., & Bonn, G. K. (2014). Pakistan Journal of Pharmaceutical Sciences, 27(3), 459-462.
- 8 Colle, D., Arantes, L. P., et al. (2012). Journal of Medicinal Food, 15(6), 549-556.
- 9 Ren, Y. S., Zheng, Y., et al. (2020). Chinese Journal of Natural Medicines, 18(2), 103-113. X
- 10 Davaatseren, M., Hur, H. J., et al. (2013a). Journal of Medicinal Food, 16(1), 26-33.
- 11 Hfaiedh, M., Brahmi, D., & Zourgui, L. (2016). Environmental Toxicology, 31(3), 339-349.
- 12 Gulfraz, M., Ahamd, D., et al. (2014). Pakistan Journal of Pharmaceutical Sciences, 27(4), 825-829.
- 13 Olas, B. (2022). Nutrients, 14(7), 1350.
- 14 Majewski, M., Lis, B., et al. (2020). Antioxidants (Basel, Switzerland), 9(2), 131.
- 15 Aremu, O. O., Oyedeji, A. O., et al. (2019). Antioxidants (Basel, Switzerland), 8(8), 309.
- 16 García-Carrasco, B., Fernandez-Dacosta, R., et al. (2015). Medical Sciences (Basel, Switzerland), 3(2), 38-54.
- 17 Davaatseren, M., Hur, H. J., et al. (2013b). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 58, 30–36.
- 18 Choi, J., Yoon, K. D., & Kim, J. (2018). Bioorganic & Medicinal Chemistry Letters, 28(3), 476-481.

- 19 Jędrejek, D., Kontek, B., et al. (2017). Chemico-Biological Interactions, 262, 29-37.
- 20 Yoon, H. S., & Park, C. M. (2019). Biomolecules, 9(7), 288.
- 21 Huang, S., Meng, N., et al. (2018). Nutrients, 10(7), 926.
- 22 Sun, Y., Wu, Y., et al. (2020). Toxins, 12(8), 496.
- 23 Park, C. M., Cho, C. W., & Song, Y. S. (2014). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 66, 56–64.
- 24 Hu, G., Wang, J., et al. (2017). BMC Complementary and Alternative Medicine, 17(1), 38.
- 25 Jeon, D., Kim, S. J., & Kim, H. S. (2017). BMC Complementary and Alternative Medicine, 17(1), 508.
- 26 Dong, L., Dongzhi, Z., et al. (2020). The American Journal of Chinese Medicine, 48(2), 445–462.
- 27 Qian, L., Zhou, Y., et al. (2014). International Journal of Biological Macromolecules, 64, 392–394.
- 28 Xu, P., Xu, X. B., et al. (2021). Polish Journal of Veterinary Sciences, 24(2), 243-251.
- 29 Sharifi-Rad, M., Roberts, T. H., et al. (2018). Phytotherapy Research: PTR, 32(11), 2131–2145.
- 30 Flores-Ocelotl, M. R., Rosas-Murrieta, N. H., et al. (2018). BMC Complementary and Alternative Medicine, 18(1), 95.
- 31 Li, Y. C., Shen, J. D., et al. (2014). Pharmaceutical Biology, 52(8), 1028-1032.
- 32 Gao, C., Kong, S., et al. (2019). Medical Science Monitor: International medical journal of experimental and clinical research,
- 33 Dufay, S., Worsley, A., et al. (2014). The Journal of Pharmacy and Pharmacology, 66(10), 1478-1490.



- Antioxidant Support
- Inflammatory Support
- Microbial Support
- Gastrointestinal Support



INTRODUCTION

Enula is a hydro-ethanol extract from the roots of *Inula helenium* and *Ipomoea purga. I. helenium* belongs to the Asteraceae/Compositae family and is commonly known as Elecampane.¹ *I. helenium* root includes volatile oils such as alantolactone, isoalantolactone, alantol, alpha- and beta-bergamotene, beta-pinene, and anethole; amino acids such as aspartic acid, serine, threonine, and glutamic acid; sterols such as stigmasterol and beta-sitosterol; and thymol derivatives.^{2,3,4} Alantolactone and isoalantolactone are considered the main constituents.^{3,5} The main phenolic compounds that may help with antioxidant support are the phenolic acids (caffeic, dicaffeoyl quinic, chlorogenic, and hydroxybenzoic), terpenes (alantolactone and isoalantolactone), and flavonoids (epicatechin, catechin gallate, dihydroquercetin pentosyl rutinoside, quercetin-3-0-beta-glucopyranoside, ferulic acid-4-0-glucoside, and kaempherol-7-0-dipentoside).⁶ The roots also include dietary fiber from fructooligosaccharides and inulin.⁷ *I. helenium* root has been used in traditional Chinese health practices for gastrointestinal support, where it is known as *tu mu xiang*.*³

Ipomoea purga is commonly known as jalap root and belongs to the Convolvulaceae family. Synonyms for *I. purga* include *Ipomoea jalapa, Ipomoea schiedeana, Convolvulus officinalis, Convolvulus purga* and *Exogonium purga*.^{8,9,10} *I. purga* is a climbing vine that is native to southern Mexico.¹⁰ The root has been used in traditional health practices to support gastrointestinal regularity,¹¹ with other potential benefits under current investigation.*¹² Constituents of *I. purga* root include convolvulin, jalapine, caffeic acid, scopoletin, valeric acid, starch, and tiglic acid.^{12,13}

Enula is made at our U.S. manufacturing facility and because our extracts are

made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

ANTIOXIDANT SUPPORT

l. helenium root extract may help with antioxidant support, as determined by DPPH, phosphomolybdenum, beta-carotene bleaching, ABTS, FRAP, and CUPRAC assays.*7,14 Flavonoids are found in all plant parts, and the relevant phenolic compounds, concentrated in the inflorescence, leaves, and root, are highly soluble in ethanol.*15 The constituent alantolactone may help to support levels of quinone reductase, glutathione S-transferase (GST), and glutathione reductase already within the normal range, in a dose-dependent manner.*16 The antioxidant support of *l. helenium* is attributed to effects on PI3K and JNK signaling pathways, with support of Nrf2 already within the normal range.*16

INFLAMMATORY SUPPORT

Isoalantolactone, a sesquiterpene lactone found in *I. helenium*, may help with healthy inflammatory support.*¹⁷ In vitro research has shown that isoalantolactone may help to maintain NF-kappa B already within the normal range.*¹⁷ Alantolactone and isoalantolactone may help to maintain levels of IgE, TNF-alpha, and IFN-gamma already within the normal range.*¹⁸ They may also help to maintain IL-4, IL-5 and IL-13 already within the normal range.*¹⁸ Additionally, the sesquiterpene lactone igalan may help with healthy inflammatory support.*¹⁹

OTHER USES

Microbial Support

l. helenium may help with microbial support, as determined by the agar-well diffusion method.*14,20 It may also help with mycelial support.*20

Gastrointestinal Support

l. purga has a long history of traditional use for supporting gastrointestinal health and regularity, 8,12 supporting healthy peristalsis.* 11

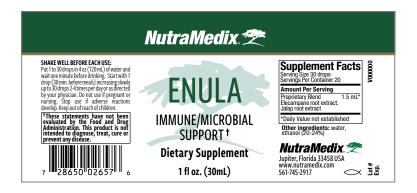
SAFETY AND CAUTIONS

Information on the adverse effects of *Inula helenium* is limited. *I. helenium* may cause allergic reactions in those with allergies to other plants in the Asteraceae/Compositae family, such as ragweed. Cases of contact dermatitis have been reported, which may be attributed to the sesquiterpene lactones alantolactone and isoalantolactone. *I. helenium* may have additive effects with CNS depressants. Large amounts of *I. helenium* may cause vomiting and diarrhea. Rarely, large amounts of *I. helenium* root may cause spasms or symptoms of paralysis.

l. purga may cause purgative effects, which are contra-indicated in pregnancy. ^{25,26} It is also contraindicated in gastrointestinal inflammation or infection. ²⁷ *l. purga* contains cathartic gluco-resins which may intensify peristalsis, increasing water elimination. ^{11,28} Consequently, it is contraindicated in those taking stimulant laxatives as it may have additive effects, leading to dehydration and electrolyte imbalance. ²⁹ In addition, *l. purga* may have additive effects with diuretic-induced potassium loss. ²⁹ Fluid and electrolyte imbalance may theoretically increase INR and risk of bleeding in those taking warfarin. ⁸ Electrolyte imbalance may also worsen the toxicity of cardiac glycosides. ³⁰

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Lunz, K., & Stappen, I. (2021). *Molecules (Basel, Switzerland)*, 26(11), 3155.
 ² Brinker, F. (2001). Herb contraindications & drug interactions (p. 85). Eclectic Medical Publications.
- ³ Eastland Herb. (2018). Eastland Herb Chinese herbal medicine: Materia medica and formula & strategies (4.3). [mobile app]. App store. https://apps.apple.com/us/app/eastland-herb-chinese-medicine/id737380894.
- 4 Stojakowska, A., Malarz, J., & Kisiel, W. (2004). Zeitschrift fur Naturforschung. C, Journal of Biosciences, 59 (7-8), 606–608.
- 5 Konishi, T., Shimada, Y., et al. (2002). Biological & Pharmaceutical Bulletin, 25(10), 1370–1372.
- ⁶ Spiridon, I., Nechita, C. B., et al. (2013). *Central European Journal of Chemistry*, 11(10), 1700-1710.
- Petkova, N., Vrancheva, R., et al. (2015). Journal of Bioscience Technology, 4(1), 101-107.
- 8 Natural Medicines. (2021, July 10). Jalap [monograph]. http://naturalmedicines.therapeuticresearch.com
- 9 Ipomoea purga (Wender.) Hayne. Worldfloraonline.org. (2021). Retrieved 10 July 2021, from http://www.worldfloraonline.org/taxon/wfo-0001296675#description.
- 10 Ipomoea purga (Wender.) Hayne | Plants of the World Online | Kew Science. Plants of the World Online. (2021). Retrieved 10 July 2021, from http://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:269627-1.
- 11 Pereda-Miranda, R., Fragoso-Serrano, M., et al. (2006). Journal of Natural Products, 69(10), 1460–1466.
- 12 Ipomoea purga (Convolvulaceae). Dr. Duke's Phytochemical and Ethnobotanical Databases U.S. Department of Agriculture. (2021). Retrieved 10 July 2021, from https://phytochem.nal.usda.gov/phytochem/plants/show/1081.
- 13 Meira, M., Pereira da Silva, E., et al. (2012). Brazilian Journal of Pharmacognosy, 22(3): 682-713.
- ¹⁴ Albayrak, S., Korkmaz Cinar, A. E., et al. (2015). Iranian Journal of Science & Technology, 39A4, 473-483.
- ¹⁵ Zlatić, N., Jakovljević, D., & Stanković, M. (2019). Plants (Basel, Switzerland), 8(6), 179.
- ¹⁶ Seo, J. Y., Lim, S. S., et al. (2008). *Phytotherapy Research: PTR*, 22(11), 1500–1505.
- ¹⁷ Ding, Y. H., Song, Y. D., et al. (2019). *Acta Pharmacologica Sinica*, 40(1), 64–74.
- 18 Wang, Q., Gao, S., et al. (2018). Phytomedicine: International journal of phytotherapy and phytopharmacology, 46, 78-84.
- ¹⁹ Dao, T., Song, K., et al. (2020). Inflammation Research: Official journal of the European Histamine Research Society, 69(3), 309–319.
- ²⁰ Deriu, A., Zanetti, S., et al. (2008). *International Journal of Antimicrobial Agents*, *31*(6), 588–590.
- ²¹ Natural Medicines. (2021, July 10). Elecampane [monograph]. http://naturalmedicines.therapeuticresearch.com
- ²² Lamminpää, A., Estlander, T., et al. (1996). *Contact Dermatitis*, *34*(5), 330–335.
- ²³ Aberer W. (2008). Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology: JDDG, 6(1), 15–24.
- ²⁴ Gardner, Z., & McGuffin, M. (2013). American Herbal Products Association's botanical safety handbook (pp. 474-475). CRC Press / Taylor & Francis.
- ²⁵ Brinker, F. (2001). Herb contraindications & drug interactions (p. 274). Eclectic Medical Publications.
- ²⁶ Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 1145). Art of Medicine Press.
- ²⁷ Brinker, F. (2001). Herb contraindications & drug interactions (p. 218-220). Eclectic Medical Publications.
- ²⁸ Ono M. (2017). *Journal of Natural Medicines*, 71(4), 591–604.
- ²⁹ Brinker, F. (2001). Herb contraindications & drug interactions (p. 234-235). Eclectic Medical Publications.
- ³⁰ Gardner, Z., & McGuffin, M. (2013). American Herbal Products Association's botanical safety handbook (pp. 477-478). CRC Press /Taylor & Francis.

GLUCOMEDIX ®



APPLICATIONS

- Blood Sugar Support
- Metabolic Support
- Cardiovascular Support
- Immune System Support
- Microbial Support



INTRODUCTION

GlucoMedix is a proprietary blend of hydro-ethanol extracts from Stevia leaf (Stevia rebaudiana) and Cat's Claw bark (Uncaria tomentosa) which is also known as Samento. S. rebaudiana is part of the Asteraceae/Compositae family, native to parts of South America, and used as a dietary supplement as well as a sweetener. The constituents responsible for the sweet taste are steviol glycosides, including stevioside, rebaudiosides A-E, steviolbioside, and dulcoside A. S. rebaudiana also contains phytosterols such as stigmasterol, beta-sitosterol, and campesterol, as well as flavonoids, diterpenes, and triterpenes, among others.

Samento is extracted from the rare pentacyclic chemotype of *U. tomentosa*, which is TOA-free, with levels in trace amounts or undetectable. This pentacyclic oxindole alkaloid (POA)-predominant, tetracyclic oxindole alkaloid (TOA)-free form of *U. tomentosa* may help with blood sugar support,² metabolic support,³ cardiovascular support,^{4,5} and immune system support.*⁶

GlucoMedix is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

BLOOD SUGAR SUPPORT

Both *S. rebaudiana* and *U. tomentosa* may help to maintain blood sugar levels already within the normal range.*2,7,8,9,10 Healthy blood glucose regulation depends upon pancreatic health, insulin secretion in response to elevated blood glucose, glucagon secretion in response to decreased blood glucose, insulin sensitivity, and a balance between glycogen synthesis and glycogenolysis. Steviol glycosides such as stevioside and rebaudioside A may help to support pancreatic health as well as maintain post-prandial insulin levels already within the normal range.*1 According to animal studies, stevioside may also help to support glycogen synthesis, 12,13 slow gluconeogenesis, 4 support healthy glucagon levels already within the normal range, support healthy insulin levels already within the normal range, and support healthy insulin sensitivity. 14,15,16 Uncaria spp. may help to inhibit the enzyme alpha-glucosidase, delaying the absorption of saccharides.*1

METABOLIC SUPPORT

U. tomentosa may help to support healthy insulin sensitivity.*3,18

OTHER USES

Cardiovascular Support
S. rebaudiana may help to maintain cholesterol levels already within the normal range.*7,19 It may also help to maintain healthy blood pressure levels already within the normal range.*20,21 U. tomentosa and S. rebaudiana have synergistic effects for cardiovascular support, as U. tomentosa may also help to maintain cholesterol levels already within the normal range through the support of liver health *3,7 health.*3,7

Immune System Support *U. tomentosa* may help to maintain a healthy immune response and support immune system homeostasis.* It may help to maintain neutrophil function as well as Th1 and Th2 cytokine levels already within the normal range.*22,23,24 *U. tomentosa* may also help to maintain CD4+CD25+Foxp3+ regulatory T cells within the normal range.*5. It should be noted that only TOA-free *U. tomentosa* (such as Samento) helps with immune support.*6

Microbial Support

S. rebaudiana may help with microbial support.*26,27,28

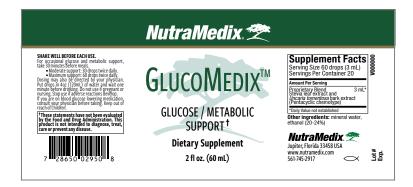
SAFETY AND CAUTIONS

S. rebaudiana is generally well tolerated. Nausea and dizziness have been known to occur, though at a similar rate to placebo, and usually resolve after the first week of use. *S. rebaudiana* may theoretically increase lithium levels due to increased diversis and decreased lithium excretion. *S. rebaudiana* may theoretically have additive effects when taken concurrently with antidiabetic or antihypertensive medications. antihypertensive medications.²⁹

U. tomentosa is generally well tolerated. Gastrointestinal effects such as nausea, constipation, and diarrhea have been reported. *U. tomentosa* may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4. *J. tomentosa* should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy. *U. tomentosa* may have additive effects with anticoagulants, generally attributed to the TOA rhynchophylline, as well as additive effects with antihypertensive drugs, generally attributed to the TOAs rhynchophylline and isorhynchophylline. As a reminder, Samento is TOA-free, with levels in trace amounts or undetectable.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

³⁴ Zhou, J., & Zhou, S. (2010). *Journal of Ethnopharmacology*, 132(1), 15–27. ³⁵ Zhou, J. Y., & Zhou, S. W. (2012). *Fitoterapia*, 83(4), 617–626.

¹ Goyal, S. K., Samsher, & Goyal, R. K. (2010). International Journal of Food Sciences and Nutrition, 61(1), 1-10. ² Domingues, A., Sartori, A., et al. (2011). Phytotherapy Research: PTR, 25(8), 1229–1235. ³ Araujo, L., Feitosa, K. B., et al. (2018). *Scientific Reports*, 8(1), 11013. 4 Potawale, S. E., Mehta, U. K., et al. (2008). *Pharmacology Online*, 2, 197-214. 5 Horie, S., Yano, S., et al. (1992). *Life Sciences*, 50(7), 491-498. ⁶ Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). Applied Sciences, 10(8), 2668. 7 Ritu, M., & Nandini, J. (2016). *Journal of the Science of Food and Agriculture*, *96*(12), 4231–4234.
8 Gregersen, S., Jeppesen, P. B., et al. (2004). *Metabolism: Clinical and experimental*, *53*(1), 73–76.
9 Misra, H., Soni, M., et al. (2011). *Journal of Pharmacy & Bioallied Sciences*, *3*(2), 242–248. ¹⁰ Ahmad, U., & Ahmad, R. S. (2018). BMC Complementary and Alternative Medicine, 18(1), 179. ¹¹ Philippaert, K., Pironet, A., et al. (2017). *Nature Communications*, 8, 14733. ¹² Yang, P. S., Lee, J. J., et al. (2009). Neuroscience Letters, 454(1), 72–75.

¹³ Hübler, M. O., Bracht, A., & Kelmer-Bracht, A. M. (1994). Research Communications in Chemical Pathology and Pharmacology, 84(1), 111–118.

¹⁴ Chen, T. H., Chen, S. C., et al. (2005). Planta Medica, 71(2), 108–113.

¹⁵ Jeppesen, P. B., Gregersen, S., et al. (2002). Phytomedicine: International journal of phytotherapy and phytopharmacology, 9(1), 9–14. ¹⁶ Jeppesen, P. B., Gregersen, S., et al. (2003). *Metabolism: Clinical and experimental*, 52(3), 372–378. ¹⁷ Wang, Z. W., Wang, J. S., et al. (2013). *Fitoterapia*, 90, 30–37. ¹⁸ Arauj, L. C. C., Furig, I. C., et al. (2017). *Journal of Diabetes & Metabolism*, 8:10(Suppl). 19 Ilias, N., Hamzah, H., et al. (2021). Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie, 143, 112207. ²⁰ Ray, J., Kumar, S., et al. (2020). International Journal of Clinical Research & Trials, 5, 142.

²¹ Chan, P., Tomlinson, B., et al. (2000). British Journal of Clinical Pharmacology, 50(3), 215–220. 22 Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). Phytomedicine: International journal of phytotherapy and phytopharmacology, 23(2), 141–148. ²³ Núñez, C., Lozada-Requena, I., et al. (2015). Revista Peruana de Medicina Experimental y Salud Publica, 32(4), 643–651. ²⁴ Winkler, C., Wirleitner, B., et al. (2004). Planta Medica, 70(3), 205–210. Mahmoudian-Sani, M. R., Asadi-Samani, M., et al. (2017). Journal of Renal Injury Prevention, 6(3), 158-163.
 Brambilla, E., Cagetti, M. G., et al. (2014). Caries Research, 48(1), 19–23.
 Preethi, D., Sridhar, T. M., et al. (2011). Journal of Ecobiotechnology, 3(7), 05-10. ²⁸ Fazal, H., Ahmad, N., et al. (2011). *Pakistan Journal of Botany*, 43(2), 1307-1313.

²⁹ Natural Medicines. (2021, March 27). Stevia [monograph]. http://naturalmedicines.therapeuticresearch.com. 30 de Paula, L. C., Fonsèca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22–30. ³¹ Budzinski, J. W., Foster, B. C., et al. (2000). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 7(4), 273–282. ³² Lamm, S., Sheng, Y., & Pero, R. W. (2001). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 8(4), 267–274. 33 Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126–130.

HORMONAL BALANCE



APPLICATIONS

- Women's Wellness Support
- Healthy Aging
- Mood Support
- Immune Support



INTRODUCTION

Hormonal Balance is a comprehensive herbal formula designed to maintain women's wellness and support healthy aging.*

Epimedium leaf (*Epimedium grandiflorum*) belongs to the Berberidaceae family and contains flavonoids, polysaccharides, lignans, phenol glycosides, and sesquiterpenes, among others.^{1,2} Epimedium species have been used to support both women's and men's health for centuries, attributed partly to their affinity with estrogen receptor alpha (ER-alpha).*3,4

In traditional Chinese health practices, related Epimedium species known collectively as yin yang huo are used to support kidney yang, which encompasses healthy aging. Today, this support is attributed to the constituent flavonoids and polysaccharides.*2

Tribulus fruit (*Tribulus terrestris*), also known as puncture vine, belongs to the Zygophyllaceae family.⁵ It contains steroidal saponins such as spirostanol and furostanol; flavonoids such as quercetin and kaempferol; alkaloids such as tribulusamide C and tribulusterine; tannins; terpenoids; and polyphenols; among others.^{6,7}

Tribulus fruit may help maintain healthy fertility by supporting the central nervous system and the anterior pituitary gland, as well as maintaining gonadal hormones, their receptors, and folliculogenesis, already within the normal range.*8 Tribulus fruit has been used for centuries in both traditional Chinese health practices, where it is known as ci ji li, and traditional Ayurvedic health practices, where it is known as Gokshura.*9,6

Jatropha stem (*Jatropha macrantha*) belongs to the Euphorbiaceae family, and is also known as Huanarpo macho.^{10,11} It has been used consistently in traditional Peruvian health practices for both women's and men's wellness.*¹² Jatropha stem

includes flavonoids, phenolic acids, lignans, coumarins, and terpenes, among others.11

Muira Puama bark (*Ptychopetalum olacoides*) belongs to the Olacaceae family and is native to the Amazon region, where it is used in traditional health practices to support healthy aging, maintain brain health, and support healthy stress management.* This support is attributed to its alkaloids, 14 including magnoflorine and menispermine; it also includes the triterpenoid lupeol.* In traditional use, Muira Puama is used as an adaptogen to support mental, physical, and sexual wellness, regardless of age.*

Maca root (*Lepidium meyenii*) belongs to the Brassicaceae family and is native to the Peruvian Andes. ^{12,17} It is sometimes called Peruvian ginseng (though it is not a true ginseng) and may support healthy aging, ^{17,18} attributed to the constituent macamides and glucosinolates.*18 Maca root has been used traditionally to support healthy sexual function, maintain healthy fertility, and support comfortable menopause.*¹²

Eurycoma root (*Eurycoma longifolia*) belongs to the Simaroubaceae family and its primary constituents include ellagic acid, quercetin, and rutin; quassinoids such as eurycomanone; and alkaloids. ^{19,20} It has been used in the traditional health practices of Southeast Asian countries to support sexual wellness and healthy stress management. *21

Eustephia bark (Eustephia coccinea) belongs to the Amaryllidaceae family and is used in the traditional health practices of Peru.*22

WOMEN'S WELLNESS

Healthy Sexual Function

Tribulus fruit (*T. terrestris*), according to a Cochrane systematic review and meta-analysis, may support healthy female sexual function.*²³ In a double-blind, placebo-controlled trial, 60 premenopausal women were randomly assigned to Tribulus fruit or a placebo, daily for four weeks. According to a standardized scale, Tribulus fruit significantly supported healthy sexual function.*²⁴ Another trial with premenopausal women found the same result, attributed to maintaining healthy female testosterone levels already within the normal range.²⁵

In a double-blind, placebo-controlled, clinical trial, menopausal women were randomly assigned to Tribulus fruit or a placebo, for 90 days. Compared to the placebo, Tribulus helped support healthy sexual function, according to standardized scales. A review of in vitro, in vivo, and human studies attributed this support to the steroidal saponin secondary metabolites protodioscin and protogracillin. Protogracillin.

Maca root (*L. meyenii*) contains phytoestrogens that may help maintain normal sexual function during menopause, according to a meta-anaysls of studies evaluating the effects of phytoestrogens on sexual wellness.* Eurycoma root (*E. longifolia*) may also help maintain testosterone levels already within the normal range in women, supporting a healthy libido.* ²⁹

Normal Fertility

Epimedium leaf (*E. grandiflorum*) may help maintain healthy oocytes during normal aging, as seen in an in vitro study with porcine oocytes and attributed to antioxidant support.*30 More studies are needed, to understand the full impact of Epimedium leaf on women's wellness.*31 Tribulus fruit (*T. terrestris*) may help support normal fertility through antioxidant support.*6,32 y, 14 days of Valerian root showed more consistent support than a single dose, and researchers concluded that Valerian helps maintain healthy slow-wave sleep.*12

Jatropha stem (*J. macrantha*) is used traditionally to support normal fertility, which may be due, in part, to antioxidant support.*11,33 Eustephia bark (*E. coccinea*) is used in traditional health practices to support uterine health.*22

Hormonal Support

Epimedium leaf (*E. grandiflorum*) may help maintain estrogen levels already within the normal range, as seen with its constituent icariin in rats.*34 Jatropha stem (*J. macrantha*) may help with hormonal support, attributed to the constituent saponins, 12 though reports on its ability to maintain blood levels of estradiol-17beta already within the normal range are mixed.*35,12 Maca root (*L. meyenii*) may help maintain blood progesterone, but not estradiol, already within the normal range.*12 Eurycoma root (*E. longifolia*) and its constituent eurypeptides may help maintain DHEA levels already within the normal range, which may help maintain sex hormones, including female testosterone, already within the normal range.*21

Perimenopausal/Menopausal Support

Epimedium leaf (*E. grandiflorum*) may help to soothe perimenopausal manifestations, supporting a healthy mood and maintaining neurotransmitter levels already within the normal range, as seen with the constituent icariin in rat models of perimenopause; more studies are needed.*34 Jatropha stem (*J. macrantha*) has been traditionally used for menopausal support.*35,12 Maca root (*L. meyeni*i), according to studies, may help with perimenopausal and menopausal support, though without changes in estradiol, follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), or sex hormone binding globulin (SHBG).*36

HEALTHY AGING

Bone Support

Epimedium leaf (*E. grandiflorum*) may help maintain normal bone density.*37 A meta-analysis of 17 studies regarding herbal bone support concluded that herbs may help maintain normal bone density in the lumbar spine, femoral neck, and femoral trochanter.*38 The most prescribed herb in the meta-analysis was Epimedium brevicornum, a close relative of Epimedium grandiflorum.³⁸ Icariin, a prenylflavonoid common to both species, may help to maintain calcium levels as well as osteoblast and osteoclast activity already within the normal range, supporting healthy osteogenesis.*39,40

Epimedium leaf, according to a double-blind, placebo-controlled trial with 58 postmenopausal women, may help maintain levels of bone-specific alkaline phosphatase (BSAP) already within the normal range. The participants were randomly assigned to an Epimedium prenylflavonoid extract or a placebo, daily for six weeks. There were no adverse effects, and the levels of BSAP were consistent with bone support.*41

Maca root (*L. meyenii*), according to mouse studies, may help maintain bone mineral density, Matrix Gla protein (a blood marker of bone formation), and femur weight, already within the normal range.*18 Human studies are needed. Eurycoma root (*E. longifolia*) may help support healthy bone density as a part of healthy aging, maintaining bone calcium already within the normal range.*21

Cognitive Support

Muira Puama bark (*P. olacoides*) has been shown to help support memory and cognition in mice through maintaining acetylcholinesterase (AChE) levels already within the normal range, though human studies are needed.*13,42 Mouse studies have also shown that Muira Puama bark ethanol extract may help support normal cognition and maintain levels of A-beta already within the normal range.*16,42

Cardiovascular Support

Tribulus fruit (*T. terrestris*) may help maintain healthy blood pressure already within the normal range.*9 Maca root (*L. meyenii*), according to a small study with 29 postmenopausal women, may help maintain diastolic blood pressure already within the normal range.*36

OTHER

Mood Support

Maca root (*L. meyenii*), according to the previous study with 29 postmenopausal women, may also help maintain a healthy mood.*³⁶ In a small, double blind, crossover study with 14 postmenopausal women, participants were randomly assigned to Maca root or a placebo, for six weeks, then switched to the other treatment for an additional six weeks. While no hormonal changes were seen, Maca root helped to maintain a normal mood and support healthy stress management, compared to placebo.*⁴³ The ethanol extract of Muira Puama bark (*P. olacoides*) may also help with mood support.*¹⁶

Immune Support

Eurycoma root (*E. longifolia*), according to a randomized, controlled trial with 126 middle-aged adults, may help with immune system support. The participants were assigned to Eurycoma root or a placebo, for four weeks. Compared to the placebo, Eurycoma root helped to maintain total, naïve, and CD4+ T cell numbers already within the normal range.*44

SAFETY AND CAUTIONS

Epimedium leaf (*E. grandiflorum*) is generally well tolerated, 41,45,46, and animal studies have not shown toxicity.2 Side effects may include dizziness, dry mouth, or thirst.45 Theoretically, Epimedium leaf may increase the risk of bleeding when taken with anticoagulant or antiplatelet medications. 45

Tribulus fruit (*T. terrestris*) is generally well tolerated. ⁴⁷⁻⁴⁹ Tribulus fruit should be avoided in pregnancy as it has affected fetal development in animal studies. ⁴⁷ It may increase the levels and adverse effects of lithium when taken concurrently. ⁴⁷

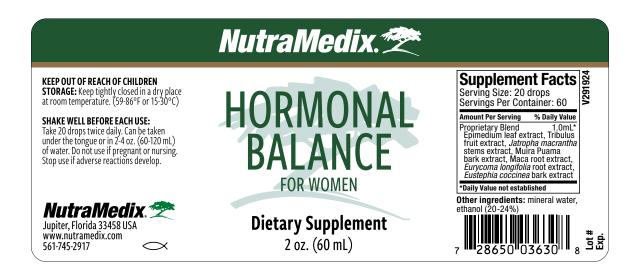
Jatropha stem (*J. macrantha*) has a long history of safe use in traditional health practices and is generally well tolerated.¹² There are no currently known interactions with pharmaceuticals.

Muira puama bark (*P. olacoides*) is generally well tolerated. In one mouse study, it had additive effects with diazepam.⁵⁰ While there are no known adverse effects or drug interactions in humans,¹⁵ it is worth noting that molecular docking studies have shown that eight compounds in Muira puama bark may bind to estrogen receptors, resulting in selective estrogen receptor modulation,⁵¹ and caution may is warranted in those with estrogen-sensitive conditions.

Maca root (*L. meyenii*) is generally well tolerated and has been used for centuries to support sexual function. No adverse events have been reported in clinical trials,18,52 and there are no currently known interactions in humans.⁵²

Eurycoma root (*E. longifolia*) is generally well tolerated and shows little inhibition of CYP isoenzymes, making CYP-related drug interactions unlikely.²¹ Due to potential effects on estrogen levels, it should be avoided in those with estrogen-receptor positive breast cancer.²¹ It may reduce the levels and effectiveness of propranolol.^{21,53}

Eustephia bark (*E. coccinea*) has a long history of safe use in traditional Peruvian medicine, though information is limited.²²



- ¹ Tan, H. L., Chan, K. G., et al. (2016). Frontiers in Pharmacology, 7, 191.
- ² Ma, H., He, X., et al. (2011). *Journal of Ethnopharmacology*, 134(3), 519–541.
- ³ Ho, C. C., & Tan, H. M. (2011). Current Urology Reports, 12(6), 470–478.
- ⁴ Dietz, B. M., Hajirahimkhan, A., et al. (2016). Pharmacological Reviews, 68(4), 1026-1073.
- ⁵ Abarikwu, S. O., Onuah, C. L., et al. (2020). *Andrologia*, *52*(3), e13509.
- ⁶ Ştefănescu, R., Tero-Vescan, A., et al. (2020). *Biomolecules, 10*(5), 752.
- ⁷ Zhu, W., Du, Y., et al. (2017). *Chemistry Central Journal*, 11(1), 60.
- ⁸ Sirotkin, A. V., & Kolesárová, A. (2021). *Physiological Research, 70*(Suppl4), S657–S667.
- ⁹ Chhatre, S., Nesari, T., et al. (2014). *Pharmacognosy Reviews, 8*(15), 45–51.
- ² Chnatre, S., Nesari, T., et al. (2014). *Pharmacognosy Reviews, 8*(15), 45–51.

 ¹⁰ Apaza T, L., Antognoni, F., et al. (2021). *Natural Product Research, 35*(24), 5843–5847.
- ¹¹ Tinco-Jayo, J. A., Aguilar-Felices, E. J., et al. (2021). *Molecules (Basel, Switzerland)*, 27(1), 115
- ¹² Oshima, M., Gu, Y., & Tsukada, S. (2003). *The Journal of Veterinary Medical Science, 65*(10), 1145–1146.
- ¹³ da Silva, A. L., Silva Martins, B. D., et al. (2009). *Psychopharmacology*, 202(1-3), 165–172.
- ¹⁴ Tian, X., Guo, S., et al. (2018). *Natural Product Research*, *32*(3), 354–357.
- ¹⁵ Natural Medicines. (2022, September 22). Muira Puama [monograph]. http://naturalmedicines.therapeuticresearch.com
- ¹⁶ Piato, A. L., Detanico, B. C., et al. (2010). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 17(3-4), 248–253.
- ¹⁷ Shin, B. C., Lee, M. S., et al. (2010). *BMC Complementary and Alternative Medicine*, 10, 44.
- Beharry, S., & Heinrich, M. (2018). Journal of Ethnopharmacology, 211, 126–170.
 Ganapathy, A., Hari Priya, V. M., & Kumaran, A. (2021). Journal of Ethnopharmacology, 267,
- ²⁰ George, A., & Henkel, R. (2014). *Andrologia*, 46(7), 708–721.
- ²¹ Rehman, S. U., Choe, K., & Yoo, H. H. (2016). *Molecules (Basel, Switzerland)*, 21(3), 331.
- ²² Bussmann, R. W., & Glenn, A. (2010). *Journal of Ethnobiology and Ethnomedicine*, 6, 30.
- ²³ Sha'ari, N., Woon, L. S., et al. (2021). *Phytomedicine: International journal of phytotherapy and phytopharmacology, 93,* 153760.
- ²⁴ Akhtari, E., Raisi, F., et al. (2014). *Daru: Journal of Faculty of Pharmacy, Tehran University of Medical Sciences*, 22(1), 40.
- ²⁵ Vale, F., Zanolla Dias de Souza, K., et al. (2018). *Gynecological Endocrinology: The official journal of the International Society of Gynecological Endocrinology, 34*(5), 442–445.
- ²⁶ Postigo, S., Lima, S. M., et al. (2016). Revista Brasileira de Ginecologia e Obstetricia: Revista da Federacao Brasileira das Sociedades de Ginecologia e Obstetricia, 38(3), 140–146.
- ²⁷ Ghanbari, A., Akhshi, N., et al. (2021). *Phytomedicine: International journal of phytotherapy and phytopharmacology, 84*, 153462.
- ²⁸ Najafi, M., & Ghazanfarpour, M. (2018). Climacteric: The journal of the International Menopause Society, 21(5), 437–445.
- ²⁹ Santos, H. O., Howell, S., & Teixeira, F. J. (2019). *Journal of Ethnopharmacology, 235,* 392–405.

- ³⁰ Yoon, J. W., Lee, S. E., et al. (2021). *Animal Bioscience, 34*(4), 546–557
- ³¹ Zhao, H., Shan, Y., et al. (2019). *Drug Design, Development and Therapy*, 13, 2997–3007.
- ³² Dakshayini, P. N., & Mahaboob Basha, P. (2018). *Journal of Innovations in Pharmaceutical* and Biological Sciences (JIPBS), 5(2), 101-107.
- ³³ Sabandar, C. W., Ahmat, N., et al. (2013). *Phytochemistry*, *85*, 7–29.
- ³⁴ Cao, L. H., Qiao, J. Y., et al. (2019). Molecules (Basel, Switzerland), 24(20), 3700.
- ³⁵ Benavides, A., Montoro, P., et al. (2006). *Journal of Pharmaceutical and Biomedical Analysis*, 40(3), 639–647.
- ³⁶ Stojanovska, L., Law, C., et al. (2015). Climacteric: The journal of the International Menopause Society, 18(1), 69–78.
- ³⁷ Indran, I. R., Liang, R. L., et al. (2016). *Pharmacology & Therapeutics*, 162, 188–205.
- 38 Lin, W. L., Lin, P. Y., et al. (2020). The American Journal of Chinese Medicine, 48(8), 1749–1768.
- ³⁹ He, C., Wang, Z., & Shi, J. (2020). Advances in Pharmacology (San Diego, Calif.), 87, 179–203.
- ⁴⁰ Ming, L. G., Chen, K. M., & Xian, C. J. (2013). *Journal of Cellular Physiology*, 228(3), 513–521.
- ⁴¹ Yong, E. L., Cheong, W. F., et al. (2021). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, *91*, 153680.
- ⁴² Figueiró, M., Ilha, J., et al. (2011). *Phytomedicine: International journal of phytotherapy* and phytopharmacology, 18(4), 327–333.
- ⁴³ Brooks, N. A., Wilcox, G., et al. (2008). *Menopause (New York, N.Y.)*, 15(6), 1157–1162.
- ⁴⁴ George, A., Suzuki, N., et al. (2016). *Phytotherapy Research: PTR*, 30(4), 627–635.
- ⁴⁵ Natural Medicines. (2021, August 26). Horny Goat Weed [monograph]. http://naturalmedicines.therapeuticresearch.com
- 46 Teo, Y. L., Cheong, W. F., et al. (2019). Planta Medica, 85(4), 347–355.
- ⁴⁷ Natural Medicines. (2022, July 11). Tribulus [monograph]. http://naturalmedicines.thera-peuticresearch.com
- ¹⁸² Sanagoo, S., Sadeghzadeh Oskouei, B., et al. (2019). *Complementary Therapies in Medicine*, 42. 95–103.
- ⁴⁹ Kamenov, Z., Fileva, S., et al. (2017). *Maturitas, 99*, 20–26.
- ⁵⁰ Brunetti, P., Lo Faro, A. F., et al. (2020). *Pharmaceuticals (Basel, Switzerland)*, 13(10), 309.
- ⁵¹ Powers, C. N., & Setzer, W. N. (2015). *In Silico Pharmacology, 3,* 4.
- ⁵² Natural Medicines. (2022, July 11). Maca [monograph]. http://naturalmedicines.therapeuticresearch.com
- ⁵³ Natural Medicines. (2022, September 29). Eurycoma Longifolia [monograph]. http://naturalmedicines.therapeuticresearch.com

HOUTTUYNIA ®



APPLICATIONS

- Microbial Support
- Immune System Support
- Inflammatory Response Support
- Gastrointestinal Support



INTRODUCTION

Houttuynia is a hydro-ethanol extract from Houttuynia cordata leaf, which is in the Saururaceae family. It is known as *yu xing cao* in traditional Chinese health practices and is found throughout Southeast Asia. Constituents include volatile oils such as alpha-pinene, d-limonene, citronellol, carvacrol, and thymol, flavonoids such as quercetin, quercitrin, isoquercitrin, and rutin; organic acids such as chlorogenic acid, palmitic acid, and linoleic acid;² phytosterols such as stigmasterol and beta-sitosterol; and water-soluble polysaccharides. H. cordata also contains houttuynoside A and houttuynamide A, in addition to amino acids, vitamins, and trace minerals.3,4,5

Houttuynia is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

MICROBIAL SUPPORT

H. cordata may help with both intracellular and extracellular microbial support. H. cordata may help with microbial support for diverse strains with dose-dependent zone diameters of inhibition, and may also help with microbial support for a variety of morphological forms.*7 Additionally, it may provide microbial support for smaller intracellular microbes and help to maintain normal

host immunity.*8,9 In addition to intracellular microbial support, *H. cordata* may help to support relevant respiratory and intestinal mucosa through maintaining cytokines/chemokines, secretory IgA (sIgA), zonula occludens-1 (ZO-1)/tight junction protein, TLR4, and NF-kappaB already within the normal range.*10 *H. cordata* may help to maintain a healthy gut-lung axis.*10 Additionally, it may help to support healthy gingival epithelium as well as balanced oral microbiota, including mycelial support.*7

IMMUNE SYSTEM SUPPORT

H. cordata may help with immune system support through helping to maintain healthy levels of CD4+ and CD8+ T cells that are already within the normal range.*11 It may help to support the innate immune response by maintaining levels of reactive nitrogen intermediates (RNI), such as nitric oxide (NO), and reactive oxygen intermediates (ROI), such as superoxide, that are already within the normal range. It may also help to support the morphological change of macrophages from the round form to the dendritic form, supporting normal phagocytic activity as well as normal NO production.*12 H. cordata may assist with immune system support through the maintenance of a healthy Th1/Th2 ratio, in addition to the maintenance of Th2-dependent cytokines IL-4 and IL-5 already within the normal range.*¹³ Additionally, it may help with IgE-mediated immune support by maintaining IL-4, TNF-alpha, and NF-kappaB already within the normal range.*¹⁴ *H. cordata* may help to maintain MIP-1-alpha, MIP-1-beta, and RANTES already within the normal range in human peripheral blood mononuclear cells (PBMCs).*15 It may also help to support health through its effect on the complement cascade.*16,17

OTHER USES

Inflammatory Response Support

H. cordata may help with antioxidant support and healthy inflammatory response support.* It may help to support healthy function of the NF-kappaB and MAPK pathways and may help to maintain cytokine levels already within the normal range.* It may also help to maintain levels of TNF-alpha, NO, IL-6, IL-8 and PGE2 already within the normal range.* The constituent houttuynamide A (becatamide) may additionally help to maintain levels of COX-1 and COX-2 already within the normal range.* In traditional Chinese health practices, H. cordata is used to clear heat.* 1,2

Gastrointestinal Support

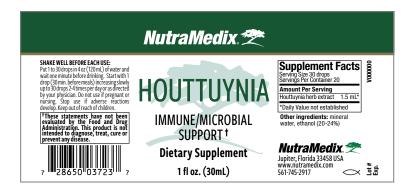
H. cordata may help to maintain intestinal homeostasis through the support of healthy gut microbiota.*23 It may help to support relaxation of intestinal smooth muscle as well as normal transit time, and may help to maintain the

SAFETY AND CAUTIONS

There are no known contraindications to the use of this herb. H. cordata has been used for centuries in Chinese Medicine, with the first known mention in Ming Yi Za Zhu (Miscellaneous Records of Famous Physicians) by Tao Hong-Jing in 500 CE.¹ In laboratory animals, oral administration of 16 mg/kg was found to be non-toxic.¹¹ In vitro and mouse studies have shown no evidence of genotoxicity or other toxicity,¹¹¹.¹8.²² and the herb is considered a safe and edible plant.²²²

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 216-217). Art of Medicine Press.
- ² Bensky, D., Clavey, S., & Stöger, E. (2004). Chinese herbal medicine materia medica (3rd ed., pp. 176-178). Seattle: Eastland Press.
- ³ Yang, L. & Jiang, J-G. (2009). *Pharmaceutical Biology*, 47(12), 1154-1161.
- 4 Kumar, M., Prasad, S. K., & Hemalatha, S. (2014). Pharmacognosy Reviews, 8(15), 22–35.
- ⁵ Chou, S. C., Su, C. R., et al. (2009). Chemical & Pharmaceutical Bulletin, 57(11), 1227-1230.
- ⁶ Li, J., Rehman, M. U., et al. (2017). Southeast Asian Journal of Tropical Medicine and Public Health, 48(6), 1260-1266.
- 7 Sekita, Y., Murakami, K., et al. (2016). BioMed Research International, 2016, 2581876.
- ⁸ Chiow, K. H., Phoon, M. C., et al. (2016). Asian Pacific Journal of Tropical Medicine, 9(1), 1–7.
- ⁹ Remali, J., & Aizat, W. M. (2021). Frontiers in Pharmacology, 11, 589044.
- 10 Zhu, H., Lu, X., et al. (2018). Journal of Ethnopharmacology, 218, 90–99.

 11 Lau, K. M., Lee, K. M., et al. (2008). Journal of Ethnopharmacology, 118(1), 79–85.
- ¹² Kim, G. S., Kim, D. H., et al. (2008). *Biological & Pharmaceutical Bulletin*, 31(11), 2012–2017.
- ¹³ Lee, J. S., Kim, I. S., et al. (2008). Journal of Ethnopharmacology, 117(1), 34–40.
 ¹⁴ Han, E. H., Park, J. H., et al. (2009). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 47(7), 1659–1666.
- ¹⁵ Cheng, B. H., Chan, J. Y., et al. (2014). Carbohydrate Polymers, 103, 244–249.
- ¹⁶ Jiang, Y., Lu, Y., et al. (2014). *Natural Product Research*, 28(6), 407–410.
- ¹⁷ Zhang, T., & Chen, D. (2008). *Journal of Ethnopharmacology*, 117(2), 351–361.
- 18 Shingnaisui, K., Dey, T., et al. (2018). Journal of Ethnopharmacology, 220, 35–43.
- ¹⁹ Lee, H. J., Seo, H. S., et al. (2013). *Molecular Medicine Reports*, 8(3), 731–736.
- ²⁰ Chun, J. M., Nho, K. J., et al. (2014). *BMC Complementary and Alternative Medicine*, 14, 234.
- ²¹ Park J. B. (2015). Phytotherapy Research: PTR, 29(9), 1381–1387.
- ²² Li, W., Zhou, P., et al. (2011). *Journal of Ethnopharmacology*, 133(2), 922–927.

 ²³ Chen, M. Y., Li, H., et al. (2019). *Chinese Journal of Natural Medicines*, 17(3), 187–197.
- ²⁴ Jiang, X. L., & Cui, H. F. (2004). World Journal of Gastroenterology, 10(10), 1513–1520.
- ²⁵ Shi, C. C., Zhu, H. Y., et al. (2020). *International Journal of Biological Macromolecules*, 158, 52–66.
- ²⁶ Kang, C. K., Hah, D. S., et al. (2012). The American Journal of Chinese Medicine, 40(5), 1019–1032.

MAGNESIUM MALATE



APPLICATIONS

- Muscle Support
- Energy Production
- Mineral Support
- Bone Health
- Sleep Support
- Antioxidant support
- Stress Management



INTRODUCTION

Magnesium is an essential mineral in the human diet. It is the second most abundant intracellular cation (Mg²⁺) and is involved in more than 350 enzymatic reactions and over 80% of metabolic functions.^{1,2,3} Magnesium is needed for cellular energy metabolism, DNA transcription, RNA synthesis, membrane stabilization, and calcium metabolism, among many other functions.^{1,2} Magnesium may help to support muscular, skeletal, and neural health.*^{1,2,4} Dietary magnesium may be found in seeds such as pumpkin and chia; nuts and their butters such as almonds, cashews and peanuts; legumes such as black beans, kidney beans, and edamame, and spinach, among others.⁵ It can also be found in hard water, due to the high mineral content. Magnesium intake is often inadequate,⁷ and subclinical deficiency occurs before serum magnesium levels are impacted. Because of this, serum magnesium levels do not reliably correlate with either total body magnesium or amounts in specific tissues.9

Malic acid is commonly found in apples and other fruits. It is often added to food products to contribute a sour taste. Malic acid in the form of malate is an important part of the Krebs cycle, which helps to metabolize food into energy in the form of ATP. It may also help to support overall muscle health.*

In magnesium malate, magnesium is bound to malic acid. Magnesium levels depend on intestinal absorption and renal excretion.² Magnesium malate has been found to be more bioavailable than many of its magnesium counterparts.* In a single-dose rat study, magnesium malate had the highest area under the curve followed by magnesium acetyl taurate, while magnesium citrate and magnesium oxide had the lowest bioavailability.*10 A small single-center, randomized, doubleblind, four-arm crossover trial with 14 healthy adults found similar results, with

dimagnesium malate significantly more bioavailable than magnesium oxide.*11 Magnesium malate may help to support muscle health and energy production more than either magnesium or malic acid alone, due to different mechanisms

Our magnesium malate is free of dairy, soy, gluten, sugar, yeast, and mold. It is cGMP NSF Certified (ANSI Standards 173 Section 8), as well as FDA (Food and Drug Administration) and FSMA (Food Safety Modernization Act) Compliant. It is also kosher certified, halal certified, and suitable for vegetarians and vegans.

MUSCLE SUPPORT

Magnesium plays an important role in energy metabolism, and may help to support and maintain skeletal muscle health. 12 It may also support skeletal muscle relaxation.*13 Malic acid may assist with skeletal muscle support by helping to maintain lactic acid levels already within the normal range.* 14 Magnesium and malic acid work synergistically to support skeletal muscle health.* Additionally, magnesium may help to support both cardiac and smooth muscle, helping to maintain both cardiac and vascular health.*15 Because of this, magnesium may help to maintain cardiac output and peripheral vascular resistance already within the normal range.*15

ENERGY PRODUCTION

Magnesium helps to create energy in the form of ATP from dietary sources, and may support the utilization of other essential nutrients.* Magnesium may also help to support healthy daytime energy levels in women.*16 In a study with healthy male volleyball players, compared to control, the magnesium group had post-exercise lactic acid levels significantly closer to normal, suggesting that magnesium supplementation can support metabolism under anaerobic conditions.*17 Malic acid may help to maintain serum lactate levels within the normal range during and after exertion.* ¹⁴ Together, magnesium and malic acid play important roles in energy production via ATP, under both aerobic and anerobic conditions. ^{14,17}

OTHER USES

Mineral Support

Given that magnesium intake is often inadequate, magnesium intake may benefit from support." For prevention of deficiency, the RDA for elemental magnesium in ages 19-30 is 310 mg/day for women and 400 mg/day for men. In ages 31 and older, the RDA is 320 mg/day for women and 420 mg/day for men.

Approximately 50% of the body's magnesium is located within bone, where it contributes to structural integrity. Magnesium is a cofactor for the synthesis, transport, and activation of vitamin D, 18,79 and may also help to regulate calcium absorption. Magnesium's role in both of these processes helps to support and maintain healthy bones. *2,18

Sleep Support

Magnesium may help to support healthy sleep by supporting healthy NMDA and GABA levels already within the normal range.*20 It may also help to maintain healthy sleep quality.*21

Antioxidant support

Magnesium may help to contribute antioxidant activity, as it is a cofactor of superoxide dismutase and other antioxidant enzymes.*22,23,24

Stress Management

Magnesium may help to support relaxation and stress management in everyday stress.*25,26

SAFETY AND CAUTIONS

Magnesium is generally well-tolerated. At higher doses, loose stools and/or gastrointestinal irritation can occur. This is less likely to occur in doses under 350 mg per day. Do not take magnesium with levodopa/carbidopa, as it may reduce the bioavailability of levodopa/carbidopa. When taken with aminoglycoside antibiotics, magnesium can increase the risk of neuronuscular weakness. Magnesium can decrease the absorption of bisphosphonates when taken concurrently, and doses should be separated by at least two hours. Magnesium may decrease the absorption of quinolone antibiotics, which should be taken at least 2 hours before, or 4-6 hours after magnesium. Magnesium may have additive effects with calcium channel blockers, and may increase the risk for ketamine toxicity. It may also increase the absorption of sulfonylureas. Use caution when taking magnesium with potassium-sparing diuretics, as these can decrease magnesium excretion and increase magnesium levels.

Malic acid is generally recognized as safe (GRAS) in food and food products. As a supplement, it is generally well-tolerated. While one study has shown that malic acid may cause loose stools, it may have been due, instead, to the magnesium that was taken concurrently.²⁹ In one animal study, malic acid derived from tagetes root was shown to decrease blood pressure.³⁶ As with magnesium, malic acid may have additive effects with antihypertensives.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



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1 Ross, A.C., Caballero, B., et al. (2014). Modern nutrition in health and disease (1th ed., pp. 159-175). Wolters Kluwer/Lippincott Williams & Wilkins.
2 Stargrove, M., Treasure, J., & McKee, D. (2007). Herb., nutrient, and drug interactions (pp. 556-582). Mosby/Elsevier.
3 Case, D. R., Wolte, J., & P. Dovle, R. (2004). Movines (Saes). Switzenhall, 75(4), 3172.
4 Gröber, U., Schmidt, J., & Kisters, K. (2015). Autrients, 7(9), 8199-8226.
5 Office of Dietary Supplements. Magnesium Ods on hit gov. (2017). Retrieved 20 June 2021, from https://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/.
8 Blaszczyk, U. & Duda-Chodak, A. (2013). Norzniki Panstwowego Zakladu Higjeny, 64(3), 165-171.
Ford, E. S. & Modedad, A. H. (2003). Journal of Nutrition, 132, 289-2882.
9 Volpe S. L. (2015). Current Sports Medicine Reports, 14(4), 279-283.
9 Fiorentini, D., Cappadone, C., et al. (2021). Nutrients, 17(4), 1136.
1 Ursal, N., Kaildag, S., et al. (2019). Biological Trace Element Research, 187(1), 128-136.
1 Crowley, D. M. (2008). Bioavailability and tolerability of various Albion manufactured organic magnesium sources compared to magnesium oxide. Albion Laboratories, Saint Clair Shores, Michigan.
1 Hayhoe, R. P. C., Lenties, M. A. H., et al. (2019). Murrition brumal, 20(1), 90.
1 Hayhoe, R. P. C., Lenties, M. A. H., et al. (2019). Murrition brumal, 20(1), 90.
2 Barna, O., Londola, P., et al. (2013). Murrition brumal, 20(1), 90.
3 Barna, O., Londola, P., et al. (2013). Murrition brumal, 20(1), 90.
4 Kaylor, E., Ernigle, H., et al. (2012). Biochemical Genetics, 5(§-6), 387-994.
5 de Baail, J. H., Hoenderop, J. G., & Bindels, R. J. (2015). Physiological Reviews, 95(1), 1-46.
6 Cao, T., Zhen, S., et al. (2018). Nutrition of Sports Sciences, 32(5), 438-445.
8 Rosanoff, A., Dai, Q., & Shapses, S. A. (2016). Albanesis in Nutrition (Bethesda, Md.), 7(1), 25-43.
9 Dai, Q., Tux, Y., et al. (2018). Nutrition (Bethesda, Md.), 7(1), 25-43.
9 Dai, Q., Tux, Y., et al. (2018). Authorition (Bethesda, Md.), 7(1), 25-43.
9 Dai, Q., Tux, Y.,
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<u>MELATONIN</u>



APPLICATIONS

- Sleep Support
- Immune Support
- Antioxidant Support



INTRODUCTION

Endogenous melatonin has many important functions in the body. Its biological roles can be receptor-dependent, such as sleep maintenance and circadian rhythm support, or receptor-independent, such as antioxidant support. While melatonin is best known as a product of the pineal gland, it can be produced by other areas in the body as well, including the retina and gastrointestinal tract.²

Melatonin can be found in animal foods such as eggs and fish, as well as in plant foods such as nuts, germinated seeds and legumes, mushrooms, and fruits.^{3,4,5,6} Studies have shown that melatonin is well-absorbed from dietary sources.^{*7} Supplemental melatonin may assist the body's natural processes that support healthy sleep, maintain healthy immunity, and support normal antioxidant function.*

Melatonin is made at our U.S. manufacturing facility using a specialized proprietary process in which we solvate synthetic melatonin powder into a water/ethanol blend. While melatonin supplements are available from both animal and synthetic sources, we use synthetic melatonin to avoid the potential risk of zoonotic infection. Because Melatonin is made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

SLEEP SUPPORT

Endogenous melatonin is a neuroendocrine hormone produced by the pineal gland that helps to regulate the 24-hour circadian rhythm.* In the body, tryptophan is converted to 5-hydroxytryptophan, then to serotonin, then to N-acetylserotonin, and finally to melatonin.³ Melatonin secretion is controlled by retinal ganglion cells that receive light and dark cues from the environment and convey this information

to the suprachiasmatic nucleus (SCN) in the hypothalamus. The SCN, in turn, triggers melatonin release from the pineal gland which regulates the sleep-wake cycle.¹

While melatonin is continually produced, blood levels are higher in the evening to help prepare for sleep.⁸ Daytime light helps to suppress melatonin secretion, promoting alertness. Soon after sunset, melatonin levels begin to rise in preparation for sleep. It should be noted that normal melatonin secretion may be delayed by external cues such as blue light from screens too close to bedtime.⁸ Melatonin levels also decrease with age, particularly after the age of 60.⁹

Exogenous melatonin may be helpful to support and maintain a normal circadian rhythm.* It may also help to support normal, healthy sleep as appropriate for shift work or a given time zone.* A meta-analysis of 17 studies involving 284 participants concluded that supplemental melatonin may help to support healthy sleep latency, maintain normal sleep efficiency, and support healthy sleep duration.* In addition, it may help to maintain a normal percentage of REM sleep and maintain melatonin levels already within the normal range.* 12,13

IMMUNE SUPPORT

Melatonin may help to support normal cytokine production.* In vitro studies have shown that melatonin may help to support Th1 cells and cytokines such as IL-2 and interferon-gamma already within the normal range.* It may also help to support healthy monocyte function and normal IL-6 production, already within the normal range.* In innate immunity, melatonin may help to maintain levels of natural killer (NK) cells already within the normal range.* In adaptive immunity, melatonin may help to maintain CD69 from CD4* helper I cells already within the normal range.*

Leukocytes both produce and respond to melatonin.*2,15,16 Endogenous melatonin interacts with calmodulin in the cytosol; with nuclear binding receptors in monocytes and lymphocytes; and with MT1 and MT2 G-protein coupled receptors in cell membranes; all of which help to regulate a healthy immune response.*17,18 Supplemental melatonin may help to maintain normal immune homeostasis.*15 In addition, melatonin may help with healthy inflammatory response support.*15

As melatonin levels decrease with age, there are repercussions for both innate immunity and adaptive immunity, including humoral and cellular immunity. This leads to a suboptimal immune response, particularly of NK cells, interferon-gamma, and associated cytokines and chemokines. For these reasons, it may be prudent to consider supplemental melatonin for healthy immune support, particularly in older individuals.

OTHER USES

Antioxidant Support

Endogenous melatonin and its metabolites help to support antioxidant activity for both reactive oxygen species (ROS) and reactive nitrogen species (RNS).*17,79 Melatonin may help to support normal free radical scavenging, maintain levels of antioxidant and prooxidant enzymes already within the normal range, and support mitochondrial function.*17 Antioxidant support is attributed to various mechanisms, from interactions between melatonin and calmodulin to the support of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAI) and glutathione peroxidase (GPx).*17,20

Melatonin also supports normal non-enzymatic antioxidant activity.*20 In the mitochondria, melatonin helps to stabilize the inner membrane and supports normal functioning of the electron transport chain, which helps to maintain normal ATP production.*17 It also helps to maintain intracellular glutathione levels already within the normal range.*18 Melatonin supports antioxidant activity in both lipophilic and lipophobic environments and is widely distributed to tissues and cells, including cell membranes, cytosol, and cellular organelles.*20 Some researchers have found melatonin's antioxidant support to be more robust than that of vitamin E.*21

SAFETY AND CAUTIONS

Melatonin is generally well tolerated when used as recommended. The most common side effects are drowsiness, dizziness, nausea, and headache. Melatonin has been used in doses up to 10 mg daily for 2 months and in doses up to 8 mg

daily for 6 months.²² Serious side effects are rare. One study in postmenopausal women taking 6 mg daily for 2 weeks found that melatonin may increase levels of VLDL and triglycerides.²³ At 3 mg per day, some study participants developed a rash, though at the same rate as placebo.²² Melatonin may cause gastrointestinal effects such as nausea and abdominal cramps, though generally at the same rate as placebo and usually with prompt resolution.^{22,24,25} In healthy adults between the ages of 60-71 years given a single dose of 3 mg melatonin, participants experienced increased postural swaying which could theoretically increase the risk of falls.²⁶ Cognitive function in older adults, however, is not affected.²⁶ Melatonin may cause a temporary dip in mood, and may worsen depression in those diagnosed.^{27,28} Reports are mixed as to whether melatonin may decrease or increase the risk of seizures.²²

Melatonin may have additive effects with anticoagulant, antiplatelet, hypoglycemic, and CNS depressant drugs. 22,29 It may decrease the effects of anticonvulsants, and extended-release nifedipine. Theoretically, melatonin may have additive effects with antihypertensive drugs, though it may also decrease the effects. Cyp1ac contraceptive drugs may increase the adverse effects of melatonin due to the alteration of endogenous melatonin. ACYP1AC and CYP2C19 substrates may increase levels of melatonin, and melatonin may increase levels of these substrates. There is insufficient safety data available in pregnancy and lactation, thus melatonin should be avoided in these states. Those using melatonin should be advised to avoid driving for 4-5 hours after consumption, as it may cause daytime drowsiness.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

¹ Blasiak, J., Reiter, R. J., & Kaarniranta, K. (2016). Oxidative Medicine and Cellular Longevity, 2016, 6819736.

33 Kitajima, T., Kanbayashi, T., et al. (2001). Psychiatry and Clinical Neurosciences, 55(3), 299-300.

34 Wright, K. P., Myers, B. L., et al. (2000). Brain Research, 873(2), 310–317.

```
<sup>2</sup> Reiter, R. J., Tan, D. X., et al. (2000). Journal of Biomedical Science, 7(6), 444–458.
<sup>3</sup> Meng, X., Li, Y., et al. (2017). Nutrients, 9(4), 367.
<sup>4</sup> Iriti, M., & Varoni, E. M. (2016). LWT - Food Science and Technology, 65, 758–761.
<sup>5</sup> Reiter, R. J., & Tan, D. X. (2002). Annals of the New York Academy of Sciences, 957, 341–344.
<sup>6</sup> Salehi, B., Sharopov, F., et al. (2019). Cells, 8(7), 681.
<sup>7</sup> Sae-Teaw, M., Johns, J., et al. (2013). Journal of Pineal Research, 55(1), 58–64.
<sup>8</sup> Wahl, S., Engelhardt, M., et al. (2019). Journal of Biophotonics, 12(12), e201900102.
<sup>9</sup> Bondy, S. C., & Campbell, A. (2020). Current Aging Science, 13(2), 92–101.
<sup>10</sup> Arendt, J., & Skene, D. J. (2005). Sleep Medicine reviews, 9(1), 25–39.
<sup>11</sup> Brzezinski, A., Vangel, M. G., et al. (2005). Sleep Medicine Reviews, 9(1), 41–50.
<sup>12</sup> Xu, H., Zhang, C., et al. (2020). Sleep Medicine, 76, 113-119.
<sup>13</sup> Kunz, D., & Mahlberg, R. (2010). Journal of Sleep Research, 19(4), 591–596.
<sup>14</sup> Garcia-Mauriño, S., Gonzalez-Haba, M. G., et al. (1997). Journal of Immunology (Baltimore, Md.: 1950), 159(2), 574–581.
<sup>15</sup> Carrillo-Vico, A., Lardone, P. J., et al. (2013). International Journal of Molecular Sciences, 14(4), 8638–8683.
16 Radogna, F., Diederich, M., & Ghibelli, L. (2010). Biochemical Pharmacology, 80(12), 1844–1852.
<sup>17</sup> Zhang, H. M., & Zhang, Y. (2014). Journal of Pineal Research, 57(2), 131–146.
<sup>18</sup> Srinivasan, V., Maestroni, G. J., et al. (2005). Immunity & Ageing, 2, 17.
<sup>19</sup> Reiter R. J. (1998). Progress in Neurobiology, 56(3), 359–384.
<sup>20</sup> Tomás-Zapico, C., & Coto-Montes, A. (2005). Journal of Pineal Research, 39(2), 99–104.
<sup>21</sup> Jou, M. J., Peng, T. I., et al. (2004). Journal of Pineal Research, 37(1), 55–70.

<sup>22</sup> Natural Medicines. (2021, December 4). Melatonin [monograph]. http://naturalmedicines.therapeuticresearch.com
<sup>23</sup> Wakatsuki, A., Okatani, Y., et al. (2001). Maturitas, 38(2), 171–177.
<sup>24</sup> Gonçalves, A. L., Martini Ferreira, A., et al. (2016). Journal of Neurology, Neurosurgery, and Psychiatry, 87(10), 1127–1132.
<sup>25</sup> Guénolé, F., Godbout, R., et al. (2011). Sleep Medicine Reviews, 15(6), 379–387.
<sup>26</sup> Lui, M., Chow, H., et al. (2019). Journal of Aging and Physical Activity, 1–6.
<sup>27</sup> van Geijlswijk, I. M., Korzilius, H. P., & Smits, M. G. (2010). Sleep, 33(12), 1605–1614.
<sup>28</sup> Carman, J. S., Post, R. M., et al. (1976). The American Journal of Psychiatry, 133(10), 1181–1186.
<sup>29</sup> Foster, B. C., Cvijovic, K., et al. (2015). Journal of Pharmacy & Pharmaceutical sciences: A publication of the Canadian Society for Pharmaceutical Sciences, Societe Canadienne des Sciences Pharmaceutiques, 18(2), 124–131.
30 Stewart L. S. (2001). The International Journal of Neuroscience, 107(1-2), 77-85.
<sup>31</sup> Lissoni, P., Barni, S., et al. (1999). European Journal of Cancer (Oxford, England: 1990), 35(12), 1688–1692.
<sup>32</sup> Lusardi, P., Piazza, E., & Fogari, R. (2000). British Journal of Clinical Pharmacology, 49(5), 423–427.
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METHYL COMPLETE



APPLICATIONS

- Methylation Support
- Metabolic Support
- Energy Support
- Neurological Support



INTRODUCTION

This formula contains ingredients to support healthy DNA methylation, a biochemical process involving the addition of a methyl group (-CH3) to various essential biochemical compounds.* Healthy methylation is powered by efficient folate and methionine cycles, which depend on active folate (5-MTHF) and active vitamin B12 (methylcobalamin), essential cofactors such as vitamin B2 (riboflavin) and active B6 (P5P), adequate methyl donors, and effective conversion of homocysteine, either recycled back to methionine or converted to cysteine with the help of B6 (P5P) and eventually to glutathione. Fully active B vitamins and additional methyl donors may help to support healthy methylation.*

Our methylation support formula is free of dairy, soy, gluten, sugar, yeast, and mold. It is cGMP NSF Certified (ANSI Standards 173 Section 8), as well as FDA (Food and Drug Administration) and FSMA (Food Safety Modernization Act) Compliant

VITAMIN B2

Vitamin B2 is water-soluble and is required for flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), two co-enzymes that are involved in energy production, cellular function, and metabolism.1 FMN is needed for the conversion of B6 to its active form, pyridoxal 5'-phosphate, and FAD is required for the conversion of tryptophan to niacin.*1 FAD is also needed for the **folate cycle**, to convert folic acid to active folate, which together with B12, helps to maintain homocysteine levels already within the normal range by recycling homocysteine back to methionine, facilitating sulfur amino acid metabolism.*2

Riboflavin can be obtained in the diet from pork, fish, and organ meats, as well as fortified foods such as grains and cereals.² The recommended dietary allowance (RDA) for individuals ages 19 and older is 1.3 mg/day for men and 1.1 mg/day for women.² The RDA during pregnancy is 1.4 mg/day, and the RDA during lactation is 1.6 mg/day, regardless of age. As adverse effects from riboflavin are extremely

rare, an upper limit (maximum intake unlikely to cause adverse effects) has not been established.²

VITAMIN B6

Vitamin B6 is water-soluble and can be in one of six forms. In this formula, vitamin B6 is in the form of pyridoxal 5'-phosphate (P5P), an active coenzyme form that does not rely on the body for conversion. Conversion of regular B6 to active P5P requires FMN, which in turn, requires adequate riboflavin. Vitamin B6 is needed for over 100 enzyme reactions, most of which are related to protein metabolism.³ It is also needed for the folate cycle. B6 in the form of P5P is a coenzyme for other enzymes in the transsulfuration pathway, converting homocysteine to cysteine.*3 As with vitamin B2, vitamin B6 helps to maintain homocysteine levels already within the normal range.*3 Vitamin B6 also helps support hemoglobin formation and neurotransmitter synthesis.*3

Vitamin B6 can be obtained in the diet from citrus, poultry, and beef, as well as fortified foods such as grains and cereals. The RDA for ages 19 and older is 1.3 mg/day for both men and women, ages 19–50. The RDAs for ages 51 and older are 1.7 mg/day for men and 1.5 mg/day for women. The RDA during pregnancy is 1.9 mg/day, and the RDA during lactation is 2.0 mg/day, regardless of age. The upper limit, or maximum intake unlikely to cause adverse effects, is 100 mg/day for both men and women.

FOLIC ACID

Folic acid in this formula is in the active form of Calcium L-Methylfolate. Folic acid is a water-soluble B vitamin formerly known as vitamin B9. It is needed for DNA and RNA synthesis, as well as amino acid metabolism.*4 Folic acid is an important part of the **folate cycle**, which helps support the **methionine cycle**. The conversion of homocysteine to methionine in the form of S-adenosylmethionine (SAM-e), an important methyl donor for other reactions, is folate-dependent.*4

Folate or folic acid in the diet can be found in abundance in leafy green vegetables as well as in fortified foods such as bread and cereal. 2 The RDA for individuals ages 19 and older, both men and women, is 400 mcg/day of dietary folate equivalents (DFE). The RDA during pregnancy is 600 mcg/day DFE and the RDA during lactation is 500 mcg/day DFE, regardless of age. The upper limit, or maximum intake unlikely to cause adverse effects, is 1,000 mcg/day.

VITAMIN B12

Vitamin B12 in this formula is in the form of methylcobalamin, an active form that does not rely on the body's conversion for efficacy, the other active form being 5-deoxyadenosylcobalamin.⁵ Vitamin B12 acts as a cofactor for the enzyme methionine synthase, which helps in the conversion of methyltetrahydrofolate to tetrahydrofolate in the folate cycle, as well as the conversion of homocysteine to methionine in the methionine cycle. It is also needed for S-adenosylmethionine (SAM-e) formation, the body's universal methyl donor.^{2,5} In addition to methylation, vitamin B12 is needed for healthy central nervous system function, normal DNA synthesis, and healthy red blood cell formation.*⁵

Vitamin B12 can be obtained in the diet from animal foods such as dairy and meat, as well as in some fortified foods. Vegetarians may obtain some B12 from nutritional yeast.² The RDA for both men and women is 2.4 mcg/day in ages 19–50 and 2.0 mcg/day in ages 51 and older.² The RDA in pregnancy is 2.6 mcg/day and the RDA in lactation is 2.8 mcg/day, regardless of age.² Because adverse

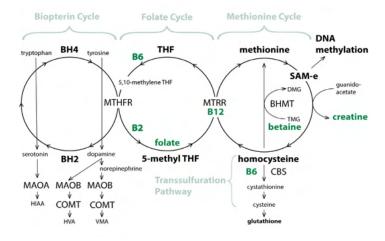
effects from vitamin B12 are so rare, an upper limit has not been established.²

CREATINE MONOHYDRATE

Creatine Monohydrate is commonly used to support healthy skeletal muscle energy metabolism and ATP production.*6 It may also help to facilitate healthy methylation and detoxification.*7 It can be obtained in the diet through eating meats and other animal foods.⁶ Supplying creatine as an ingredient in this formula may help to spare SAM-e generated by the methionine cycle for other purposes.

BETAINE ANHYDROUS

Betaine anhydrous is also known as trimethylglycine (TMG) and occurs naturally in the body from the oxidation of choline. It can be obtained in the diet from seafood, wheat bran, and spinach.⁸ As a methyl donor in the methionine cycle, it may help to recycle homocysteine back to methionine, maintaining levels of homocysteine already within the normal range.*9,10



METHYLATION SUPPORT

Methylation, the addition of methyl groups (-CH3), is essential to processes as varied as DNA replication, neurotransmitter production, antioxidant activity, and healthy detoxification, among others.* Normal methylation can be challenged by various factors, including a lack of B vitamins and cofactors; an inability to convert B vitamins and cofactors to their active forms, resulting in a lack of methyl donors; and various single-nucleotide polymorphisms (SNPs) which may affect methylation efficiency.

Supplementation with B vitamins, particularly in their active forms, may help to support normal methylation, bypassing the need for conversion; help maintain homocysteine levels already within the normal range; and help maintain glutathione levels already within the normal range, supporting normal detoxification.* Efficient methylation may support normal cellular metabolism, as well as healthy energy production and storage.* Normal levels of homocysteine are associated with normal antioxidant activity, a healthy inflammatory response, and normal cognitive and cardiovascular health.*¹¹

Vitamin B2 is required for the conversion of vitamin B6 to the active form P5P;1 it is also a cofactor for MTHFR, the enzyme that converts folic acid to active methylfolate in the folate cycle. Both methylfolate and methylcobalamin (B12) help to recycle homocysteine to methionine, which is then converted to S-adenosylmethionine (SAM-e), the body's universal methyl donor.¹² Adequate levels of SAM-e may help to stabilize BH4 in the biopterin cycle, maintaining neurotransmitters such as MAO and serotonin already within the normal range.*¹³ SAM-e may also help to maintain homocysteine levels already within the normal range.*¹⁴ After donating a methyl group, SAM-e converts to homocysteine, which can either be recycled back to methionine with the help of methylfolate or methylcobalamin (B12),¹⁵ or converted to cysteine through the transsulfuration pathway with the help of cofactor P5P (B6), supporting normal glutathione production and helping with healthy antioxidant support.*¹⁶

Vitamin B6 is needed for the folate cycle, the transsulfuration pathway, and methylation.¹⁷ In this formula, it is present in the active form of pyridoxal 5'-phosphate (P5P), which does not rely on the body's ability to convert it. Vitamin B6 may help with folate recycling and may help to maintain homocysteine levels already within the normal range.*18,19

Vitamin B12 is in the active form of methylcobalamin, the other active form being adenosylcobalamin. As a methyl donor, methylcobalamin may help to maintain normal methylation, independent of MTHFR status, as it is not reliant on the body's ability to convert it. B12 is needed for both the folate cycle and the methionine cycle, the latter of which is responsible for making SAM-e.²⁰

In the active form of Calcium L-Methylfolate, folate helps to make SAM-e, the body's universal methyl donor, via the methionine cycle.12.17 As such, SAM-e is involved in a number of processes, including the synthesis of creatine, which is made from the transamination of amino acids arginine, glycine, and methionine.²¹ This methylation support formula includes creatine, which may help to spare SAM-e for other purposes.*

Creatine monohydrate may also help with methylation support.*7 It is generated by the methionine cycle, and both rat and human studies have found that it may help to maintain homocysteine levels already within the normal range and may help with antioxidant support.*22,7 A double-blind, placebo-controlled human study found that creatine may help to maintain normal energy homeostasis in the brain, supporting healthy cognition.*23 As 40% of the methyl groups produced as SAM-e are used for creatine synthesis, supplemental creatine may help spare some of these to be used for other purposes.*24

Betaine anhydrous, also known as trimethylglycine (TMG), occurs naturally in the body from the oxidation of choline and is a cofactor in the recycling of homocysteine to methionine.*25 As such, betaine anhydrous may act on the methionine cycle to maintain levels of homocysteine already within the normal range.*9,10

SAFETY AND CAUTIONS

Riboflavin is generally well tolerated. The most common adverse effects are bright yellow urine and dose-dependent nausea. Theoretically, taking riboflavin with tetracycline antibiotics may decrease their effects.²⁶

Vitamin B6 is generally well tolerated in doses less than 100 mg/day. Common adverse effects include gastrointestinal symptoms such as heartburn, abdominal pain, loss of appetite, nausea, and vomiting, though somnolence and headache have also been reported. Theoretical interactions with B6 include additive effects with antihypertensive medications as well as decreased levels and effects of phenobarbital and phenytoin.²⁷

Vitamin B12 is generally well tolerated in oral form and side effects are uncommon. There are no currently known drug interactions. While large doses of folic acid can mask a B12 deficiency, this would not be expected at the dosages recommended for this product.²⁸

Folic acid is generally well tolerated under doses of 1 mg/day. It may reduce the effectiveness of methotrexate. When taken with phenobarbital or primidone, it may increase the risk of seizures. When taken with phenytoin, it may reduce serum levels and effectiveness.²⁹

Creatine monohydrate is generally well tolerated.³⁰ Common side effects include gastrointestinal effects such as diarrhea and stomach upset, muscle cramps, and dehydration.³¹ There are no currently known drug interactions.³¹

Betaine anhydrous is generally well tolerated. It may cause gastrointestinal side effects such as nausea, vomiting, or diarrhea. There are currently no known drug interactions.³²

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

1 ODS. (2022). Office of Dietary Supplements - Riboflavin. Retrieved 23 April 2022, from https://ods.od.nih.gov/factsheets/Riboflavin-HealthProfessional/#en1

2 Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline. (1998). National Academies Press (US).

3 ODS. (2022). Office of Dietary Supplements - Vitamin B6. Retrieved 23 April 2022, from https://ods.od.nih.gov/factsheets/ VitaminB6-HealthProfessional/

4 ODS. (2022). Office of Dietary Supplements - Folate. Retrieved 24 April 2022, from https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/

5 ODS. (2022). Office of Dietary Supplements - Vitamin B12. Retrieved 23 April 2022, from https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/

6 Ostojic, S. M. (2021). Journal of Functional Foods, 83(2021), 104568.

7 Bozack, A. K., Howe, C. G., et al. (2021). European Journal of Nutrition, 60(4), 1921-1934.

8 Craig S. A. (2004). The American Journal of Clinical Nutrition, 80(3), 539-549.

9 Mütze, U., Gleich, F., et al. (2022). Journal of Inherited Metabolic Disease, 10.

10 Valayannopoulos, V., Schiff, M., et al. Orphanet Journal of Rare Diseases, 14(1), 66.

11 Ford, T. C., Downey, L. A., et al. (2018). Nutrients, 10(12), 1860.

12 Amenyah, S. D., McMahon, A., et al. (2020). Biochimie, 173, 17–26.

13 Miller, A. L. (2008). Alternative Medicine Review: A journal of clinical therapeutic, 13(3), 216–226.

14 Jacques, P. F., Kalmbach, R., et al. (2002). The Journal of Nutrition, 132(2), 283–288.

15 Vaccaro, J. A., & Naser, S. A. (2021). Healthcare (Basel, Switzerland), 10(1), 61.

16 Dalto, D. B., & Matte, J. J. (2017). Nutrients, 9(3), 189.

17 Anderson, O. S., Sant, K. E., & Dolinoy, D. C. (2012). The Journal of Nutritional Biochemistry, 23(8), 853–859.

18 Obeid, R., Kirsch, S. H., et al. (2016). European Journal of Nutrition, 55(3), 1021–1028.

19 Stach, K., Stach, W., & Augoff, K. (2021). Nutrients, 13(9), 3229.

20 Froese, D. S., Fowler, B., & Baumgartner, M. R. (2019). Journal of Inherited Metabolic Disease, 42(4), 673-685.

21 Salazar, J. H. (2014). Laboratory Medicine 45(1), e19-e20.

22 Deminice, R., Portari, G. V., et al. (2009). The British Journal of Nutrition, 102(1), 110-116.

23 Rae, C., Digney, A. L., et al. (2003). Proceedings. Biological Sciences, 270(1529), 2147–2150.

24 Joncquel-Chevalier Curt, M., Voicu, P. M., et al. (2015). Biochimie, 119, 146-165.

25 Zhou, R. F., Chen, X. L., et al. (2017). Scientific Reports, 7(1), 679.

26 Natural Medicines. (2022, April 23). Riboflavin [monograph]. http://naturalmedicines.therapeuticresearch.com

27 Natural Medicines. (2022, April 23). Vitamin B6 [monograph]. http://naturalmedicines.therapeuticresearch.com

28 Natural Medicines. (2022, April 23). Vitamin B12 [monograph]. http://naturalmedicines.therapeuticresearch.com

29 Natural Medicines. (2022, April 23). Folic Acid [monograph]. http://naturalmedicines.therapeuticresearch.com

30 Almeida, D., Colombini, A., & Machado, M. (2020). The Journal of Sports Medicine and Physical Fitness, 60(7), 1034–1039.

31 Natural Medicines. (2022, April 23). Creatine [monograph]. http://naturalmedicines.therapeuticresearch.com 32 Natural Medicines. (2022, April 23). Betaine Anhydrous [monograph]. http://naturalmedicines.therapeuticresearch.com

MOODMEDIX ®



APPLICATIONS

- Mood/Emotional Support
- Inflammatory Response Support
- Immune System Support
- Neurological Support



INTRODUCTION

MoodMedix is a proprietary blend of hydro-ethanol extracts from turmeric root (Curcuma longa) and Cat's Claw bark (Uncaria tomentosa) which is also known as Samento. The active constituents of C. longa are considered to be the curcuminoids, particularly the well-studied curcumin. *C. longa* root also contains proteins, fatty acids, minerals and polysaccharides. *C. longa* may help with occasional mood and emotional support as well as healthy inflammatory response support.*2,3 Samento is extracted from a rare pentacyclic chemotype of *U. tomentosa*, verified by independent 3rd party HPLC testing to be free of TOAs, with levels in trace amounts or undetectable. This pentacyclic oxindole alkaloid (POA)-predominant, tetracyclic oxindole alkaloid (TOA)-free form of U. tomentosa may help with healthy inflammatory response support, immune system support, and neurological support.*4,5

MoodMedix is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

MOOD/EMOTIONAL SUPPORT

C. longa may help with emotional support and occasional low mood.*2,6,7 A healthy mood is dependent on normal levels of neurotransmitters such as serotonin, norepinephrine, and dopamine, among others.8 The monoamine oxidase (MAO) enzymes help to break down these neurotransmitters and prevent levels from becoming elevated; however, they may also contribute to decreased levels.9 C. longa may help to support MAO-A and MAO-B levels already within the normal range, which may help to maintain levels of serotonin already within the normal range. The Brain-derived neurotrophic factor (BDNF) is important for neuronal health and function, helping to support normal cognition and a healthy emotional state. 12 C. longa may help to support BDNF levels and salivary cortisol levels already within the normal range.*13

OTHER USES

Inflammatory Response Support
Both *C. longa* and *U. tomentosa* (pentacyclic chemotype) may help to maintain and support a healthy inflammatory response.*3,5,15 *C. longa* may help to support CRP, TNF-alpha, and IL-6 levels already within the normal range.*3 *U. tomentosa* may help to support NF-kappa B levels already within the normal range in a dose-dependent manner,^{16,17} thus supporting both TNF-alpha and IL-1-beta already within the normal range.*

Immune System Support *U. tomentosa* (pentacyclic chemotype) may help to maintain a healthy immune response and support immune system homeostasis.* *U. tomentosa* may help to maintain neutrophil function as well as Th1 and Th2 levels already within the normal range.* 19,20,21 lt should be noted that only TOA-free *U. tomentosa* (such as Samanta) belos with homeostatic immuno support. *4 Samento) helps with homeostatic immune support.*4

Neurological Support

 $\it U.~tomentosa~may~help~to~support~neurological~health~and~help~to~maintain~healthy~neurocognitive~function.* ^22,23$

SAFETY AND CAUTIONS

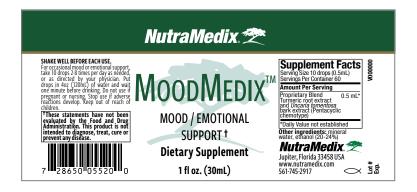
U. tomentosa and *C. longa* are generally well tolerated. Gastrointestinal effects such as nausea, constipation, and diarrhea have been reported with both, though generally not at greater rates than with placebo. ^{24,25,26,27} Both may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4.^{28,29}

C. longa may have additive effects with anticoagulant drugs,³⁰ warfarin,³¹ and antidiabetic drugs,³² C. longa may increase blood levels of amlodipine,³³ sulfasalazine,³⁴ and tacrolimus,³⁵ the last of which is attributed to CYP3A4 inhibition. The antioxidant activity of C. longa may oppose the prooxidant action of alkylating drugs and antitumor antibiotics.³⁶ C. longa can cause gallbladder contractions and should be used with caution in gallbladder disease.³⁷ It is possible that C. longa may increase the risk of hepatotoxicity when taken in high doses with hepatotoxic drugs.³⁸

U. tomentosa should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy.³⁹ *U. tomentosa* may have additive effects with anticoagulants, generally attributed to the TOA rhynchophylline,⁴⁰ as well as additive effects with antihypertensive drugs, generally attributed to the TOAs rhynchophylline and isorhynchophylline.^{41,42} As a reminder, Samento is TOA-free, with levels in trace amounts or undetectable.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

¹ Ashraf, K., Sultan, S., et al. (2017). *International Journal of Green Pharmacy*, 11(4). ² Sanmukhani, J., Satodia, V., et al. (2014). Phytotherapy Research: PTR, 28(4), 579-585. ³ Uchio, R., Muroyama, K., et al. (2019). *Nutrients*, 11(8), 1822. 4 Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). Applied Sciences, 10(8), 2668. ⁵ Liang, J. H., Wang, C., et al. (2020). Fitoterapia, 147, 104772. ⁶ Al-Karawi, D., Al Mamoori, D. A., & Tayyar, Y. (2016). *Phytotherapy Research: PTR*, 30(2), 175–183. ⁷ Fusar-Poli, L., Vozza, L., et al. (2020). Critical Reviews in Food Science and Nutrition, 60 (15), 2643–2653. 8 Sheffler, Z., Reddy, V., & Pillarisetty, L. (2021). Physiology, Neurotransmitters. Ncbi.nlm.nih.gov. Retrieved 6 May 2021, from https://www.ncbi.nlm.nih.gov/books/NBK539894/. Laban, T., & Saadabadi, A. (2021). Monoamine Oxidase Inhibitors (MAOI). Ncbi.nlm.nih.gov. Retrieved 6 May 2021, from https://www.ncbi.nlm.nih.gov/books/NBK539848/. ¹⁰ Yu, Z. F., Kong, L. D., & Chen, Y. (2002). *Journal of Ethnopharmacology*, 83(1-2), 161–165. 11 Kulkarni, S. K., Bhutani, M. K., & Bishnoi, M. (2008). *Psychopharmacology*, 201(3), 435-442. ¹² Phillips C. (2017). Neural Plasticity, 2017, 7260130. ¹³ Wynn, J. K., Green, M. F., et al. (2018). Schizophrenia Research, 195, 572-573. ¹⁴ Yu, J. J., Pei, L. B., et al. (2015). *Journal of Clinical Psychopharmacology*, 35(4), 406–410. ¹⁵ Mur, E., Hartig, F., et al. (2002). *The Journal of Rheumatology*, 29(4), 678–681. 16 Sandoval-Chacón, M., Thompson, J. H., et al. (1998). Alimentary Pharmacology & Therapeutics, 12(12), 1279-1289. ¹⁷ Allen-Hall, L., Arnason, J. T., et al. (2010). Journal of Ethnopharmacology, 127(3), 685–693. ¹⁸ Fan, C., Song, Q., et al. (2019). Frontiers in Cellular Neuroscience, 12, 516. 19 Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). Phytomedicine: International journal of phytotherapy and phytopharmacology, 23(2), 141–148. ²⁰ Núñez, C., Lozada-Requena, I., et al. (2015). Revista Peruana de Medicina Experimental y Salud Publica, 32(4), 643–651. ²¹ Winkler, C., Wirleitner, B., et al. (2004). *Planta Medica*, 70(3), 205–210. ²² Snow, A. D., Castillo, G. M., et al. (2019). *Scientific Reports*, 9(1), 561. ²³ Mohamed, A. F., Matsumoto, K., et al. (2000). The Journal of Pharmacy and Pharmacology, 52(12), 1553–1561 ²⁴ Chuengsamarn, S., Rattanamongkolgul, S., et al. (2012). Diabetes Care, 35(11), 2121–2127. 25 Sharma, R. A., McLelland, H. R., et al. (2001). Clinical Cancer Research: An official journal of the American Association for Cancer Research, 7(7), 1894–1900. ²⁶ de Paula, L. C., Fonseca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22–30. ²⁷ Kuptniratsaikul, V., Dajpratham, P., et al. (2014). Clinical Interventions in Aging, 9, 451–458. ²⁸ Hou, X.-L., Takahashi, K., et al. (2007). *International Journal of Pharmaceutics*, 337(1–2), 169–177. ²⁹ Budzinski, J. W., Foster, B. C., et al. (2000). Phytomedicine: International journal of phytotherapy and phytopharmacology, 7(4), 273–282. 30 Srivastava, K. C., Bordia, A., & Verma, S. K. (1995). Prostaglandins, Leukotrienes, and Essential Fatty Acids, 52(4), 223–227. 31 Medsafe. (2021). Beware turmeric/curcumin containing products can interact with warfarin. Medsafe.govt.nz. Retrieved 25 March 2021, from https://medsafe.govt.nz/safety/EWS/2018/Turmeric.asp. 32 Jain, S. K., Rains, J., et al. (2009). *Antioxidants & Redox Signaling*, 11(2), 241–249. 33 Jiang, N., Zhang, M., et al. (2020). Pharmaceutical Biology, 58(1), 465–468. 34 Kusuhara, H., Furuie, H., et al. (2012). British Journal of Pharmacology, 166(6), 1793–1803. 35 Nayeri, A., Wu, S., et al. (2017). *Transplantation Proceedings*, 49(1), 198–200. ³⁶ Somasundaram, S., Edmund, N. A., et al. (2002). Cancer Research, 62(13), 3868–3875. 37 Rasyid, A., Rahman, A. R., et al. (2002). Asia Pacific Journal of Clinical Nutrition, 11(4), 314–318. 38 Lombardi, N., Crescioli, G., et al. (2021). British Journal of Clinical Pharmacology, 87(3), 741. 39 Lamm, S., Sheng, Y., & Pero, R. W. (2001). Phytomedicine: International journal of phytotherapy and phytopharmacology, 8(4), 267–274.

40 Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126–130.

⁴¹ Zhou, J., & Zhou, S. (2010). *Journal of Ethnopharmacology*, 132(1), 15–27. 42 Zhou, J. Y., & Zhou, S. W. (2012). *Fitoterapia*, 83(4), 617–626.



- Inflammatory Response Support
- Antioxidant Support
- Gastrointestinal Support
- Microbial Support
- Neurological Support



INTRODUCTION

Mora™ is a hydro-ethanol extract made from Achillea millefolium (flowers), Rubus fruticosus (leaves) and Calycophyllum spruceanum (bark).

A. millefolium belongs to the Asteraceae/Compositae family and is commonly known as yarrow. Synonyms for A. millefolium include A. borealis, A. magna, and A. lanulosa. A. millefolium includes phenolic acids such as gallic acid, 2-OH-benzoic acid, chlorogenic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, sinapic acid, ferulic acid, and cinnamic acid. It also includes flavonoid aglycones and glycosides such as myricetin, luteolin, kaempherol, rutin, and hyperoside. A. millefolium has been used traditionally for gastrointestinal support.

R. fruticosus belongs to the Rosaceae family and is commonly known as blackberry. Synonyms for R. fruticosus include R. plicatus, R. affinis, R. canadensis, R. millspaughii, and R. laciniatus. A. fruticosus leaves have been traditionally used for microbial support. The leaves contain phenolic acids such as neo-chlorogenic acid, caffeic acid, gallic acid, p-coumaric acid, and ellagic acid; flavonols such as quercetin, quercetin-3-0-galactoside, quercetin-3-0-glucuronide, and kaempferol; flavan-3-ols such as catechin, epicatechin, and epicatechin gallate methyl gallate; ellagitannins such as sanguiin H-6/lambertianin C, and casuarinin; anthocyanins such as cyanidin-3-0-glucoside; and triterpene acids such as rubinic acid and rubusic acid. They also contain tannins, villosin, gallic acid, and iron. Constitutional parameters are the Publicages family and in commonth language.

C. spruceanum belongs to the Rubiaceae family and is commonly known as capirona.⁸ A synonym for this plant is *Eukylista spruceana*.⁹ It is native to the Amazon rainforest and is sometimes called the "Tree of Youth."¹⁰ It has been used in traditional medicine for healthy inflammatory response support.*¹¹ Constituents of *C. spruceanum* include seco-iridoids 6'-O-acetyldiderroside, 7-methoxydiderroside, 8-O-tigloyldiderroside, kingiside, secoxyloganin, and diderroside, as well as iridoids loganin and loganetin.¹² Others constituents

include gardenoside, cyanidin, 5-hydroxymorin, 5-hydroxy-6-methoxycoumarin-7-glucoside, and taxifolin.¹⁰

Mora is made at our U.S. manufacturing facility and because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

INFLAMMATORY RESPONSE SUPPORT

A. millefolium may provide inflammatory support through the maintenance of cytokines such as INOS, COX-2, and IL-6 already within the normal range, as shown in preclinical studies.* It may also provide inflammatory support through the maintenance of human neutrophil elastase already within the normal range. In mice, A. millefolium helped to support normal dermal thickness and to maintain IgE levels already within the normal range. In Additionally, it may help to support normal filaggrin expression already within the normal range. In the healthy inflammatory response support from A. millefolium is partly attributed to its phenolic compounds, particularly apigenin, luteolin, and dicaffeoylquinic acids. In Apigenin may help to maintain IL-6, IL-8, and prostaglandin synthesis already within the normal range. In Fruticosus leaves contain cyanidin-3-0-glucoside which may help with healthy inflammatory response support by way of TNF-alpha and COX-2 inhibition.

ANTIOXIDANT SUPPORT

A. millefolium may provide antioxidant support, as quantified by DPPH assay, 6 which is attributed to its phenolic compounds. 7 R. fruticosus may also assist with antioxidant support. 18,19 The phenolic content of R. fruticosus has been determined spectrophotometrically, and the free radical scavenging capacity was determined via DPPH assay. 18 The constituent cyanidin-3-O-glucoside may provide particularly robust antioxidant support. 7 C. spruceanum may also help with antioxidant support, as quantified by DPPH, ABTS, singlet oxygen, superoxide anion radical, and beta-carotene bleaching methods. 10,11 In vivo antioxidant support was seen in Caenorhabditis elegans (C. elegans). 10

GASTROINTESTINAL SUPPORT

A. millefolium may help with gastrointestinal support.*20 It may help to support and maintain healthy gastrointestinal mucosa,²¹ attributed to antioxidant activity as measured by glutathione (GSH) and superoxide dismutase (SOD) levels in rats.*22 It may help to support intestinal smooth muscle relaxation,²⁰ attributed to the flavonoid content,³ and may also help to support hepatobiliary health, attributed to choleretic support from the dicaffeoylquinic acids.*3 Additionally, it may help to support normal gastric emptying, attributed to the constituent choline.*23 Ellagitannins from R. fruticosus may help to support healthy gastrointestinal mucosa through maintaining NF-kappaB already within the normal range.*24

OTHER USES

Microbial Support

A. millefolium may help with microbial support, 25 and may help with mycelial support.*25 R. fruticosus may also help with microbial support.*26 The most robust microbial support occurs with the hydro-alcoholic leaf extract, as quantified by a 6-11 mm zone of inhibition.*26

Neurological Support

A. millefolium may help to support a calm, healthy mood, the mechanism of which is not yet understood, though it is known to be independent of GABA receptor action. 27,28 R. fruticosus may also help to support a calm, healthy mood. 429

SAFETY AND CAUTIONS

Oral consumption of *A. millefolium* is generally well tolerated. There have been reports of urticaria or atopic dermatitis from topical exposure, which is generally attributed to the presence of sesquiterpene lactones.³⁰ Large amounts may cause diuretic effects.³¹ As *A. millefolium* may support diuresis, lithium dosage needs to be closely monitored and may need to be lowered.¹ *A. millefolium* may cause allergic reactions in those with allergies to other plants in the Asteraceae/Compositae family, such as ragweed.³² It may also have mild estrogenic effects.³³ *A. millefolium* is contraindicated in pregnancy.

R. fruticosus is generally well tolerated. There is little information available on potential side effects. Insufficient data is available to determine the safety of R. fruticosus leaf in pregnancy.*4

Data is currently limited for C. spruceanum, which has shown no evidence of toxicity in mice.³⁴

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

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<sup>1</sup> Natural Medicines. (2021, July 14). Yarrow [monograph]. http://naturalmedicines.therapeuticresearch.com
<sup>2</sup> Georgieva, L., Gadjalova, A., et al. (2015). International Food Research Journal, 22(4) 1347-1352.
<sup>3</sup> Benedek, B., & Kopp, B. (2007). Wiener medizinische Wochenschrift (1946), 157(13-14), 312-314.
4 Natural Medicines. (2021, July 14). Blackberry [monograph]. http://naturalmedicines.therapeuticresearch.com
<sup>5</sup> Verma, R., Gangrade, T., et al. (2014). Pharmacognosy Reviews, 8(16), 101–104.
<sup>6</sup> Ferlemi, A. V., & Lamari, F. N. (2016). Antioxidants (Basel, Switzerland), 5(2), 17.
7 Zia-Ul-Haq, M., Riaz, M., et al. (2014). Molecules (Basel, Switzerland), 19(8), 10998–11029.
<sup>8</sup> Polesna, L., Polesny, Z., et al. (2011). Pharmaceutical Biology, 49(2), 125–136.
9 Calycophyllum spruceanum (Benth.) Hook.f. ex K.Schum. Worldfloraonline.org. (2021). Retrieved 15 July 2021, from http://www.worldfloraonline.org/taxon/wfo-0000782163.
<sup>10</sup> Peixoto, H., Roxo, M., et al. (2018). Molecules (Basel, Switzerland), 23(3), 534.
<sup>11</sup> de Vargas, S. F., Almeida, P. D., et al. (2016). BMC Complementary and Alternative Medicine, 16, 83.
<sup>12</sup> Cardona Zuleta, L. M., Cavalheiro, A. J., et al. (2003). Phytochemistry, 64(2), 549–553.
<sup>13</sup> Ngo, H., Hwang, E., et al. (2020). The American Journal of Chinese Medicine, 48(5), 1121–1140.
14 Villalva, M., Jaime, L., et al. (2019). Food Research International (Ottawa, Ont.), 115, 128–134.
<sup>15</sup> Rathee, P., Chaudhary, H., et al. (2009). Inflammation & Allergy Drug Targets, 8(3), 229–235.
16 Guz, L., Adaszek, Ł., et al. (2019). Polish Journal of Veterinary Sciences, 22(2), 369–376.
<sup>17</sup> Barut, E. F., Barut, B., et al. (2017). Turkish Journal of Biochemistry, 42(4), 493-502.
18 Asnaashari, M., Tajik, R., & Khodaparast, M. H. (2015). Journal of Food Science and Technology, 52(8), 5180–5187.
19 Zielonka-Brzezicka, J., Nowak, A., et al. (2016). Pomeranian Journal of Life Sciences, 62(4), 52-59.
<sup>20</sup> Moradi, M. T., Rafieian-Koupaei, M., et al. (2013). African Journal of Traditional, Complementary, and Alternative Medicines: AJTCAM, 10(6), 499–503.
<sup>21</sup> Cavalcanti, A. M., Baggio, C. H., et al. (2006). Journal of Ethnopharmacology, 107(2), 277–284.
<sup>22</sup> Potrich, F. B., Allemand, A., et al. (2010). Journal of Ethnopharmacology, 130(1), 85–92.
<sup>23</sup> Borrelli, F., Romano, B., et al. (2012). Neurogastroenterology and Motility: The official journal of the European Gastrointestinal Motility Society, 24(2), 164–e90.
<sup>24</sup> Sangiovanni, E., Vrhovsek, U., et al. (2013). PloS One, 8(8), e71762.
<sup>25</sup> Stojanović, G., Radulović, N., et al. (2005). Journal of Ethnopharmacology, 101(1-3), 185–190.
<sup>26</sup> Weli, A. M., Al-Saadi, H. S., et al. (2020). Toxicology Reports, 7, 183–187.
<sup>27</sup> Baretta, I. P., Felizardo, R. A., et al. (2012). Journal of Ethnopharmacology, 140(1), 46–54.
<sup>28</sup> Sarris, J., McIntyre, E., & Camfield, D. A. (2013). CNS Drugs, 27(3), 207–219.
<sup>29</sup> Riaz, M., Zia-Ul-Haq, M., et al. (2014). Turkish Journal of Medical Sciences, 44(3), 454–460.
30 Jovanović, M., Poljacki, M., et al. (2004). Medicinski Pregled, 57 (5-6), 209-218.
31 de Souza, P., Crestani, S., et al. (2013). Journal of Ethnopharmacology, 149(1), 157–161.
<sup>32</sup> Hausen, B. M., Breuer, J., et al. (1991). Contact Dermatitis, 24(4), 274–280.
```

33 Saeidnia, S., Gohari, A., et al. (2011). Daru: Journal of Faculty of Pharmacy, Tehran University of Medical Sciences, 19(3), 173–186.

34 da Silva, A., Amorim, R., et al. (2018). Journal of Ethnopharmacology, 219, 103-109.

- Men's Wellness Support
- Healthy Aging
- Mood Support
- Immune Support



INTRODUCTION

Natural Boost is a comprehensive herbal formula designed to help maintain men's wellness and support healthy aging.*

Epimedium leaf (*Epimedium grandiflorum*) belongs to the Berberidaceae family and includes flavonoids, polysaccharides, lignans, phenol glycosides, and sesquiterpenes, among others.^{1,2} In traditional Chinese health practices, related Epimedium species known collectively as yin yang huo are used to support kidney yang, which encompasses healthy aging.* Today, this support is attributed to the constituent flavonoids and polysaccharides.*² Icarin, one of its flavonoids, may help maintain phosphodiesterase 5 (PDE-5) and testosterone levels already within the normal range.*³

Tribulus fruit (*Tribulus terrestris*), also known as puncture vine, belongs to the Zygophyllaceae family.⁴ It contains steroidal saponins such as spirostanol and furostanol; flavonoids such as quercetin and kaempferol; alkaloids such as tribulusamide C and tribulusterine; tannins; terpenoids; and polyphenols; among others.^{5,6}

Tribulus fruit may help maintain normal fertility by supporting the central nervous system and the anterior pituitary gland, as well as maintaining gonadal hormones and their receptors, already within the normal range.*7 Tribulus fruit has been used for centuries in both Chinese traditional health practices, where it is known as ci ji li, and traditional Ayurvedic health practices, where it is known as Gokshura.*8,5

L-arginine HCl is an essential amino acid needed for protein synthesis, specifically for nitric oxide synthase (NOS).*9,10

Jatropha stem (*Jatropha macrantha*) belongs to the Euphorbiaceae family, and is also known as Huanarpo macho. 11,12 lt has been used in traditional Peruvian

health practices for both men's and women's wellness.*13 lts contents include flavonoids, phenolic acids, lignans, coumarins, and terpenes, among others.12

Muira Puama bark (*Ptychopetalum olacoides*) belongs to the Olacaceae family and is native to the Amazon region, where it is used in traditional health practices to support healthy aging, maintain brain health, and support healthy stress management.* This support is attributed to its alkaloids, including magnoflorine and menispermine; it also includes the triterpenoid lupeol. In traditional use, it is used as an adaptogen to support mental, physical, and sexual wellness regardless of age.*

Maca root (*Lepidium meyenii*) belongs to the Brassicaceae family and is native to the Peruvian Andes.^{13,18} It is sometimes called Peruvian ginseng (though it is not a true ginseng) and may support healthy aging,^{18,19} attributed to the constituent macamides and glucosinolates.*¹⁹ Maca root has been used traditionally to support healthy sexual function and maintain healthy fertility.*¹³

Ginkgo leaf (*Ginkgo biloba*) belongs to the Ginkgoaceae family and contains flavonoids, terpenoids, and organic acids. It has been used in traditional Chinese health practices, where it is known as yin xing ye, since the 16th century.*20

Eurycoma root (*Eurycoma longifolia*) belongs to the Simaroubaceae family and its primary constituents include ellagic acid, quercetin, and rutin; quassinoids such as eurycomanone; and alkaloids.^{21,22} It has been used in the traditional health practices of Southeast Asian countries to support sexual wellness and healthy stress management.*²³

Eustephia bark (*Eustephia coccinea*) belongs to the Amaryllidaceae family and is used in the traditional health practices of Peru.²⁴

Saffron pistil (*Crocus sativus*) belongs to the Iridaceae family and its main constituents include crocin, picrocrocin and safranal.²⁵ It is used in traditional health practices as well as cooking.*²⁶

MEN'S WELLNESS

Healthy Sexual Function

Epimedium leaf (*E. grandiflorum*) contains icariin, a component that has been shown in rat studies to support healthy sexual function though maintaining endothelial nitric oxide synthetase (eNOS) already within the normal range.*²⁷ According to in vitro studies, it may also help to maintain levels of PDE-5 already within the normal range.*²⁸

Tribulus fruit (*T. terrestris*) may help support healthy sexual function, as seen in a 12-week randomized controlled trial.*²⁹ The mechanism is thought to be maintenance of eNOS already within the normal range and corresponding effects on the corpus cavernosum epithelium.*³⁰

L-arginine is an amino acid used in protein synthesis that may help maintain levels of nitric oxide (NO) already within the normal range, supporting normal sexual function.*31 In two randomized controlled trials with over 100 participants each, L-arginine supplementation helped maintain healthy sexual function, compared with placebo.*32,33

Jatropha stem (*J. macrantha*) may help maintain nitric oxide already within the normal range and support normal sexual function, as seen in rat studies.*12 Muira Puama bark, in a combination formula taken twice daily for three months, helped support healthy sexual function, according to a standardized scale.*34

Eurycoma root (*E. longifolia*) may help support healthy sexual function. In a randomized controlled trial, 45 healthy older men were randomly assigned to one of four groups: control + placebo, control + Eurycoma root, exercise + placebo, or exercise + Eurycoma root, daily for six months. While all of the intervention groups experienced some support, the exercise + Eurycoma root group experienced the most support in maintaining testosterone levels already within the normal range and supporting healthy sexual function.*35 Eurycoma root may help to maintain PDE-5 enzyme levels as well as aromatase-mediated estrogen levels already within the normal range.*21,23,4

Saffron pistil (*C. sativus*) may help maintain normal sexual function, according to a four-week randomized controlled trial with 36 men.*36 A meta-analysis of six trials found similar evidence for healthy sexual function support.*37

Normal Fertility

Epimedium leaf (*E. grandiflorum*) may help maintain a healthy epididymal sperm count already within the normal range, compared to control, as found in rat studies.*38

Tribulus fruit (*T. terrestris*) may help support healthy male fertility through maintaining spermatogenesis already within the normal range.*6 In a systematic review of seven human studies, six studies found Tribulus fruit to support normal fertility, helping maintain sperm count, motility, and morphology already within the normal range.*39

Maca root (*L. meyenii*) may support normal sperm motility and help maintain sperm concentration already within the normal range, according to a systematic review and meta-analysis of five randomized, controlled trials. A very small clinical study with nine healthy men taking maca root for four months found that maca helped maintain normal sperm count, sperm motility, and seminal volume, already within the normal range, though a larger double-blind placebocontrolled study with 69 men found evidence for only sperm concentration support.

Eurycoma root (E. longifolia), in a meta-analysis of two studies with a total of 139 participants, was found to support healthy sexual function in some men, though not all.*43 The quassinoid eurycomanone may maintain health sperm quality already within the normal range.*4

Hormonal Support

Epimedium leaf (*E. grandiflorum*) may help maintain normal testosterone levels already within the normal range, as found in rat studies.*38 While a randomized, single-blind placebo-controlled study suggested that Tribulus fruit supplementation for six weeks may help maintain testosterone levels already within the normal range in humans,44 the evidence is mixed.*45,46

L-arginine supplementation, according to a randomized controlled trial with 108 male participants, may help maintain testosterone levels already within the normal range.*32 Jatropha stem (*J. macrantha*) combined with Maca root (*L. meyenii*), according to a study with mice, may help maintain testosterone levels already within the normal range, attributed to the component saponins; human studies are needed.*13

Eurycoma root (*E. longifolia*), according to a meta-analysis of nine studies, five of which were randomized, controlled trials, may help maintain testosterone levels already within the normal range.*47 In a randomized, controlled trial, 32 men were randomly assigned to Eurycoma root or a placebo for two weeks. Compared to the placebo, the Eurycoma root group experienced significant support for maintaining testosterone levels already within the normal range, though without evidence of support for maintaining luteinizing hormone (LH), follicle-stimulating hormone (FSH), or sex hormone binding globulin (SHBG) already within the normal range.*48

HEALTHY AGING

Cardiovascular Support

Tribulus fruit (*T. terrestris*) may help maintain angiotensin-converting enzyme (ACE) already within the normal range, ⁴⁹ as well as healthy blood pressure already within the normal range. ^{*8} Larginine may be converted to nitric oxide, supporting vasodilation and maintaining normal blood flow. ^{*31} It may also help maintain healthy systolic and diastolic blood pressure already within the normal range, according to a review of meta-analyses. ^{*9} Ginkgo leaf (G. biloba) may help support cardiovascular health by maintaining insulin sensitivity and a healthy insulin response, already within the normal range. ^{*50}

Saffron pistil (*C. sativus*), according to meta-analysis of ten studies with 622 participants, may help maintain diastolic blood pressure already within the normal range.*51 It may also, according to a meta-analysis of nine studies with 595 participants, help maintain waist circumference and fasting blood glucose levels already within the normal range.*52 Another meta-analysis of 25 randomized, controlled trials also found that Saffron pistil may help maintain fasting blood glucose already within the normal range, though a decrease in waist circumference was non-significant.*53

Cognitive Support

Muira Puama bark (*P. olacoides*), according to mouse studies, may support memory and cognition through maintaining acetylcholinesterase (AChE) levels already within the normal range, though human studies are needed.*14,54 Mouse studies have also shown that Muira Puama bark ethanol extract may help maintain levels of A-beta already within the normal range.*54

Ginkgo leaf (*G. biloba*), according to one randomized, controlled trial, may help with neurocognitive support by maintaining brain-derived neurotropic factor (BDNF) levels already within the normal range.*55 Another study found that ginkgo may help maintain cerebral blood flow already within the normal range.*56

Bone Support

Eurycoma root (*E. longifolia*) may help support healthy bone density, maintaining bone calcium levels already within the normal range during healthy aging.*23 The constituent eurypeptides may help maintain DHEA already within the normal range, which may help maintain sex hormones such as testosterone already within the normal range.*23

OTHER

Mood and Sleep Support

According to a meta-analysis of nine randomized trials, Saffron pistil (*C. sativus*) may help maintain a healthy mood.*⁵⁷ According to a meta-analysis of 21 randomized trials, saffron pistil may help maintain both mood and sleep already within the normal range.*⁵⁸ Other meta-analyses suggest that saffron pistil may help maintain healthy sleep duration and normal sleep quality.*^{59,60}

Immune Support

Eurycoma root (*E. longifolia*), according to a four-week randomized, controlled trial with 126 middle-aged adults, may help maintain total, naïve, and CD4+ T cell numbers already within the normal range.*61

SAFETY AND CAUTIONS

Epimedium leaf (*E. grandiflorum*) is generally well tolerated, ^{41,45,46}, and animal studies have not shown toxicity.2 Side effects may include dizziness, dry mouth, or thirst.45 Theoretically, Epimedium leaf may increase the risk of bleeding when taken with anticoagulant or antiplatelet medications. ⁴⁵

Tribulus fruit (*T. terrestris*) is generally well tolerated. ⁴⁷⁻⁴⁹ Tribulus fruit should be avoided in pregnancy as it has affected fetal development in animal studies. ⁴⁷ It may increase the levels and adverse effects of lithium when taken concurrently. ⁴⁷

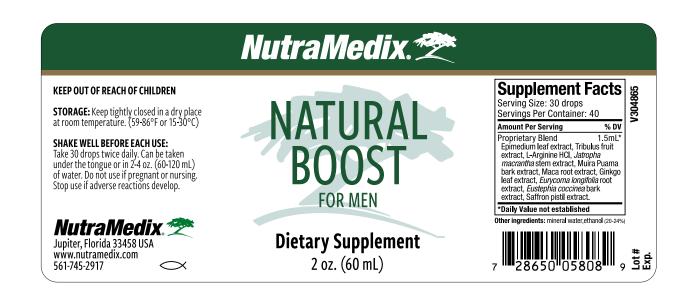
Jatropha stem (*J. macrantha*) has a long history of safe use in traditional health practices and is generally well tolerated.¹² There are no currently known interactions with pharmaceuticals.

Muira puama bark (*P. olacoides*) is generally well tolerated. In one mouse study, it had additive effects with diazepam.⁵⁰ While there are no known adverse effects or drug interactions in humans,¹⁵ it is worth noting that molecular docking studies have shown that eight compounds in Muira puama bark may bind to estrogen receptors, resulting in selective estrogen receptor modulation,⁵¹ and caution may is warranted in those with estrogen-sensitive conditions.

Maca root (*L. meyenii*) is generally well tolerated and has been used for centuries to support sexual function. No adverse events have been reported in clinical trials,18,52 and there are no currently known interactions in humans.⁵²

Eurycoma root (*E. longifolia*) is generally well tolerated and shows little inhibition of CYP isoenzymes, making CYP-related drug interactions unlikely.²¹ Due to potential effects on estrogen levels, it should be avoided in those with estrogen-receptor positive breast cancer.²¹ It may reduce the levels and effectiveness of propranolol.^{21,53}

Eustephia bark (*E. coccinea*) has a long history of safe use in traditional Peruvian medicine, though information is limited.²²



- ¹ Tan, H. L., Chan, K. G., et al. (2016). Frontiers in Pharmacology, 7, 191.
- ² Ma, H., He, X., et al. (2011). Journal of Ethnopharmacology, 134(3), 519–541.
- ³ Niu, Y., Lin, G., et al. (2022). *Translational Andrology and Urology*, 11(7), 1007–1022.
- ⁴ Abarikwu, S. O., Onuah, C. L., & Singh, S. K. (2020). Andrologia, 52(3), e13509.
- ⁵ Ștefănescu, R., Tero-Vescan, A., et al. (2020). *Biomolecules, 10*(5), 752.
- ⁶ Zhu, W., Du, Y., et al. (2017). Chemistry Central Journal, 11(1), 60.
- ⁷ Sirotkin, A. V., & Kolesárová, A. (2021). *Physiological Research*, 70(Suppl4), S657–S667.
- ⁸ Chhatre, S., Nesari, T., et al. (2014). Pharmacognosy Reviews, 8(15), 45-51.
- ⁹ McRae, M. P. (2016). Journal of Chiropractic Medicine, 15(3), 184–189.
- ¹⁰ Natural Medicines. (2021, October 13). L-Arginine [monograph]. http://natural-medicines.therapeuticresearch.com
- ¹¹ Apaza T, L., Antognoni, F., et al. (2021). *Natural Product Research*, *35*(24), 5843–5847.
- ¹² Tinco-Jayo, J. A., Aguilar-Felices, E. J., et al. (2021). *Molecules (Basel, Switzerland)*, 27(1), 115.
- ¹³ Oshima, M., Gu, Y., & Tsukada, S. (2003). *The Journal of Veterinary Medical Science*, *65*(10), 1145–1146.
- ¹⁴ da Silva, A. L., Silva Martins, B. D., et al. (2009). *Psychopharmacology*, 202(1-3), 165–172.
- ¹⁵ Tian, X., Guo, S., et al. (2018). *Natural Product Research*, 32(3), 354–357.
- ¹⁶ Natural Medicines. (2020, September 22). Muira Puama [monograph]. http://naturalmedicines.therapeuticresearch.com
- ¹⁷ Piato, A. L., Detanico, B. C., et al. (2010). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 17(3-4), 248–253.
- ¹⁸ Shin, B. C., Lee, M. S., et al. (2010). *BMC Complementary and Alternative Medicine*, 10, 44.
- ¹⁹ Beharry, S., & Heinrich, M. (2018). *Journal of Ethnopharmacology*, 211, 126–170.
- ²⁰ Eastland Herb. (2018). Eastland Herb Chinese herbal medicine: Materia medica and formula & strategies (4.3). [mobile app]. App store. https://apps.apple.com/us/app/eastland-herb-chinese-medicine/id737380894.
- ²¹ Ganapathy, A., Hari Priya, V. M., & Kumaran, A. (2021). *Journal of Ethnopharmacology, 267*, 113536.
- ²² George, A., & Henkel, R. (2014). Andrologia, 46(7), 708-721.
- ²³ Rehman, S. U., Choe, K., & Yoo, H. H. (2016). *Molecules (Basel, Switzerland)*, 21(3), 331.
- ²⁴ Bussmann, R. W., & Glenn, A. (2010). *Journal of Ethnobiology and Ethnomedicine*, 6, 30.
- ²⁵ Khazdair, M. R., Boskabady, M. H., et al. (2015). *Avicenna Journal of Phytomedicine*, *5*(5), 376–391.
- $^{\rm 26}$ Natural Medicines. (2022, September 6). Saffron [monograph]. http://natural-medicines.therapeuticresearch.com
- ²⁷ Liu, Q. W., Yang, Z. H., et al. (2021). *Andrology, 9*(1), 342–351.
- ²⁸ Chau, Y., Li, F. S., Levsh, O., & Weng, J. K. (2019). *PloS One, 14*(9), e0222803.
- ²⁹ Kamenov, Z., Fileva, S., et al. (2017). *Maturitas, 99*, **20–26**.
- ³⁰ Do, J., Choi, S., et al. (2013). Korean Journal of Urology, 54, 183-188.
- ³¹ Maccallini, C., & Amoroso, R. (2022). *Molecules (Basel, Switzerland), 27*(20), 6820.
- ³² El Taieb, M., Hegazy, E., & Ibrahim, A. (2019). *The Journal of Sexual Medicine*, *16*(9), 1390–1397.
- ³³ Abu El-Hamd, M., & Hegazy, E. M. (2020). *Andrologia*, *52*(7), e13640.
- ³⁴ Nguyen, S., Rajfer, J., & Shaheen, M. (2018). *Translational andrology and uroloay*, 7(2), 266–273.
- ³⁵ Leitão, A. E., Vieira, M., et al. (2021). *Maturitas*, *145*, 78–85.
- ³⁶ Modabbernia, A., Sohrabi, H., et al. (2012). *Psychopharmacology*, 223(4), 381–388.

- ³⁷ Maleki-Saghooni, N., Mirzaeii, K., et al. (2018). *Avicenna Journal of Phytomedicine*, *8*(3), 198–209.
- ³⁸ Chen, M., Hao, J., et al. (2014). *Molecules (Basel, Switzerland), 19*(7), 9502–9514.
- ³⁹ Sanagoo, S., Sadeghzadeh Oskouei, B., et al. (2019). *Complementary Therapies in Medicine*, 42, 95–103.
- ⁴⁰ Lee, H. W., Lee, M. S., et al. (2022). Frontiers in Pharmacology, 13, 934740.
- ⁴¹ Gonzales, G. F., Cordova, A., et al. (2001). Asian Journal of Andrology, 3(4), 301–303.
- ⁴² Alcalde, A. M., & Rabasa, J. (2020). Andrologia, 52(10), e13755.
- ⁴³ Kotirum, S., Ismail, S. B., & Chaiyakunapruk, N. (2015). *Complementary Therapies in Medicine*, *23*(5), 693–698.
- ⁴⁴ Fernández-Lázaro, D., Mielgo-Ayuso, J., et al. (2021). Nutrients, 13(11), 3969.
- 45 Santos, H. O., Howell, S., & Teixeira, F. J. (2019). *Journal of Ethnopharmacology*, 235, 392–405.
- ⁴⁶ Kovac, J. R., Pan, M., et al. (2016). *American Journal of Men's Health, 10*(6), NP109–NP117.
- ⁴⁷ Leisegang, K., Finelli, R., et al. (2022). *Medicina (Kaunas, Lithuania)*, *58*(8), 1047.
- ⁴⁸ Chan, K. Q., Stewart, C., et al. (2021). Andrologia, 53(4), e14001.
- ⁴⁹ Kamrani Rad, S. Z., Javadi, B., et al. (2019). *Avicenna Journal of Phytomedicine*, *9*(4), 291–309.
- ⁵⁰ Siegel, G., Ermilov, E., et al. (2014). *Atherosclerosis*, 237(2), 584–588.
- ⁵¹ Pourmasoumi, M., Hadi, A., et al. (2019). *Pharmacological Research, 139*, 348–359.
- 52 Rahmani, J., Bazmi, E., et al. (2020). *Complementary Therapies in Medicine, 49,* 102298.
- ⁵³ Tahmasbi, F., Araj-Khodaei, M., et al. (2022). *Phytotherapy Research: PTR*, *36*(9), 3394–3414.
- ⁵⁴ Figueiró, M., Ilha, J., et al. (2011). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, *18*(4), 327–333.
- ⁵⁵ Sadowska-Krępa, E., Kłapcińska, B., et al. (2017). Nutrients, 9(8), 803.
- ⁵⁶ Mashayekh, A., Pham, D. L., et al. (2011). *Neuroradiology*, *53*(3), 185–191.
- ⁵⁷ Tóth, B., Hegyi, P., et al. (2019). *Planta Medica*, 85(1), 24-31.
- ⁵⁸ Ghaderi, A., Asbaghi, O., et al. (2020). *Complementary Therapies in Medicine,* 48, 102250.
- ⁵⁹ Lian, J., Zhong, Y., et al. (2022). *Sleep Medicine*, *92*, 24–33.
- ⁶⁰ Munirah, M. P., Norhayati, M. N., & Noraini, M. (2022). *International Journal of Environmental Research and Public Health*, 19(18), 11658.
- ⁶¹ George, A., Suzuki, N., et al. (2016). *Phytotherapy Research: PTR*, *30*(4), 627–635.
- ⁶² Natural Medicines. (2021, August 26). Horny Goat Weed [monograph]. http://naturalmedicines.therapeuticresearch.com
- ⁶³ Natural Medicines. (2022, July 11). Tribulus [monograph]. http://naturalmedicines.therapeuticresearch.com
- ⁶⁴ Brunetti, P., Lo Faro, A. F., et al. (2020). *Pharmaceuticals (Basel, Switzerland)*, 13(10), 309.
- 65 Powers, C. N., & Setzer, W. N. (2015). In Silico Pharmacology, 3, 4.
- 66 Natural Medicines. (2022, July 11). Maca [monograph]. http://naturalmedicines.theraneuticresearch.com
- ⁶⁷ Natural Medicines. (2022, August 2). Ginkgo [monograph]. http://naturalmedicines.therapeuticresearch.com
- ⁶⁸ Natural Medicines. (2022, September 29). Eurycoma Longifolia [monograph]. http://naturalmedicines.therapeuticresearch.com

- Supports Healthy Inflammatory Response
- Antioxidant
- Immune System Support
- Microbial Support



INTRODUCTION

Noni is a liquid extract made from the fruit of the Indian Mulberry (*Morinda citrifolia*) tree. *M. citrifolia* belongs to the Rubiaceae family. Noni is believed to have originated in the Indonesian archipelago and have spread during the Polynesian migration. While Noni is native to Southeast Asia and Australasia, it is now cultivated on multiple continents in nutrient-rich volcanic soil. Polynesians have used *M. citrifolia* in traditional folk healing for over 2,000 years, including the fruit, flowers, leaves, bark, stems, and roots. The fruit has been consumed as a food for hundreds of years, particularly in times of famine, and in 2003, was approved as a novel food by the European Commission. Other names for Indian Mulberry (Morinda citrifolia) include hog apple, Hawaiian Noni, canarywood, cheese fruit, and mengkudu.

In traditional Chinese health practices, the root of related species *Morinda officinalis*, known as *ba ji tian*, has been used for centuries, with the oldest known written mention dating back to the second century *Shen Nong Ben Cao Jing*, or *Shen Nong's Herbal Classic.*⁵ Noni fruit from *M. citrifolia*, a new addition to the traditional Chinese materia medica, is described as having an affinity for the kidney, liver, and spleen, and is used for deficiency conditions, tendon health, and bone health.*6

Constituents of Noni fruit include polysaccharides such as homogalacturonan and rhamnogalacturonan I, iridoids such as asperuloside and asperulosidic acid, flavonoid glycosides such as rutin and narcissoside, anthraquinones such as ribiadin and damnacanthal, lignans such as 3,3'-bisdemethylpinoresinol and morindolin, and coumarins such as scopoletin, in addition to carotenoids, phytosterols, and others.\(^1\) Some sources suggest that anthraquinones, particularly alizarin, rubiadin, and lucidin, are absent in ripe Noni fruit, attributing their presence in some samples to the inadvertent inclusion of fruit skin, seeds, or leaves.\(^2\) Noni also contains potassium (K\(^4\)), calcium (Ca\(^2\)), sodium (Na\(^4\)),

magnesium (Mg²⁺), and vitamin C.¹

Noni is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

SUPPORTS HEALTHY INFLAMMATORY RESPONSE

Healthy inflammatory response support has been seen both in vitro and in vivo, and current ethnobotanical use for this purpose persists in the Fiji islands and beyond. Noni may help to maintain phase II enzyme function already within the normal range through the support of quinone reductase (QR), which may help to support a healthy inflammatory response by promoting normal cell signaling. Noni fruit may also help to maintain TNF-alpha levels already within the normal range, as 5-lipooxygenase (5-LOX) and Nrf2 levels already within the normal range.

Constituent flavonoids such as quercetin and kaempferol may contribute antioxidant activity to support a healthy inflammatory response.*8,70 Constituent flavonoids may also help to maintain histamine release, leukocyte migration, prostaglandin E2 (PGE2) and leukotriene-B4 (LTB-4) already within the normal range.*4 Additionally, flavonoids may help to maintain IL-2 secretion and T-cell proliferation already within the normal range via the MAPK and phospholipase-C pathways.*4 Constituent iridoids may help to maintain COX-1, COX-2, PGE2, and nitric oxide (NO) already within the normal range.*4,7,8

A heteropolysaccharide including homogalacturonan and rhamnogalacturonan was found to contribute healthy inflammatory response support both in vitro and in vivo, via mechanisms including maintaining leukocyte migration already within the normal range, nociception already within a normal and comfortable range, and bradykinin already within the normal range.**

Noni fruit was comparable to positive control in maintaining metalloproteinase 9 (MMP-9) already within the normal range in human monocytes, as well as comparable to positive control for comfort in a study with mice, validating centuries of ethnobotanical use for healthy inflammatory response support. Additionally, Noni may help to maintain levels of high-sensitivity C-reactive protein (hsCRP) already within the normal range (p<0.05; p<0.001). 12,13

ANTIOXIDANT

Noni fruit may contribute antioxidant activity, as evidenced by Oxygen Radical Absorbance Capacity (ORAC) assay, 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, and peroxynitrite (ONOO') assay. *8,14* The phenolic content has been verified by the Folin-Ciocalteu method. *8* The antioxidant activity is attributed to the constituent iridoid glycosides, ascorbic acid, and phenolic compounds such as flavonoids, *4.8* and has been seen both in vitro and in vivo. *8* The constituent phenolics may support both antioxidant activity and a healthy inflammatory response. *10* Noni may help to maintain levels of malondialdehyde (MDA) already within the normal range (p<0.001). *13* It may also help to maintain plasma superoxide anion radicals (p<0.01; p<0.001) and lipid hydroperoxide (p<0.001; p<0.001) already within the normal range. *15*

OTHER USES

Immune System Support

Noni fruit may help with immune system support for innate, cell-mediated, and humoral immunity, generally attributed to the constituent polysaccharides.*4 Noni's polysaccharides help to promote a normal cytokine and chemokine response and to support normal phagocytic neutrophil activity.*4

Microbial Support

Noni fruit may offer microbial support, attributed to the constituents acubin, L-asperuloside, and alizarin.*3

SAFETY AND CAUTIONS

Noni is considered safe when used appropriately,¹⁶ and has been used safely in 2,000 years of ethnobotanical practice.¹ Upon ingestion of Noni puree, the constituent scopoletin peaks after two hours, has a half-life of four hours, and is excreted in the urine.^{16,18} Small clinical trials have used Noni without significant side effects, ^{17,18} though there have been reports of nausea and abdominal discomfort with the use of dehydrated Noni fruit.¹⁸ While there have been case reports of hepatotoxicity as evidenced by elevated liver enzymes, these were mostly, though not solely, attributed to multiple-ingredient formulas or prior history of liver toxicity.^{19,20,21} It remains unclear whether the hepatotoxicity was due to Noni, additional ingredients, possible contaminants, or other factors in the medical history.^{19,20,21} In most cases, elevated liver enzymes returned to normal levels after discontinuing Noni;^{19,21} the one case with a prior history of toxic hepatitis from acetaminophen experienced liver failure and required a liver transplant.²⁰

Noni may have additive effects with antihypertensive medications.¹⁶ Noni should be used with caution in chronic kidney disease, as its potassium content may contribute to hyperkalemia.⁴ Due to Noni's relatively high potassium content of approximately 56 mEq of potassium per liter, it should be used with caution in patients taking medications that may raise potassium levels, including potassium-sparing diuretics such as amiloride and spironolactone, ACE inhibitors (ACEIs) such as lisinopril and captopril, and angiotensin receptor blockers (ARBs) such as losartan and valsartan, due to the risk of hyperkalemia.¹⁶ Taking Noni with potentially hepatotoxic drugs may theoretically increase the risk of hepatotoxicity.^{16,20} There has been one case report regarding Noni decreasing the effectiveness of coumadin; however, it is noted that the Noni was part of a combination product with over 115 other substances, many of which were high in vitamin K.²³ Use during pregnancy and lactation should be avoided, as there is insufficient reliable evidence of safety in these circumstances.¹⁶

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Potterat, O., & Hamburger, M. (2007). Planta Medica, 73(3), 191–199.
- ² Bussmann, R. W., Hennig, L., et al. (2013). Evidence-Based Complementary and Alternative Medicine: eCAM, 2013, 208378.
- ³ Wang, M. Y., West, B. J., et al. (2002). Acta Pharmacologica Sinica, 23(12), 1127–1141.
- ⁴ Lohani, M., Majrashi, M., et al. (2019). Complementary Therapies in Medicine, 47, 102206.
- ⁵ Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 891-892). Art of Medicine Press.
- 6 Liu, J. L., Zhang, R., et al. (2020). Zhongguo Zhong Yao Za Zhi = Zhongguo Zhongyao Zazhi = China Journal of Chinese Materia Medica, 45(5), 984–990.
- 7 Nitteranon, V., Zhang, G., et al. (2010). Food Research International, 44, 2271-2277.
- B Dussossoy, E., Brat, P., et al. (2011). Journal of Ethnopharmacology, 133(1), 108–115.
- 9 Basar, S., Uhlenhut, K., et al. (2010). *Phytotherapy Research: PTR*, 24(1), 38–42.
- ¹⁰ Serafini, M. R., Santos, R. C., et al. (2011). *Journal of Medicinal Food*, 14(10), 1159–1166.
- ¹¹ Sousa, S. G., Oliveira, L. A., et al. (2018). *Carbohydrate Polymers*, 197, 515–523.
- ¹² Wang, M. Y., Peng, L., et al. (2012). *The Scientific World Journal*, 2012, 594657.
- ¹³ Yilmaz, M. I., Romano, M., et al. (2020). Scientific Reports, 10(1), 9018.
- ¹⁴ Su, B. N., Pawlus, A. D., et al. (2005). *Journal of Natural Products*, 68(4), 592–595.
- 15 Wang, M. Y., Lutfiyya, M. N., et al. (2009). Chemistry Central Journal, 3, 13.
- 16 Natural Medicines. (2021, September 8). Noni [monograph]. http://naturalmedicines.therapeuticresearch.com
- ¹⁷ Prapaitrakool, S., & Itharat, A. (2010). Journal of the Medical Association of Thailand = Chotmaihet Thangphaet, 93 (7, Suppl.), S204–S209.
- ¹⁸ Issell, B. F., Gotay, C. C., et al. (2009). *Journal of Dietary Supplements*, 6(4), 347–359.
- 19 Millonig, G., Stadlmann, S., & Vogel, W. (2005). European Journal of Gastroenterology & Hepatology, 17(4), 445–447.
- ²⁰ Stadlbauer, V., Fickert, P., et al. (2005). World Journal of Gastroenterology, 11(30), 4758–4760.
- ²¹ Yuce, B., Gulberg, V., et al. (2006). *Digestion*, 73(2-3), 167–170.
- ²² Mueller, B. A., Scott, M. K., et al. (2000). American journal of kidney diseases: The Official Journal of the National Kidney Foundation, 35(2), 310–312.
- ²³ Carr, M. E., Klotz, J., & Bergeron, M. (2004). American Journal of Hematology, 77(1), 103.

- Microbial Support
- Antioxidant Support
- Inflammatory Response Support



INTRODUCTION

This product is a synergistic blend of Elecampane (Inula helenium) root, Jalapa (Ipomoea purga) root, Blackberry (R. fruticosus) leaves, and Capirona (Calycophyllum spruceanum) bark. It is designed to assist with comprehensive microbial support, with additional antioxidant support and healthy inflammatory response support.*

Our liquid extracts are made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

I. helenium belongs to the Asteraceae/Compositae family.¹ The root includes volatile oils such as alantolactone, isoalantolactone, alantol, alpha- and beta-bergamotene, beta-pinene, and anethole; amino acids such as aspartic acid, serine, threonine, and glutamic acid; sterols such as stigmasterol and beta-sitosterol; and thymol derivatives.²-⁴ Alantolactone and isoalantolactone are considered the main constituents.³-5 The main phenolic compounds that may help with antioxidant support are the phenolic acids (caffeic, dicaffeoyl quinic, chlorogenic, and hydroxybenzoic), terpenes (alantolactone and isoalantolactone), and flavonoids (epicatechin, catechin gallate, dihydroquercetin pentosyl rutinoside, quercetin-3-0-beta-glucopyranoside, ferulic acid-4-0-glucoside, and kaempherol-7-Odipentoside).⁴ The roots also include dietary fiber from fructooligosaccharides and inulin. † *I. helenium* root has been used in traditional Chinese health practices for gastrointestinal support, where it is known as tu mu xiang. *³ *I. helenium* may help with microbial support, as determined by the agarwell diffusion method. *8.9 It may also help with mycelial support. *9

Ipomoea purga is commonly known as jalap root and belongs to the Convolvulaceae family. Synonyms for *I. purga* include *Ipomoea jalapa, Ipomoea schiedeana, Convolvulus officinalis, Convolvulus purga* and *Exogonium purga*.¹⁰⁻¹² *I. purga* is a climbing vine that is native to southern Mexico.12 The root has been used in traditional health practices to support gastrointestinal regularity, ¹³ with other potential benefits under current investigation.* ¹⁴ Constituents of *I. purga* root include convolvulin, jalapine, caffeic acid, scopoletin, valeric acid, starch,

and tiglic acid. ^14,15 *I. purga* has a long history of traditional use for supporting healthy gastrointestinal regularity and maintaining healthy peristalsis. *10,13,14

R. fruticosus belongs to the Rosaceae family and is commonly known as blackberry. Synonyms for *R. fruticosus* include *R. plicatus*, *R. affinis*, *R. canadensis*, *R. millspaughii*, and *R. laciniatus*.¹⁶ *R. fruticosus* leaves have been traditionally used for microbial support.*¹⁷ The leaves contain phenolic acids such as neo-chlorogenic acid, caffeic acid, gallic acid, p-coumaric acid, and ellagic acid; flavonols such as quercetin, quercetin-3-0-galactoside, quercetin-3-0-glucuronide, and kaempferol; flavan-3-ols such as catechin, epicatechin, and epicatechin gallate methyl gallate; ellagitannins such as sanguiin H-6/lambertianin C, and casuarinin; anthocyanins such as cyanidin-3-0-glucoside; and triterpene acids such as rubinic acid and rubusic acid.^{18,19} They also contain tannins, villosin, gallic acid, and iron.¹⁷ *R. fruticosus* may also help with microbial support,²⁰ antioxidant support,^{19,21} healthy inflammatory response support,¹⁹ neurological support,²² and gastrointestinal support.*²³

C. spruceanum belongs to the Rubiaceae family and is commonly known as Capirona. A synonym for this plant is *Eukylista spruceana*. It is native to the Amazon rainforest and is sometimes called the Tree of Youth. It has been used in traditional health practices for healthy inflammatory response support. Constituents of *C. spruceanum* include seco-iridoids 6'-O-acetyldiderroside, 7-methoxydiderroside, 8-O-tigloyldiderroside, kingiside, secoxyloganin, and diderroside, as well as iridoids loganin and loganetin. Other constituents include gardenoside, cyanidin, 5-hydroxymorin, 5-hydroxy-6-methoxycoumaringlucoside, and taxifolin. *C. spruceanum* may also help with antioxidant support. Takes to the support of the suppor

MICROBIAL SUPPORT

I. helenium may help with microbial support, as determined by the agar-well diffusion method.*8,9 It may also help with mycelial support.*9 *R. fruticosus* may also help with microbial support. The most robust microbial support occurs with the hydro-alcoholic leaf extract, as quantified by a 6-11 mm zone of inhibition.*20

ANTIOXIDANT SUPPORT

I. helenium root extract may help with antioxidant support, as determined by DPPH, phosphomolybdenum, beta-carotene bleaching, ABTS, FRAP, and CUPRAC assays.*7.8 Flavonoids are found in all plant parts, and the relevant phenolic compounds, concentrated in the inflorescence, leaves, and root, are highly soluble in ethanol.*29 The constituent alantolactone may help to support levels of quinone reductase, glutathione S-transferase (GST), and glutathione reductase already within the normal range, in a dose-dependent manner.*30 The antioxidant support of I. helenium is attributed to effects on PI3K and JNK signaling pathways, with support of Nrf2 already within the normal range.*30

The phenolic content of *R. fruticosus has* been determined spectrophotometrically, and the free radical scavenging capacity was determined via DPPH assay.*21 The constituent cyanidin-3-O-glucoside may provide particularly robust antioxidant support.*19 *C. spruceanum* may also help with antioxidant support, as quantified by DPPH, ABTS, singlet oxygen, superoxide anion radical, and beta-carotene bleaching methods.*26,27 In vivo antioxidant support was seen in *Caenorhabditis elegans* (C. elegans).*26

INFLAMMATORY RESPONSE SUPPORT

Isoalantolactone, a sesquiterpene lactone found in I. helenium, may help with healthy inflammatory support.*31 In vitro research has shown that isoalantolactone may help to maintain NF-kappa B already within the normal range.*31 Alantolactone and isoalantolactone may help to maintain levels of IgE, TNF-alpha, and IFN-gamma already within the normal range.*32 They may also help to maintain IL-4, IL-5 and IL-13 already within the normal range.*32 Additionally, the sesquiterpene lactone igalan may help with healthy inflammatory support.*33 R. fruticosus leaves contain cyanidin-3-Oglucoside which may help with healthy inflammatory response support by way of TNF-alpha and COX-2 inhibition.*1

SAFETY AND CAUTIONS

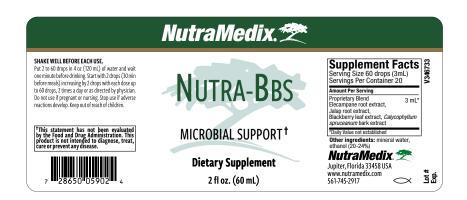
Information on the adverse effects of Inula helenium is limited. I. helenium may cause allergic reactions in those with allergies to other plants in the Asteraceae/ Compositae family, such as ragweed.³⁴ Cases of contact dermatitis have been reported, which may be attributed to the sesquiterpene lactones alantolactone and isoalantolactone. 35,36 I. helenium may have additive effects with CNS depressants.³⁴ Large amounts of I. helenium may cause vomiting and diarrhea.³⁷ Rarely, large amounts of *I. helenium* root may cause spasms or symptoms of paralysis.3

1. purga may cause purgative effects, which are contra-indicated in pregnancy.38,39 It is also contraindicated in gastrointestinal inflammation or infection.⁴⁰ *I. purga* contains cathartic gluco-resins which may intensify peristalsis, increasing water elimination.^{13,41} Consequently, it is contraindicated in those taking stimulant laxatives as it may have additive effects, leading to dehydration and electrolyte imbalance. ⁴² In addition, *I*. purga may have additive effects with diuretic-induced potassium loss. 42 Fluid and electrolyte imbalance may theoretically increase INR and risk of bleeding in those taking warfarin.¹⁰ Electrolyte imbalance may also worsen the toxicity of cardiac glycosides.⁴³

R. fruticosus is generally well tolerated. There is little information available on potential side effects. Insufficient data is available to determine the safety of R. fruticosus leaf in pregnancy.16 Data is currently limited for C. spruceanum, which has shown no evidence of toxicity in mice. 44

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

1 Lunz, K., & Stappen, I. (2021). Molecules (Basel, Switzerland), 26(11), 3155.

2 Brinker, F. (2001). Herb contraindications & drug interactions (p. 85). Eclectic Medical Publications.

3 Eastland Herb. (2018). Eastland Herb - Chinese herbal medicine: Materia medica and formula & strategies (4.3). [mobile app].

App store. https://apps.apple.com/us/app/eastland-herb-chinese-medicine/id737380894. 4 Stojakowska, A., Malarz, J., & Kisiel, W. (2004). Zeitschrift fur Naturforschung. C, Journal of Biosciences, 59(7-8), 606-608.

5 Konishi, T., Shimada, Y., et al. (2002). Biological & Pharmaceutical Bulletin, 25(10), 1370–1372.

6 Spiridon, I., Nechita, C. B., et al. (2013). Central European Journal of Chemistry, 11(10), 1700-1710.

7 Petkova, N., Vrancheva, R., et al. (2015). Journal of Bioscience Technology, 4(1), 101-107.

8 Albayrak, S., Korkmaz Cinar, A. E., et al. (2015). Iranian Journal of Science & Technology, 39A4, 473-483.

9 Deriu, A., Zanetti, S., et al. (2008). International Journal of Antimicrobial Agents, 31(6), 588-590.

10 Natural Medicines. (2021, July 10). Jalap [monograph]. http://naturalmedicines.therapeuticresearch.com 11 Ipomoea purga (Wender.) Hayne. Worldfloraonline.org. (2021). Retrieved 10 July 2021, from http://www.worldfloraonline.org/ taxon/wfo-0001296675#description.

12 Ipomoea purga (Wender.) Hayne | Plants of the World Online | Kew Science. Plants of the World Online. (2021). Retrieved 10 July 2021, from http://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:269627-1.

13 Pereda-Miranda, R., Fragoso-Serrano, M., et al. (2006). Journal of Natural Products, 69(10), 1460-1466.

14 Ipomoea purga (Convolvulaceae). Dr. Duke's Phytochemical and Ethnobotanical Databases U.S. Department of Agriculture.

(2021). Retrieved 10 July 2021, from https://phytochem.nal.usda.gov/phytochem/plants/show/1081.

15 Meira, M., Pereira da Silva, E., et al. (2012). Brazilian Journal of Pharmacognosy, 22(3), 682-713.

16 Natural Medicines. (2021, July 14). Blackberry [monograph]. http://naturalmedicines.therapeuticresearch.com

17 Verma, R., Gangrade, T., et al. (2014). Pharmacognosy Reviews, 8(16), 101-104.

18 Ferlemi, A. V., & Lamari, F. N. (2016). Antioxidants (Basel, Switzerland), 5(2), 17.

19 Zia-Ul-Haq, M., Riaz, M., et al. (2014). Molecules (Basel, Switzerland), 19(8), 10998-11029.

20 Weli, A. M., Al-Saadi, H. S., et al. (2020). Toxicology Reports, 7, 183-187.

21 Asnaashari, M., Tajik, R., & Khodaparast, M. H. (2015). Journal of Food Science and Technology, 52(8), 5180-5187.

22 Riaz, M., Zia-Ul-Haq, M., et al. (2014). Turkish Journal of Medical Sciences, 44(3), 454-460.

23 Sangiovanni, E., Vrhovsek, U., et al. (2013). PloS One, 8(8), e71762.

24 Polesna, L., Polesny, Z., et al. (2011). Pharmaceutical Biology, 49(2), 125-136.

25 Calycophyllum spruceanum (Benth.) Hook.f. ex K.Schum. Worldfloraonline.org. (2021). Retrieved 15 July 2021, from http:// www.worldfloraonline.org/taxon/wfo-0000782163.

26 Peixoto, H., Roxo, M., et al. (2018). Molecules (Basel, Switzerland), 23(3), 534.

27 de Vargas, S. F., Almeida, P. D., et al. (2016). BMC Complementary and Alternative Medicine, 16, 83.

28 Cardona Zuleta, L. M., Cavalheiro, A. J., et al. (2003). Phytochemistry, 64(2), 549–553.

29 Zlatić, N., Jakovljević, D., & Stanković, M. (2019). Plants (Basel, Switzerland), 8(6), 179.

30 Seo, J. Y., Lim, S. S., et al. (2008). Phytotherapy Research: PTR, 22(11), 1500-1505.

31 Ding, Y. H., Song, Y. D., et al. (2019). Acta Pharmacologica Sinica, 40(1), 64-74.

32 Wang, Q., Gao, S., et al. (2018). Phytomedicine: International journal of phytotherapy and phytopharmacology, 46, 78-84. 33 Dao, T., Song, K., et al. (2020). Inflammation Research: Official journal of the European Histamine Research Society, 69(3),

34 Natural Medicines. (2021, July 10). Elecampane [monograph]. http://naturalmedicines.therapeuticresearch.com

35 Lamminpää, A., Estlander, T., et al. (1996). Contact Dermatitis, 34(5), 330-335.

36 Aberer W. (2008). Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology: JDDG, 6(1), 15-24.

37 Gardner, Z., & McGuffin, M. (2013). American Herbal Products Association's botanical safety handbook (pp. 474-475). CRC Press /Taylor & Francis.

38 Brinker, F. (2001). Herb contraindications & drug interactions (p. 274). Eclectic Medical Publications.

39 Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 1145). Art of Medicine Press.

40 Brinker, F. (2001). Herb contraindications & drug interactions (p. 218-220). Eclectic Medical Publications.

41 Ono, M. (2017). Journal of Natural Medicines, 71(4), 591-604.

 $42\,Brinker, F.\,(2001).\,Herb\,contraindications\,\&\,drug\,interactions\,(p.\,234-235).\,Eclectic\,Medical\,Publications.$

43 Gardner, Z., & McGuffin, M. (2013). American Herbal Products Association's botanical safety handbook (pp. 477-478). CRC Press /Taylor & Francis.

44 da Silva, A., Amorim, R., et al. (2018). Journal of Ethnopharmacology, 219, 103-109.

- Microbial Support
- Immune System Support
- Inflammatory Response Support



INTRODUCTION

This product is a synergistic blend of Samento (*Uncaria tomentosa*), Stevia (*Stevia rebaudiana*) and Banderol (*Otoba parvifolia*). It is designed to assist with comprehensive microbial support.* Our liquid extracts are made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herb in its original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

Samento is a hydro-ethanol extract from *U. tomentosa* (bark), also known as Cat's Claw. It is traditionally used for health promotion by indigenous tribes of the Peruvian Amazon, and ongoing research continues to elucidate its health-supporting effects.*1 U. tomentosa exists in two chemotypes, one of which contains more tetracyclic oxindole alkaloids (TOA) and the other of which contains more pentacyclic oxindole alkaloids (POA). Samento is made from the bark of this rare, TOA-free pentacyclic phenotype which not only meets but exceeds the standards of the U.S. Pharmacopoeia (USP 42), requiring no less than 0.3% of POAs and no more than 0.05% TOAs.² Samento is verified by independent third-party HPLC testing to be free of TOAs, with levels in trace amounts or undetectable.³

U. tomentosa (bark) includes other active constituents such as esters (ex. carboxyl alkyl), glycosides (ex. quinovic acid), organic acids (ex. oleanolic, ursolic, palmitoleic), procyanidins, sterols (ex. sitosterol), and triterpenes, as well as catechin, rutin, 3,4-dehydro-5-carboxystrictosidine, and many others.⁴ *U. tomentosa* may assist with microbial support,⁵⁻⁷ immune system support,⁴ healthy inflammatory response support,^{8,9} cardiovascular support,¹⁰ neurological support,¹¹⁻¹³ blood glucose and metabolic support,^{14,15} and antioxidant support.*¹⁶

Stevia is a hydro-ethanol extract from Stevia leaf (*Stevia rebaudiana*). *S. rebaudiana* is part of the Asteraceae/Compositae family, native to Brazil and Paraguay, and used as a dietary supplement as well as a sweetener. The constituents responsible for the sweet taste are steviol glycosides, including stevioside, rebaudioside A-F, steviolbioside, isosteviol, and dulcoside A, of which stevioside and rebaudioside A are the most abundant. The Steviol glycosides are approximately 250-300 times sweeter than sucrose. *S. rebaudiana* also contains phytosterols such as stigmasterol, beta-sitosterol, and campesterol, as well as flavonoids, diterpenes, triterpenes, vitamins, and minerals. The

S. rebaudiana may help with microbial support, ^{19,20,21} inflammatory response support, ²² and antioxidant support. *23-25 *S. rebaudiana* may also assist with cardiovascular and metabolic support, helping to maintain blood pressure, ²⁶⁻²⁸ lipid levels, ²⁹⁻³² and blood glucose, ³³⁻³⁸ already within the normal range.* It may also support satiety and healthy eating habits. *25,39-41

Banderol is a hydro-ethanol extract from the bark of wild *Otoba parvifolia*, including mineral water and 20-24% alcohol. *O. parvifolia* is also known as Banderilla tree and belongs to the Myristicaceae family.⁴² It is sustainably harvested from the Amazon basin ecosystem, and has been used by indigenous groups in the region for hundreds of years. Traditionally, *O. parvifolia* bark has been used for microbial support.*⁴³ The proprietary hydro-ethanolic extraction and enhancement process maximizes the bioavailability of isoflavones and other beneficial constituents.*⁴² Banderol may help with microbial support.*⁴⁷ It may also help with healthy inflammatory response support.*⁴⁷

MICROBIAL SUPPORT

U. tomentosa (bark) may assist with a broad range of microbial support.**57 *S. rebaudiana* (leaf) may help with diverse types of microbial support, including a variety of morphological forms.**19-21 It may also help with mycelial support.**48 *O. parvifolia* (bark) may help with diverse microbial support for various types and morphological forms.**44-46 Independently, both *O. parvifolia* and *U. tomentosa* assist with microbial support.**7 In combination, they exhibit more robust support.**7

ANTIOXIDANT SUPPORT

Polyphenols and flavonoids in *S. rebaudiana* leaves may contribute antioxidant support to help with normal oxidative stress.*23,48 *S. rebaudiana* may help to maintain superoxide dismutase (SOD) levels already within the normal range, contributing antioxidant support.*25

IMMUNE SYSTEM SUPPORT

U. tomentosa (pentacyclic chemotype) may help to support immune system homeostasis.* Research suggests that POAs help to maintain lymphocyte proliferation-regulating factor levels already within the normal range,⁴⁹ CD4* CD25* Foxp3* levels already within the normal range, and Th2 levels already within the normal range.* It should be noted that TOAs inhibit the effect of POAs on lymphocyte-proliferation-regulating factor in a dose-dependent manner, thus TOA-free *U. tomentosa* is required for adequate immune support.* The specific POA mitraphylline may help to support healthy neutrophil function and maintain levels of Th1, Th2, and Th17 already within the normal range.* Mitraphylline may also help to support healthy apoptosis.*

INFLAMMATORY RESPONSE SUPPORT

U. tomentosa (pentacyclic chemotype) may help to maintain and support a healthy inflammatory response.*8,9 *U. tomentosa* may help to support NF-kappaB levels already within the normal range in a dose-dependent manner,^{53,54} thus supporting both TNF-alpha and IL-1-beta already within the normal range.*54

U. tomentosa and its most prevalent POA alkaloid, mitraphylline, may help

to maintain levels of IL-1-alpha, IL-2, IL-4, IL-6, IL-8, and IL-17 already within the normal range, 55-58 in addition to supporting healthy function of the MAP kinase pathway.*54,58

S. rebaudiana may help with healthy inflammatory response support.*22 Stevioside and its metabolite steviol may assist with cytokine support, helping to maintain healthy levels of TNF-alpha, IL-1-beta, IL-6, and NF-kappaB already within the normal range.*22 It may also help to maintain levels of cytokine-governing lipopolysaccharides already within the normal range.*48

O. parvifolia (bark) may help support a healthy inflammatory response.* O. parvifolia has been studied in mice, in which Banderol's inflammatory response support was found comparable to the positive control.*47

SAFETY AND CAUTIONS

All three herbs are generally well tolerated. With *U. tomentosa*, gastrointestinal effects such as nausea, vomiting, constipation or diarrhea have been reported.⁵⁰ With S. rebaudiana, nausea and dizziness have been known to occur, though at a similar rate to placebo, and usually resolves after the first week of use.³⁰ A mouse study using 500 times the human dose of Banderol showed no evidence of side effects or toxicity.51

U. tomentosa should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy. 52 Both *U. tomentosa* and *S.* rebaudiana may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4. 53,28 O. parvifolia inhibits the uptake transporters OATP1B1 and OATP1B3, so caution is warranted with medications that are substrates or inhibitors of OATP1B1 and OATP1B3.54

S. rebaudiana may theoretically increase lithium levels due to increased diuresis and decreased lithium excretion. 55 S. rebaudiana may theoretically have additive effects when taken concurrently with antidiabetic or antihypertensive medications.55 While TOA-containing U. tomentosa may have additive effects with antihypertensives and anticoagulants,56-58 Samento is TOA-free, with levels in trace amounts or undetectable.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

1 Muhammad, I., Dunbar, D. C., et al. (2001). Phytochemistry, 57(5), 781-785.

2 Convention USP, editor. United States Pharmacopeia and National Formulary (USP 42-NF 37). 42nd ed. Rockville (MD): Convention, United States Pharmacopeial; 2018.

3 Vilchez, L. (2019). Informe Tecnico N IT050-2019 Samento-Stevia Liquid Extract.

4 Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). Applied Sciences, 10(8), 2668.

5 Ccahuana-Vasquez, R. A., Santos, S. S., et al. (2007). Brazilian Oral Research, 21(1), 46-50.

6 Yepes-Perez, A. F., Herrera-Calderón, O., et al. (2021). Evidence-Based Complementary and Alternative Medicine: eCAM, 2021, 6679761.

7 Datar, A., Kaur, N., et al. (2010). Townsend Letter, 7, 1-4.

8 Aquino, R., De Feo, V., et al. (1991). Journal of Natural Products, 54(2), 453-459.

9 Mur, E., Hartig, F., et al. (2002). The Journal of Rheumatology, 29(4), 678-681.

10 Horie, S., Yano, S., et al. (1992). Life Sciences, 50(7), 491-498.

11 Snow, A. D., Castillo, G. M., et al. (2019). Scientific Reports, 9(1), 561.

12 Mohamed, A. F., Matsumoto, K., et al. (2000). The Journal of Pharmacy and Pharmacology, 52(12), 1553-1561.

13 Frackowiak, T., Baczek, T., et al. (2006). Zeitschrift fur Naturforschung. C, Journal of Biosciences, 61(11-12), 821-826.

14 Domingues, A., Sartori, A., et al. (2011). Phytotherapy Research: PTR, 25(8), 1229-1235.

15 Araujo, L., Feitosa, K. B., et al. (2018). Scientific Reports, 8(1), 11013

16 Sandoval, M., Okuhama, N. N., et al. (2002). Phytomedicine: International journal of phytotherapy and phytopharmacology,

17 Goyal, S. K., Samsher, & Goyal, R. K. (2010). International Journal of Food Sciences and Nutrition, 61(1), 1-10.

18 Momtazi-Borojeni, A. A., Esmaeili, S. A., et al. (2017). Current Pharmaceutical Design, 23(11), 1616–1622.

19 Theophilus, P. A., Victoria, M. J., et al. (2015). European Journal of Microbiology & Immunology, 5(4), 268-280.

20 Preethi, D., Sridhar, T. M., et al. (2011). Journal of Ecobiotechnology, 3(7), 05-10.

21 Kedik, S. A., Yartsev, E. I., & Stanishevskaya, I. E. (2009). Pharmaceutical Chemistry Journal, 43(4), 198-199.

22 Boonkaewwan, C., & Burodom, A. (2013). Journal of the Science of Food and Agriculture, 93(15), 3820-3825.

23 El-Mesallamy, A., Mahmoud, S. A., et al. (2018). Acta Scientiarum Polonorum. Technologia Alimentaria, 17(3), 289-297.

24 Dusek, J., Carazo, A., et al. (2017). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 109 (Pt 1), 130-142.

25 Nordentoft, I., Jeppesen, P. B., et al. (2008). Diabetes, Obesity & Metabolism, 10(10), 939-949.

26 Chan, P., Tomlinson, B., et al. (2000). British Journal of Clinical Pharmacology, 50(3), 215–220.

27 Melis, M. S. (1997). Phytomedicine: International journal of phytotherapy and phytopharmacology, 3(4), 349-352.

28 Lee, C. N., Wong, K. L., et al. (2001). Planta Medica, 67(9), 796-799.

29 Adisakwattana, S., Intrawangso, J., et al. (2012). Food Technology & Biotechnology, 50(1), 11-16.

30 Ahmad, U., Ahmad, R. S., et al. (2018). Lipids in Health and Disease, 17(1), 175.

31 Ritu, M., & Nandini, J. (2016). Journal of the Science of Food and Agriculture, 96(12), 4231-4234.

32 Holvoet, P., Rull, A., et al. (2015). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 77, 22-33.

33 Gregersen, S., Jeppesen, P. B., et al. (2004). Metabolism: Clinical and Experimental, 53(1), 73-76.

34 Toskulkao, C., Sutheerawatananon, M., et al. (1995). Journal of Nutritional Science and Vitaminology, 41(1), 105-113.

35 Philippaert, K., Pironet, A., et al. (2017). Nature Communications, 8, 14733.

36 Jeppesen, P. B., Dyrskog, S. E., et al. (2006). The Review of Diabetic Studies: RDS, 3(4), 189-199.

37 Mond-Radzman, N. H., Ismail, W. I., et al. (2013). Evidence-Based Complementary and Alternative Medicine: eCAM, 2013,

38 Aghajanyan, A., Movsisyan, Z., & Trchounian, A. (2017). BioMed Research International, 2017, 9251358

39 Farhat, G., Berset, V., & Moore, L. (2019). Nutrients, 11(12), 3036.

40 Stamataki, N. S., Scott, C., et al. (2020). The Journal of Nutrition, 150(5), 1126-1134.

41 Gu, W., Rebsdorf, A., et al. (2019). Endocrinology, Diabetes & Metabolism, 2(4), e00093.

42 Jaramillo-Vivanco, T. & Balslev, H. (2020). Phytotaxa, 441(12); 143-175.

43 Weiss, J. (2018). Molecules, 24(1), 137.

44 Goc, A., & Rath, M. (2016). Therapeutic Advances in Infectious Disease, 3(3-4), 75-82.

45 Weniger, B., Robledo, S., et al. (2001). Journal of Ethnopharmacology, 78(2-3), 193-200.

46 Rocha, L. G., Almeida, J. R., et al. (2003). Phytomedicine: International journal of phytotherapy and phytopharmacology, 12(6-7), 514-535.

47 Allende, A. (2005). NutraMedix Laboratories, LLC.

48 Marcinek, K. & Krejpcio, Z. (2016). Journal für Verbraucherschutz und Lebensmittelsicherheit, 11, 3-8.

49 Keplinger, K., Laus, G., et al. (1999). Journal of Ethnopharmacology, 64(1), 23-34.

50 Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, 23(2), 141-148.

51 Núñez, C., Lozada-Requena, I., et al. (2015). Revista Peruana de Medicina Experimental y Salud Publica, 32(4), 643-651.

52 De Martino, L., Martinot, J. L., et al. (2006). Journal of Ethnopharmacology, 107(1), 91-94.

53 Sandoval-Chacón, M., Thompson, J. H., et al. (1998). Alimentary Pharmacology & Therapeutics, 12(12), 1279-1289.

54 Allen-Hall, L., Arnason, J. T., et al. (2010). Journal of Ethnopharmacology, 127(3), 685-693.

55 Lemaire, I., Assinewe, V., et al. (1999). Journal of Ethnopharmacology, 64(2), 109-115

56 Sandoval, M., Charbonnet, R. M., et al. (2000). Free Radical Biology & Medicine, 29(1), 71-78.

57 Rojas-Duran, R., González-Aspajo, G., et al. (2012). Journal of Ethnopharmacology, 143(3), 801-804.

58 Allen-Hall, L., Cano, P., et al. (2007). Journal of Ethnopharmacology, 109(2), 312-317.

59 de Paula, L. C., Fonseca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22-30. 60 Allende, A. (2006). NutraMedix Laboratories, LLC.

61 Lamm, S., Sheng, Y., et al. (2001). Phytomedicine: International journal of phytotherapy and phytopharmacology, 8(4),

62 Budzinski, J. W., Foster, B. C., et al. (2000). Phytomedicine: International journal of phytotherapy and phytopharmacology,

7(4), 273-282. 63 Natural Medicines. (2021, March 27). Stevia [monograph]. http://naturalmedicines.therapeuticresearch.com.

64 Zhou, J., & Zhou, S. (2010). Journal of Ethnopharmacology, 132(1), 15-27.

65 Zhou, J. Y., & Zhou, S. W. (2012). Fitoterapia, 83(4), 617-626.

66 Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126-130.



- Microbial Support
- Immune System Support
- Inflammatory Response Support



INTRODUCTION

This product is a synergistic blend of hydro-ethanol extracts from Cumanda (Campsiandra angustifolia) bark and Houttuynia (Houttuynia cordata) leaf. It is designed to assist with comprehensive microbial support, with additional antioxidant support and healthy inflammatory response support.* Our liquid extracts are made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

Cumanda is an extract from the bark of *Campsiandra angustifolia* also known as *Campsiandra angustifolia* Benth., *Campsiandra angustifolia* var. *angustifolia*, and huacapurana.^{1,2} It belongs to the *Fabaceae/Leguminosae* family and the Caesalpinaceae subfamily, which contains many species of *Campsiandra*.³⁻⁶ While huacapurana is a more general name that can apply to several *Campsiandra* species, *C. angustifolia* is considered the authentic Peruvian huacapurana.²

C. angustifolia is a medium-sized tree native to Peru and Northern Brazil that is used by local people for food as well as health.² Constituents found within the bark include proanthocyanidins, flavonoids, gallotannins, and caffeoylquinic acid.⁷ Secondary metabolites include steroids, flavonoids, saponins and tannins.⁸ In traditional historical use, it has been used for microbial support, healthy inflammatory response support, and gastrointestinal support, Cumanda is most known for its robust and diverse microbial support. Lagrange 1.

Houttuynia is a hydro-ethanol extract from *Houttuynia cordata* leaf, which is in the Saururaceae family. It is known as yu xing cao in traditional Chinese health practices and is found throughout Southeast Asia. Constituents include volatile oils such as alpha-pinene, d-limonene, citronellol, carvacrol, and thymol;¹⁵ flavonoids such as quercetin, quercitrin, isoquercitrin, and rutin;¹⁵ organic acids such as chlorogenic acid, palmitic acid, and linoleic acid;16 phytosterols such as stigmasterol and beta-sitosterol;¹⁶ and water-soluble polysaccharides.¹⁷ *H. cordata* also contains houttuynoside A and houttuynamide A, in addition to amino acids, vitamins, and trace minerals.¹⁷⁻¹⁹

H. cordata (leaf) may help with microbial support, $^{20\cdot24}$ immune system support, $^{25\cdot31}$ healthy inflammatory response support, $^{32\cdot36}$ and gastrointestinal support. $^{*37\cdot39}$

MICROBIAL SUPPORT

C. angustifolia (bark) may help with single-celled microbial support, and thus, may help to maintain health of erythrocytes and macrophages. 6.12,13 It may also help with microbial support of varied gram status. 13,14 Additionally, C. angustifolia may help with mycelial support.

H. cordata may help with both intracellular and extracellular microbial support. It may help with microbial support for diverse strains with dose-dependent zone diameters of inhibition, and may also help with microbial support for a variety of morphological forms. Additionally, it may provide microbial support for smaller intracellular microbes and help to maintain normal host immunity. In addition to intracellular microbial support, *H. cordata* may help to support relevant respiratory and intestinal mucosa through maintaining cytokines/chemokines, secretory IgA (sIgA), zonula occludens-1 (ZO-1)/tight junction protein, TLR4, and NF-kappaB already within the normal range. Additionally, it may help to support healthy gingival epithelium as well as balanced oral microbiota, including mycelial support.

IMMUNE SUPPORT

H. cordata may help with immune system support through maintaining healthy levels of CD4+ and CD8+ T cells that are already within the normal range.*25 lt may help to support the innate immune response by maintaining levels of reactive nitrogen intermediates (RNI), such as nitric oxide (NO), and reactive oxygen intermediates (ROI), such as superoxide, that are already within the normal range. It may also help to support the morphological change of macrophages from the round form to the dendritic form, supporting normal phagocytic activity as well as normal NO production.*26 *H. cordata* may assist with immune system support through the maintenance of a healthy Th1/Th2 ratio, in addition to the maintenance of Th2-dependent cytokines IL-4 and IL-5 already within the normal range.*27 Additionally, it may help with IgE-mediated immune support by maintaining IL-4, TNF-alpha, and NF-kappaB already within the normal range.*28 *H. cordata* may help to maintain MIP-1-alpha, MIP-1-beta, and RANTES in human peripheral blood mononuclear cells (PBMCs) already within the normal range.*29 It may also help to support health through its effect on the complement cascade.*30,31

INFLAMMATORY RESPONSE SUPPORT

H. cordata may help with antioxidant support and healthy inflammatory response support.*32 It may help to support healthy function of the NF-kappaB and MAPK pathways and may help to maintain cytokine levels already within the normal range.*32 It may also help to maintain levels of TNF-alpha, NO, IL-6, IL-8 and PGE2 already within the normal range.*33,34 The constituent houttuynamide A (becatamide) may additionally help to maintain levels of COX-1 and COX-2 already within the normal range.*35,36 In traditional Chinese health practices, *H. cordata* is used to clear heat.*15,16

SAFETY AND CAUTIONS

C. angustifolia (bark) has been used traditionally by native South American peoples for some time. Despite this, information on interactions and adverse events is sparse. Currently, there are no known cautions or interactions, though this may change with additional research and new knowledge. Theoretically, C. angustifolia may have additive effects with PDE-5 inhibitors. 75

There are no known contraindications to the use of H. cordata. It has been used for centuries in traditional Chinese health practices, with the first known mention in Ming Yi Za Zhu (Miscellaneous Records of Famous Physicians) by Tao Hong-Jing in 500 CE. In laboratory animals, oral administration of 16 mg/ kg was found to be non-toxic.25 In vitro and mouse studies have shown no evidence of genotoxicity or other toxicity, ^{25,32,40} and the herb is considered a safe and edible plant.*

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- 11 Campsiandra angustifolia Benth. The Plant List. Theplantlist.org. (2021). Retrieved 10 December 2021, from http://www. theplantlist.org/tpl1.1/record/ild-20132.
- 2 Tropical Plants Database, Ken Fern. tropical.theferns.info. (2021). Retrieved 10 December 2021, from http://tropical.theferns. info/viewtropical.php?id=Campsiandra+angustifolia.
- 3 Campsiandra angustifolia Benth.-Encyclopedia of Life. Eol.org. (2021). Retrieved 10 December 2021, from https://eol.org/
- 4 Campsiandra angustifolia. Worldfloraonline.org. (2021). Retrieved 10 December 2021, from http://www.worldfloraonline.org/ search?query=campsiandra+angustifolia.
- 5 Farji-Brener, A. G., Durán, S., et al. (2005). Revista de Biologia Tropical, 53(1-2), 63-71.
- 6 Ruiz, L., Ruiz, L., et al. (2011). Journal of Ethnopharmacology, 133(2), 917-921.
- 7 Schmeda-Hirschmann, G., Burgos-Edwards, A., et al. (2019). Journal of Ethnopharmacology, 229, 167-179.
- 8 Flores, P.C. & Andoa, D. H. (2014). UNAP Repositorio Institucional Digital. https://repositorio.unapiquitos.edu.pe/ handle/20.500.12737/4399
- 9 Ganapathy, A. A., Hari Priya, V. M., & Kumaran, A. (2021). Journal of Ethnopharmacology, 267, 113536.
- 10 de Pascoa Júnior, J. G., & de Souza, C. L. L. (2021). Research, Society and Development, 10(14), e163101419965.
- 11 Huaranca Acostupa, R. J., Armas Bardales, J. J., & Vigo Teco, R. M. (2013). Conoc Amaz, 4(2), 77-86.
- 12 Kvist, L. P., Christensen, S. B., et al. (2006). Journal of Ethnopharmacology, 106(3), 390-402.
- 13 Vasquez-Ocmin, P., Cojean, S., et al. (2018). Journal of Ethnopharmacology, 210, 372.
- 14 Roumy, V., Ruiz Macedo, J. C., et al. (2020). Journal of Ethnopharmacology, 249, 112411.
- 15 Chen, J., Chen, T., & Crampton, L. (2004). Chinese medical herbology and pharmacology (pp. 216-217). Art of Medicine Press. 16 Bensky, D., Clavey, S., & Stöger, E. (2004). Chinese herbal medicine materia medica (3rd ed., pp. 176-178). Seattle: Eastland
- 17 Yang, L. & Jiang, J-G. (2009). Pharmaceutical Biology, 47(12), 1154-1161.
- 18 Kumar, M., Prasad, S. K., & Hemalatha, S. (2014). Pharmacognosy Reviews, 8(15), 22-35.

- 19 Chou, S. C., Su, C. R., et al. (2009). Chemical & Pharmaceutical Bulletin, 57(11), 1227-1230.
- 20 Li, J., Rehman, M. U., et al. (2017). Southeast Asian Journal of Tropical Medicine and Public Health, 48(6), 1260-1266.
- 21 Sekita, Y., Murakami, K., et al. (2016). BioMed Research International, 2016, 2581876
- 22 Chiow, K. H., Phoon, M. C., et al. (2016). Asian Pacific Journal of Tropical Medicine, 9(1), 1-7.
- 23 Remali, J., & Aizat, W. M. (2021). Frontiers in Pharmacology, 11, 589044.
- 24 Zhu, H., Lu, X., et al. (2018). Journal of Ethnopharmacology, 218, 90-99.
- 25 Lau, K. M., Lee, K. M., et al. (2008). Journal of Ethnopharmacology, 118(1), 79-85.
- 26 Kim, G. S., Kim, D. H., et al. (2008). Biological & Pharmaceutical Bulletin, 31(11), 2012-2017.
- 27 Lee, J. S., Kim, I. S., et al. (2008). Journal of Ethnopharmacology, 117(1), 34-40.
- 28 Han, E. H., Park, J. H., et al. (2009). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 47(7), 1659-1666
- 29 Cheng, B. H., Chan, J. Y., et al. (2014). Carbohydrate Polymers, 103, 244-249.
- 30 Jiang, Y., Lu, Y., et al. (2014). Natural Product Research, 28(6), 407-410.
- 31 Zhang, T., & Chen, D. (2008). Journal of Ethnopharmacology, 117(2), 351-361.
- 32 Shingnaisui, K., Dey, T., et al. (2018). Journal of Ethnopharmacology, 220, 35-43.
- 33 Lee, H. J., Seo, H. S., et al. (2013). Molecular Medicine Reports, 8(3), 731-736.
- 34 Chun, J. M., Nho, K. J., et al. (2014). BMC Complementary and Alternative Medicine, 14, 234.
- 35 Park J. B. (2015). Phytotherapy Research: PTR, 29(9), 1381-1387.
- 36 Li, W., Zhou, P., et al. (2011). Journal of Ethnopharmacology, 133(2), 922–927.
- 37 Chen, M. Y., Li, H., et al. (2019). Chinese Journal of Natural Medicines, 17(3), 187-197.
- 38 Jiang, X. L., & Cui, H. F. (2004). World Journal of Gastroenterology, 10(10), 1513-1520.
- 39 Shi, C. C., Zhu, H. Y., et al. (2020). International Journal of Biological Macromolecules, 158, 52–66.
- 40 Kang, C. K., Hah, D. S., et al. (2012). The American Journal of Chinese Medicine, 40(5), 1019-1032.



- Antioxidant Support
- Detox Support
- Immune System Support
- Blood Glucose Support
- Microbial Support
- Inflammatory Response Support
- Digestive Support



INTRODUCTION

Parsley is a hydro-ethanol extract from the stems and leaves of *Petroselinum* crispum. Parsley is a biennial plant that is part of the Apiaceae/Umbelliferae family and is thought to have originated in the Mediterranean region. Synonyms for P. crispum include Petroselinum hortense, Petroselinum sativum, Petroselinum vulgare, Ápium petroselinum, Apium crispum, and Carum petroselinum.

P. crispum contains phenolic compounds and flavonoids including apigenin, apiin, luteolin, chrysoeriol, quercetin, and isorhamnetin. *P. crispum* also contains the essential oils myristicin and apiole; the carotenoids beta-carotene, lutein, violaxanthin, and neoxanthin; and coumarins. ^{3,4}

Parsley is made at our U.S. manufacturing facility. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

ANTIOXIDANT SUPPORT

P. crispum may help to support and maintain a healthy cellular antioxidant enzyme system.* It may contribute antioxidant support, as quantified by DPPH assay and chemoluminescence.* Antioxidant support has also been quantified by beta-carotene bleaching assay. The antioxidant activity is attributed to the phenolic components apiol, myristicin, and apiin.* While apiol and myristicin have similar chemical structures, apiol demonstrates more than five-fold the free radical scavenging activity of myristicin, though myristicin is the more abundant radical scavenging activity of myristicin, though myristicin is the more abundant constituent.*8 In a rat study, *P. crispum* helped to maintain total antioxidant capacity and malondialdehyde levels already within the normal range.*9 In a randomized crossover trial with 14 healthy volunteers, seven women and seven

men, *P. crispum* supported statistically significant maintenance of superoxide dismutase (SOD) and erythrocyte glutathione reductase.*10

DETOX SUPPORT

P. crispum may contribute cleansing support and help ease Herxheimer-like reactions.* It may help to support liver health through contributing antioxidant support and may help to maintain nitric oxide (NO) levels already within the normal range.* *11 P. crispum* may help to support urinary tract health through maintaining urinary pH already within the normal range.* 12,13 It may also help to support and maintain liver health.* 14

IMMUNE SYSTEM SUPPORT

P. crispum may help with immune support.*15 Preclinical studies suggest that P. crispum may help to support and maintain homeostasis of both cellular and humoral arms of adaptive immunity.*15

OTHER USES

Blood Glucose SupportP. crispum may help to maintain blood glucose levels already within the normal range.* It may also help to maintain glycation already within the normal range.* During fructose metabolism, P. crispum may help to maintain levels of ketohexokinase-C already within the normal range.*

Microbial Support

P. crispum may help with microbial support *19,20,21 Microbial support has been determined by the agar well diffusion method.*20,21 While both cold water and hot water extracts may help with microbial support, the zone of inhibition for the tested organisms was greatest with the hot water extract of *P. crispum*.*20 In a seed extract of *P. crispum*, the zones of inhibition were, in some cases, comparable to positive control.*21

Inflammatory Response support *P. crispum* may help with healthy inflammatory response support.*22 In a rat study, the ethanolic extract of *P. crispum* was shown to help with healthy hepatic inflammatory response support; this was partly attributed to antioxidant activity.*14

Digestive Support

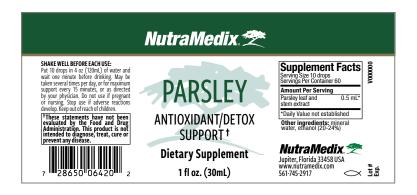
P. Crispum may help with digestive support.* It may help to support and maintain healthy gastrointestinal mucosa as well as normal stool consistency.*23,24

SAFETY AND CAUTIONS

P. crispum is generally recognized as safe (GRAS) in the U.S. and is usually well tolerated.²⁵ It is a source of salicylates.² *P. crispum* may have estrogenic effects comparable to that found in the isoflavone glycosides of soybeans.²⁶ There have been cases of rare allergic reactions to *P. crispum*, including anaphylaxis.^{27,28} According to animal research, it may have antiplatelet effects; this may have additive effects with antiplatelet drugs and/or anticoagulants.²⁹ It may also have hypoglycemic effects, which may have additive effects with hypoglycemic medications.³⁰ *P. crispum* may have an aquaretic effect, which may interfere with diuretic therapy.³¹ It has been shown to prolong the effects of pentobarbital in animal studies.³² *P. crispum* may inhibit cytochrome P450 (CYP1A2) which may inhibit levels of CYP1A2 substrates.³³ It is rich in vitamin K and high doses may interfere with warfarin therapy.³⁴ *P. crispum* is contraindicated in pregnancy, due to antifertility effects attributed to apiol.³⁵ It is also contraindicated in inflammatory kidney conditions.³⁶ inflammatory kidney conditions.36

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Mahmood, S., Hussain, S., & Malik, F. (2014). *Pakistan Journal of Pharmaceutical Sciences*, 27(1), 193–202.
- ² Natural Medicines. (2021, July 7). Parsley [monograph]. http://naturalmedicines.therapeuticresearch.com
- 3 Farzaei, M. H., Abbasabadi, Z., et al. (2013). Journal of Traditional Chinese Medicine = Chung i tsa chih ying wen pan, 33(6), 815–826.
- 4 Francis, G. W. & Isaksen, M. (1989). *Chromatographia*, 27, 549-551, 5 Akıncı, A., Eşrefoğlu, M., et al. (2017). *Balkan Medical Journal*, 34(1), 53-59.

- Fejes, S., Blázovics, A., et al. (2000). Phytotherapy Research: PTR, 14(5), 362–365.
 Wong, P. Y. Y. & Kitts, D. D. (2006). Food Chemistry, 97, 505-515.
 Zhang, H., Chen, F., et al. (2006). Food Research International, 39, 833-839.
- 9 Haidari, F., Keshavarz, S. A., et al. (2011). Iranian Journal of Pharmaceutical Research: IJPR, 10(4), 811-819.
- ¹⁰ Nielsen, S. E., Young, J. F., et al. (1999). *The British Journal of Nutrition*, 81(6), 447–455. ¹¹ Salahshoor, M. R., Abdolmaleki, A., et al. (2020). *Comparative Clinical Pathology*, 29(1).
- ¹² Nirumand, M. C., Hajialyani, M., et al. (2018). International Journal of Molecular Sciences, 19(3), 765.
- ¹³ Al-Yousofy, F., Gumaih, H., et al. (2017). Américan Journal of Clinical and Experimental Urology, 5(3), 55–62.
- ¹⁴ Al-Howiriny, T. A., Al-Sohaibani, M. O., et al. (2003). *Journal of Natural Remedies*, 3(1), 54-62.
- ¹⁵ Yousofi, A., Daneshmandi, S., et al. (2012). *Immunopharmacology and Immunotoxicology*, 34(2), 303–308.
- 16 Tunali, T., Yarat, A., et al. (1999). Phytotherapy Research: PTR, 13(2), 138–141.

 17 Ramkissoon, J. S., Mahomoodally, M. F., et al. (2012). Journal of Medicinal Food, 15(12), 1116–1123.

- ¹⁸ Le, M. T., Lanaspa, M. A., et al. (2016). *PloS One*, 11(6), e0157458.

 ¹⁹ Linde, G. A., Gazim, Z. C., et al. (2016). *Genetics and Molecular Research: GMR*, 15(3), 10.4238/gmr.15038538.

 ²⁰ Aljanaby, A. A. J. J. (2013). *Research on Chemical Intermediates*, 39, 3709-3714.
- ²¹ Seyyednejad, S. M., Maleki, S., et al. (2008). Asian Journal of Biological Sciences, 1(1), 51-55.
- ²² Al-khrazraji, S. M. (2015) *IOSR Journal of Pharmacy*, *5*(9), 17-23.

 ²³ Al-Howiriny, T., Al-Sohaibani, M., et al. (2003). *The American Journal of Chinese Medicine*, *31*(5), 699–711.
- ²⁴ Kreydiyyeh, S. I., Usta, J., et al. (2002). Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, 8(5), 382–388.
- 25 CFR Code of Federal Regulations Title 21. Accessdata.fda.gov. (2021). Retrieved 7 July 2021, from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=1828showFR=1.
- ²⁶ Yoshikawa, M., Uemura, T., et al. (2000). Chemical & Pharmaceutical Bulletin, 48(7), 1039–1044.
- ²⁷ Foti, C., Cassano, N., et al. (2011). Annals of Allergy, Asthma & Immunology: Official publication of the American College of Allergy, Asthma, & Immunology, 106(5), 447–448.
- ²⁸ Arslan, S., Ucar, R., & Caliskaner, A. Z. (2014). Medical Archives (Sarajevo, Bosnia and Herzegovina), 68(6), 426–427.

 ²⁹ Gadi, D., Bnouham, M., et al. (2009). Journal of Ethnopharmacology, 125(1), 170–174.
- 30 Yanardağ, R., Bolkent, S., et al. (2003). Biological & Pharmaceutical Bulletin, 26(8), 1206–1210.
- ³¹ Kreydiyyeh, S. I., & Usta, J. (2002). *Journal of Ethnopharmacology*, 79(3), 353–357.
- ³² Jakovljevic, V., Raskovic, A., et al. (2002). European Journal of Drug Metabolism and Pharmacokinetics, 27(3), 153–156.
- 33 Peterson, S., Lampe, J. W., et al. (2006). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 44(9), 1474–1484.
- 34 Bolton-Smith, C., Price, R. J., et al. (2000). The British Journal of Nutrition, 83(4), 389–399.
 35 Farnsworth, N. R., Bingel, A. S., et al. (1975). Journal of Pharmaceutical Sciences, 64(4), 535–598.
- 36 American Botanical Council. Herbalgram.org. (2021). Retrieved 7 July 2021, from https://www.herbalgram.org/resources/expanded-commission-e/parsley-herb-and-root/

QUERCETIN



APPLICATIONS

- Immune Health
- Zinc and Vitamin C Absorption
- Healthy Inflammatory Response Support
- Healthy Cardiovascular Support
- Antioxidant Support



INTRODUCTION

Quercetin is a yellow polyphenol bioflavonoid.*\textsup Of the six flavonoid subgroups, quercetin is classified as a flavonol.\textsup NutraMedix Quercetin is in the form of quercetin dihydrate, which is chemically known as 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one dihydrate (IUPAC) with a molecular formula of $C_{15}H_{14}O_{9}$.\textsup 3,4,5 It is also called pentahydroxyflavone dihydrate.

Quercetin is available in several forms. While flavonoid forms such as quercetin dihydrate are insoluble in water, they are highly available under physiological conditions in the presence of biological salts, especially to phagocytic and dendritic cells.* Quercetin dihydrate has the greatest bioavailability in comparison to the glycoside, aglycone, and rutinoside forms.*7

Quercetin bioavailability is determined by absorption, metabolism, and elimination, the last two of which are fairly rapid.³ The gut microbiome and individual genetics are also factors. Dietary fat and/or fiber may help to increase absorption, so it is recommended to take quercetin with meals or snacks.^{6,8} Daily consumption is recommended for optimal support as the half-life is between 11 and 28 hours.³

Quercetin can be found in many plants, including foods such as yellow and red onions, kale, apples, berries, grapes, citrus, red wine, and tea.^{3,9} It can also also be found in botanicals such as elderberry, St. John's wort, milk thistle, green tea, ginkgo, and pagoda tree.¹⁰ NutraMedix Quercetin is purified from the flowers of *Sophora japonica*, commonly known as the pagoda tree. *S. japonica* buds (*huai mi*) and flowers (*huai hua*) have been used in traditional Chinese health practices for centuries to clear heat.* centuries to clear heat."

NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers. Our Quercetin is free of gluten, sugar, soy, and dairy. It is also free of GMOs, mold, and yeast.

IMMUNE HEALTH

Quercetin may help to maintain the Th1/Th2 ratio already within the normal range.* It may also support healthy basophil and mast cell stability, consequently maintaining Ca2+ influx, histamine, leukotrienes and prostaglandins already within the normal range.* It Rat studies have shown that the greatest amount of absorbed quercetin can be found in the lung tissue, which may help to support a healthy correction. healthy seasonal immune response.

Quercetin may help to maintain levels of cytokines such as IL-1-alpha, IL-6, IL-8, and TNF-alpha already within the normal range.*3,14 It may also help maintain leukotrienes and PGD2 already within the normal range,14 serum IgE and eosinophil levels already within the normal range,2 and NF-kappaB and MAPK already within the normal range.*13,16,17

Additionally, Quercetin may help to maintain healthy dendritic cell function already within the normal range, supporting the connection between innate and adaptive immunity.*¹⁷ It may also help to maintain upper respiratory health (p=0.020; p=0.004).*^{18,19}

ZINC AND VITAMIN C ABSORPTION

Quercetin and other dietary polyphenols act as zinc ionophores, supporting zinc's entrance into cells independently of zinc transporters.*20 In studies with mouse cells, quercetin coadministered with zinc showed more effective intracellular zinc support than zinc administered alone.*20

Quercitin and vitamin C have a synergistic relationship; bioflavonoids such as quercetin may help to increase the absorption of vitamin C, and vitamin C may help to recycle oxidized quercetin.*21,22,23

OTHER USES

Healthy Inflammatory Response Support
Quercetin may help with healthy inflammatory response through supporting
normal function of the lipoxygenase (LOX) and cyclooxygenase (COX) pathways, helping
to maintain arachidonic acid metabolism already within the normal range.*1,3 Quercetin
may help to maintain levels of TNF-alpha already within the normal range,3 PDE4
already within the normal range,1 and IL-1, IL-5, and IL-13 already within the normal

Healthy Cardiovascular Support

Quercetin may help to support cardiovascular health.* It may help to maintain blood pressure already within the normal range (p=0.049),²⁴ help to maintain fasting plasma insulin (p<0.03) and insulin sensitivity (p<0.04) already within the normal range,²⁵ and help to maintain nitric oxide (NO) and plasma endothelin-1 already within the normal range (p<0.05).*²⁶

Antioxidant Support

Quercetin may help to support healthy oxidative balance by maintaining levels of glutathione (GSH) already within the healthy range.*27

SAFETY AND CAUTIONS

Quercetin is generally well tolerated and has been safely used in amounts up to one gram daily for up to 12 weeks.^{28,29} Side effects may include headache and tingling of the extremities.³⁰ Quercetin may have additive effects with hypoglycemic and antihypertensive medications.^{31,32,33} It may increase the levels and adverse effects of cyclosporine,³⁴ diclofenac,³⁵ losartan,³⁶ pravastatin,³⁷ and quetiapine.³⁸ It may also increase the levels and adverse effects of CYP2C8, CYP2C9, CYP2D6, and CYP2AB substrates: OATB substrates and P. Rukschrates. CYP3A4 substrates; OAT1 and OAT3 substrates; OATP substrates; and P-glycoprotein substrates.³⁰ Additionally, quercetin may decrease the levels and effectiveness of midazolam and of quinolone antibiotics.^{39,29} Quercetin should be avoided in pregnancy and breastfeeding.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). *Journal of Nutritional Science*, 5, e47.
- ² Al-Ishaq, R. K., Abotaleb, M., et al. (2019). *Biomolecules*, 9(9), 430.
- ³ Li, Y., Yao, J., et al. (2016). *Nutrients*, 8(3), 167.
- 4 PubChem. (2021). Quercetin. Retrieved 28 August 2021, from https://pubchem.ncbi.nlm.nih.gov/compound/Quercetin
- 5 PubChem. (2021). Quercetin dihydrate. Retrieved 29 August 2021, from https://pubchem.ncbi.nlm.nih.gov/compound/5284452
- ⁶ Dabeek, W. M., & Marra, M. V. (2019). *Nutrients*, 11(10), 2288.
- Jaffe R, Mani J. Chapter 29 Polyphenolics evoke healing responses: Clinical evidence and role of predictive biomarkers. Polyphenols: Mechanisms of action in human health and disease. January 2018:403-413.
- ⁸ Guo, Y., Mah, E., et al. (2013). *Molecular Nutrition & Food Research*, *57*(5), 896–905.
- 9 Jafarinia, M., Sadat Hòsseini, M., et al. (2020). Allergy, Asthma, and Clinical Immunology: Official journal of the Canadian Society of Allergy and Clinical Immunology, 16, 36.
- 10 Drugs and Lactation Database (LactMed) [Internet]. (2021). Bethesda (MD): National Library of Medicine (US). Available from: https://www.ncbi.nlm.nih.gov/books/NBK501922/
- 11 Eastland Herb. (2018). Eastland Herb Chinese herbal medicine: Materia medica and formula & strategies (4.3). [mobile app]. App store. https://apps.apple.com/us/app/eastland-herb-chinese-medicine/id737380894.
- ¹² Mlcek, J., Jurikova, T., et al. (2016). *Molecules (Basel, Switzerland)*, 21(5), 623.
- ¹³ Karuppagounder, V., Arumugam, S., et al. (2016). *Drug Discovery Today*, 21(4), 632–639.
- ¹⁴ Weng, Z., Zhang, B., et al. (2012). *PloS One*, 7(3), e33805.
- ¹⁵ de Boer, V. C., Dihal, A. A., et al. (2005). *The Journal of Nutrition*, 135(7), 1718–1725.
- ¹⁶ Chen, H., Lu, C., et al. (2017). *International Immunopharmacology*, 48, 110–117.
- ¹⁷ Huang, R. Y., Yu, Y. L., et al. (2010). *Journal of Immunology (Baltimore, Md.: 1950)*, 184(12), 6815–6821.
- ¹⁸ Heinz, S. A., Henson, D. A., et al. (2010). *Pharmacological Research*, 62(3), 237–242.
- ¹⁹ Nieman, D. C., Henson, D. A., et al. (2007). Medicine and Science in Sports and Exercise, 39(9), 1561–1569.
- ²⁰ Dabbagh-Bazarbachi, H., Clergeaud, G., et al. (2014). Journal of Agricultural and Food Chemistry, 62(32), 8085–8093.
- ²¹ Vinson, J. A., & Bose, P. (1988). *The American Journal of Clinical Nutrition*, 48(3), 601–604.
- ²² Boots, A. W., Kubben, N., et al. (2003). Biochemical and Biophysical Research Communications, 308(3), 560–565.
- ²³ Bors, W., Michel, C., & Schikora, S. (1995). Free Radical Biology & Medicine, 19(1), 45–52.
- ²⁴ Brüll, V., Burak, C., et al. (2015). The British Journal of Nutrition, 114(8), 1263–1277.
- ²⁵ Dower, J. I., Geleijnse, J. M., et al. (2015). *The American Journal of Clinical Nutrition*, 101(5), 914–921.
- ²⁶ Loke, W. M., Hodgson, J. M., et al. (2008). The American Journal of Clinical Nutrition, 88(4), 1018–1025.
- ²⁷ Xu, D., Hu, M. J., et al. (2019). *Molecules (Basel, Switzerland)*, 24(6), 1123.
- ²⁸ Khorshidi, M., Moini, A., et al. (2018). *Phytotherapy Research*: *PTR*, 32(11), 2282–2289.
- ²⁹ Shoskes, D. A., Zeitlin, S. I., et al. (1999). *Urology*, 54(6), 960–963.
- ³⁰ Natural Medicines. (2021, August 28). Quercetin [monograph]. http://naturalmedicines.therapeuticresearch.com
- ³¹ Ahrens, M. J., & Thompson, D. L. (2013). *Journal of Medicinal Food*, 16(3), 211–215.
- 32 Larson, A., Witman, M. A., et al. (2012). Nutrition Research (New York, N.Y.), 32(8), 557–564.
- 33 Edwards, R. L., Lyon, T., et al. (2007). The Journal of Nutrition, 137(11), 2405-2411.
- 34 Choi, J. S., Choi, B. C., & Choi, K. E. (2004). American Journal of Health-System Pharmacy: AJHP: Official journal of the American Society of Health-System Pharmacists, 61(22), 2406–2409.
- 35 Bedada, S. K., & Neerati, P. (2018). *Phytotherapy Research: PTR*, 32(2), 305–311.
- 36 Zhao, Q., Wei, J., & Zhang, H. (2019). Xenobiotica: The fate of foreign compounds in biological systems, 49(5), 563–568.
- 37 Wu, L. X., Guo, C. X., et al. (2012). British Journal of Clinical Pharmacology, 73(5), 750–757.
- 38 Bhutani, P., Rajanna, P. K., & Paul, A. T. (2020). Xenobiotica: The fate of foreign compounds in biological systems, 50(12), 1483–1489.
- ³⁹ Duan, K. M., Wang, S. Y., et al. (2012). *Journal of Clinical Pharmacology*, *52*(6), 940–946.

RELAXMEDIX ®



APPLICATIONS

- Relaxation/Sleep Support
- Stress Management Support
- Immune System Support
- Inflammatory Response Support
- Neurological Support



INTRODUCTION

RelaxMedix is a proprietary blend of hydro-ethanol extracts from Valerian root (Valeriana officinalis) and Cat's Claw bark (Uncaria tomentosa), also known as Samento. Constituents of V. officinalis include, among others, the sesquiterpene valerenic acid and iridoid valepotriates. V. officinalis and its constituent valerenic acid may act as a GABA agonist as well as a partial HT agonist. 2,3,4,5 V. officinalis may also act as an A_1 receptor agonist. *6 Activity at these receptors may account for valerian's role in the support of relaxation, sleep, and a healthy stress response.* Samento is extracted from the rare pentacyclic chemotype of *U. tomentosa*, which is TOA-free. This pentacyclic oxindole alkaloid (POA)-predominant, tetracyclic oxindole alkaloid (TOA)-free form of *U. tomentosa* may help with immune system support and inflammatory response support.*7,8

RelaxMedix is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

RELAXATION/SLEEP SUPPORT

According to a recent systematic review and meta-analysis of human trials, V. officinalis may help to support relaxation and sleep in occasional sleeplessness.*6 It may help to support both quality and quantity of sleep, with fewer nighttime awakenings.*9 V. officinalis may also support sleep through skeletal muscle relaxation, as seen in a mouse study.*4

STRESS MANAGEMENT SUPPORT

Valerian may help with stress management support during occasional stress.*10 One human trial with healthy individuals compared the effects of valerian alone, kava alone, and no treatment, on mental stress during cognitive testing. All three groups underwent initial cognitive testing, then were administered either valerian, kava, or nothing for 7 days. All three groups then underwent a subsequent session of cognitive testing. While both the valerian and kava groups experienced a decrease in systolic blood pressure after the intervention, only the valerian group experienced a lower heart rate during mental stress. While neither intervention affected performance, it appeared to mitigate the perception of mental stress by decreasing physiological reactivity.*10 A similar decrease in physiological reactivity was seen in a separate randomized, controlled trial.*11 In mice, one study found that constituent valepotriates may help to support healthy stress management, which a rat study attributed to modulation of the HPA axis.*¹² As shown in a mouse study, *U. tomentosa* may also help to support stress management.*13

OTHER USES

Immune System Support

U. tomentosa (pentacyclic chemotype) may help to maintain a healthy immune response and support immune system homeostasis.* U. tomentosa may help to maintain neutrophil function as well as Th1 and Th2 levels already within the normal ranges.* 13,14,15 It should be noted that only TOA-free U. tomentosa (such as Samento) helps with immune support.*7

Together, V. officinalis and U. tomentosa have synergistic effects.* It is known that both stress and insufficient sleep have depressant effects on the immune system.¹⁶ V. officinalis may help to maintain immune system health through the support of relaxation and sleep, while TOA-free *U. tomentosa* (pentacyclic chemotype) may help to support immune system health more directly.⁷⁷

Inflammatory Response Support

U. tomentosa (pentacyclic chemotype) may help to maintain a healthy inflammatory response.*8,17 It may help to support NF-kappa B levels already within the normal range in a dose-dependent manner;18,19 thus supporting both TNF-alpha and IL-1-beta within the normal ranges.*18

Neurological Support

U. tomentosa may help to support neurological health and help to maintain healthy neurocognitive function.*20,2

SAFETY AND CAUTIONS

V. officinalis (root) is generally well tolerated. Common side effects include drowsiness, dizziness, and occasional gastrointestinal effects. As *V. officinalis* supports relaxation, it may have additive effects when taken with sedative substances such as alcohol, ²³ benzodiazepines, ²⁴ or CNS depressants. ²⁵ Because *V. officinalis* mildly inhibits glucuronidation, it is possible that *V. officinalis* may increase levels of drugs metabolized by UGT1A1 and UGT2B7. ²⁶ While rare, there have been isolated case reports of hepatoxicity, particularly in higher doses, with multi-ingredient formulas, or concurrent with alcohol abuse. ²⁷ *V. officinalis* is considered as a recommended doses for shorter periods. ²⁷ In extended use, it should be tapered rather than stopped abruptly, to avoid rebound effects.²

U. tomentosa (bark) is generally well tolerated. Gastrointestinal effects such as nausea, vomiting, constipation and diarrhea have been reported.²⁸ It should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy.²⁹ *U. tomentosa* may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4.³⁰ *U. tomentosa* may have additive effects with anticoagulants, generally attributed to the TOA rhynchophylline, ³¹ as well as additive effects with antihypertensive drugs, generally attributed to the TOAs rhynchophylline and isorhynchophylline.^{32,33} As a reminder, Samento is TOA-free.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

33 Zhou, J. Y., & Zhou, S. W. (2012). Fitoterapia, 83(4), 617–626.

¹ Pilerood, S. A. & Prakash, J. (2013). International Journal of Food, Nutrition, and Dietetics, 1(1). ² Dietz, B. M., Mahady, G. B., et al. (2005). Brain Research Molecular Brain Research, 138(2), 191–197. ³ Benke, D., Barberis, A., et al. (2009). *Neuropharmacology*, 56(1), 174–181. 4 Caudal, D., Guinobert, I., et al. (2017). Journal of Traditional and Complementary Medicine, 8(2), 335–340. ⁵ Gordan, A., Taheri, E., & Saeidi, J. (2019). Journal of Pharmaceutical Research International, 29 (2), 1-10. ⁶ Shinjyo, N., Waddell, G., & Green, J. (2020). Journal of Evidence-Based Integrative Medicine, 25, 2515690X20967323. 7 Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). Applied Sciences, 10(8), 2668. 8 Liang, J. H., Wang, C., et al. (2020). Fitoterapia, 147, 104772. ⁹ Abdellah, S. A., Berlin, A., et al. (2019). Journal of Traditional and Complementary Medicine, 10(2), 116–123. ¹⁰ Cropley, M., Cave, Z., et al. (2002). *Phytotherapy Research: PTR*, 16(1), 23–27. ¹¹ Mineo, L., Concerto, C., et al. (2017). *Neuropsychobiology*, 75(1), 46–51. ¹² Shi, S. N., Shi, J. L., et al. (2014). Evidence-Based Complementary and Alternative Medicine: eCAM, 2014, 325948. ¹³ Bigliani, M. C., Rosso, M. C., et al. (2013). *Natural Product Research*, 27(18), 1682–1685.

¹⁴ Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 23(2), 141–148. 15 Núñez, C., Lozada-Requena, I., et al. (2015). Revista Peruana de Medicina Experimental y Salud Publica, 32(4), 643-651. ¹⁶ Asif, N., Iqbal, R., & Nazir, C. F. (2017). American Journal of Clinical and Experimental Immunology, 6(6), 92–96. ¹⁷ Mur, E., Hartig, F., et al. (2002). *The Journal of Rheumatology*, 29(4), 678–681. 18 Sandoval-Chacón, M., Thompson, J. H., et al. (1998). Alimentary Pharmacology & Therapeutics, 12(12), 1279–1289. ¹⁹ Allen-Hall, L., Arnason, J. T., et al. (2010). *Journal of Ethnopharmacology*, 127(3), 685–693. ²⁰ Snow, A. D., Castillo, G. M., et al. (2019). *Scientific Reports*, 9(1), 561. ²¹ Mohamed, A. F., Matsumoto, K., et al. (2000). The Journal of Pharmacy and Pharmacology, 52(12), 1553–1561. ²² Hadley, S., & Petry, J. J. (2003). *American Family Physician*, 67(8), 1755–1758. ²³ Chen, D., Klesmer, J., et al. (2002). *The American Journal on Addictions*, 11(1), 75–77.

²⁴ Donovan, J. L., DeVane, C. L., et al. (2004). *Drug Metabolism and Disposition: The biological fate of chemicals*, 32(12), 1333–1336. ²⁵ Houghton P. J. (1999). The Journal of Pharmacy and Pharmacology, 51(5), 505–512. Alkharfy, K. M., & Frye, R. F. (2007). Xenobiotica: The fate of foreign compounds in biological systems, 37(2), 113–123.
 Natural Medicines. (2021, March 20). Valerian [monograph]. http://naturalmedicines.therapeuticresearch.com. ²⁸ de Paula, L. C., Fonseca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22–30. ²⁹ Lamm, S., Sheng, Y., & Pero, R. W. (2001). Phytomedicine: International journal of phytotherapy and phytopharmacology, 8(4), 267–274. ³⁰ Budzinski, J. W., Foster, B. C., et al. (2000). Phytomedicine: International journal of phytotherapy and phytopharmacology, 7(4), 273–282. ³¹ Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126–130. ³² Zhou, J., & Zhou, S. (2010). Journal of Ethnopharmacology, 132(1), 15–27.

- Immune System Support
- Inflammatory Response Support
- Cardiovascular Support
- Neurological Support
- Blood Glucose and Metabolic Support

Antioxidant Support

Microbial Support



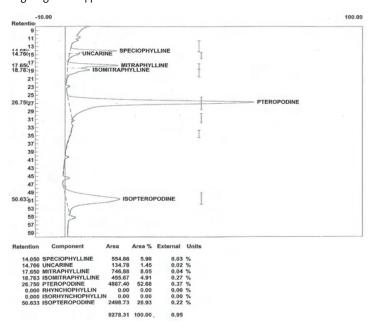
INTRODUCTION

Samento is a hydro-ethanol extract from the bark of pentacyclic chemotype *Uncaria tomentosa*, also known as Cat's Claw. The proprietary hydro-ethanolic extraction and enhancement process maximizes the bioavailability of phenolics, alkaloids, and other beneficial constituents. *U. tomentosa* is traditionally used for health promotion by indigenous tribes of the Peruvian Amazon, and ongoing research continues to elucidate its health-supporting effects. *U. tomentosa* exists in two chemotypes, one of which contains more tetracyclic oxindole alkaloids (TOA) and the other of which contains more pentacyclic oxindole alkaloids (POA). Samento is made from the bark of this rare pentacyclic phenotype. Samento is verified by independent 3rd party HPLC testing to be free of TOAs, with levels in trace amounts or undetectable. Samento not only meets but exceeds the standards of the U.S. Pharmacopoeia (USP 42) for *U. tomentosa*, which requires no less than 0.3% of POAs and no more than 0.05% TOAs. TOAS.

U. tomentosa (bark) includes other active constituents such as esters (ex. carboxyl alkyl), glycosides (ex. quinovic acid), organic acids (ex. oleanolic, ursolic, palmitoleic), procyanidins, sterols (ex. sitosterol), and triterpenes, as well as catechin, rutin, 3,4-dehydro-5-carboxystrictosidine, and many others.⁴ Samento liquid extract is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herb in its original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers. Samento is currently the only commercially available, naturally occurring TOA-free U. tomentosa.

WHY PENTACYCLIC CHEMOTYPE MATTERS (POAS VS. TOAS)

U. tomentosa (bark) most commonly contains both Pentacyclic Oxindole Alkaloids (POAs) and Tetracyclic Oxindole Alkaloids (TOAs). The POAs include speciophylline, uncarine F, mitraphylline, isomitraphylline, pteropodine, and isopteropodine, while the TOAs include rhynchophylline and isorhynchophylline.⁵ The preferred chemotype contains only POAs, which are recognized for helping to support immune system homeostasis.* POAs contribute to immune support by helping to maintain lymphocyte-proliferation-regulating factor levels already within the normal range.* Alternatively, TOAs block the effects of POAs, negating their support of immune health.* 5,6



IMMUNE SYSTEM SUPPORT

U. tomentosa (pentacyclic chemotype) may help to support immune system homeostasis.* Research suggests that POAs help to maintain lymphocyte-proliferation-regulating factor levels already within the normal range, 5 CD4 + CD25 + Foxp3 + levels already within the normal range, and Th2 levels already within the normal range.* It should be noted that TOAs inhibit the effect of POAs on lymphocyte-proliferation-regulating factor in a dose-dependent manner, thus TOA-free *U. tomentosa* is required for adequate immune support.* The specific POA mitraphylline may help to support healthy neutrophil function and maintain levels of Th1, Th2, and Th17 already within the normal range.* Mitraphylline may also help to support healthy apoptosis.* Mitraphylline

INFLAMMATORY RESPONSE SUPPORT

U. tomentosa (pentacyclic chemotype) may help to maintain and support a healthy inflammatory response.**11,12 *U. tomentosa* may help to support NF-kappaB levels already within the normal range in a dose-dependent manner,^{13,14} thus supporting both TNF-alpha and IL-1-beta already within the normal range.**14 *U. tomentosa* and its most prevalent POA alkaloid, mitraphylline, may help to maintain levels of IL-1-alpha, IL-2, IL-4, IL-6, IL-8, and IL-17 already within the normal range,^{15,16,17,18} in addition to supporting healthy function of the MAP kinase pathway.**14,18

OTHER USES

Cardiovascular Support
U. tomentosa may help to maintain blood pressure already within the normal range, attributed to the constituent hirsutine."

Neurological Support

U. tomentosa may help to support neurological health and help to maintain healthy neurocognitive function, 20,21 potentially due to the POA mitraphylline.*22

Blood Glucose and Metabolic Support

U. tomentosa may help to support healthy insulin levels and to maintain blood glucose levels already within the normal range.*7,23

Antioxidant Support

U. tomentosa may give antioxidant support, helping to maintain levels of oxidative stress already within the normal range, ²⁴ attributed to the constituent flavan-3-ol monomers, alkaloids, and polyphenols.*4

Microbial Support

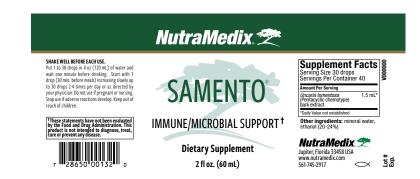
U. tomentosa may assist with a broad range of microbial support.*25,26,27

SAFETY AND CAUTIONS

U. tomentosa (bark) is generally well tolerated. Gastrointestinal effects such as nausea, vomiting, constipation or diarrhea have been reported.²⁸ It should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy.²⁹ U. tomentosa may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4.30 U. tomentosa may have additive effects with anticoagulants, generally attributed to the TOA's rhynchophylline and isorhynchophylline, 31 as well as additive effects with antihypertensive drugs, generally attributed to the TOAs rhynchophylline and isorhynchophylline. 32,33 As a reminder, Samento is TOA-free, with levels in trace amounts or undetectable.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- ¹ Muhammad, I., Dunbar, D. C., et al. (2001). Phytochemistry, 57(5), 781-785.
- ² Vilchez, L. (2019). Informe Tecnico N IT050-2019 Samento-Stevia Liquid Extract.
- ³ Convention USP, editor. United States Pharmacopeia and National Formulary (USP 42-NF 37), 42nd ed. Rockville (MD): Convention, United States Pharmacopeial; 2018.
- ⁴ Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). *Applied Sciences*, 10(8), 2668.
- ⁵ Keplinger, K., Laus, G., et al. (1999). Journal of Ethnopharmacology, 64(1), 23–34.
- 6 Wurm, M., Kacani, L., et al. (1998). Planta Medica, 64(8), 701–704.
- Domingues, A., Sartori, A., et al. (2011). Phytotherapy Research: PTR, 25(8), 1229–1235.
- 8 Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, 23(2), 141–148.
- 9 Núñez, C., Lozada-Requena, I., et al. (2015). Revista Peruana de Medicina Experimental y Salud Publica, 32(4), 643–651.
- ¹⁰ De Martino, L., Martinot, J. L., et al. (2006). *Journal of Ethnopharmacology, 107*(1), 91–94.
- ¹¹ Aquino, R., De Feo, V., et al. (1991). *Journal of Natural Products*, 54(2), 453-459.
- ¹² Mur, E., Hartig, F., et al. (2002). *The Journal of Rheumatology*, 29(4), 678–681.
- 13 Sandoval-Chacón, M., Thompson, J. H., et al. (1998). Alimentary Pharmacology & Therapeutics, 12(12), 1279-1289.
- $^{14} \, \text{Allen-Hall, L., Arnason, J. T., et al. (2010)}. \textit{Journal of Ethnopharmacology, 127} (3), 685-693.$
- ¹⁵ Lemaire, I., Assinewe, V., et al. (1999). Journal of Ethnopharmacology, 64(2), 109–115.
- ¹⁶ Sandoval, M., Charbonnet, R. M., et al. (2000). Free Radical Biology & Medicine, 29(1), 71–78.
- 17 Rojas-Duran, R., González-Aspajo, G., et al. (2012). Journal of Ethnopharmacology, 143(3), 801–804.
- 18 Allen-Hall, L., Cano, P., et al. (2007). Journal of Ethnopharmacology, 109(2), 312–317.
- ¹⁹ Horie, S., Yano, S., et al. (1992). *Life Sciences*, 50(7), 491–498.
- ²⁰ Snow, A. D., Castillo, G. M., et al. (2019). *Scientific Reports*, *9*(1), 561.
- ²¹ Mohamed, A. F., Matsumoto, K., et al. (2000). The Journal of Pharmacy and Pharmacology, 52(12), 1553-1561.
- ²² Frackowiak, T., Baczek, T., et al. (2006). Zeitschrift fur Naturforschung. C, Journal of Biosciences, 61(11-12), 821–826.
- ²³ Araujo, L., Feitosa, K. B., et al. (2018). *Scientific Reports*, 8(1), 11013.
- ²⁴ Sandoval, M., Okuhama, N. N., et al. (2002). Phytomedicine: International journal of phytotherapy and phytopharmacology, 9(4), 325–337.
- ²⁵ Ccahuana-Vasquez, R. A., Santos, S. S., et al. (2007). Brazilian Oral Research, 21(1), 46–50.
- ²⁶ Yepes-Perez, A. F., Herrera-Calderón, O., et al. (2021). Evidence-Based Complementary and Alternative Medicine: eCAM, 2021, 6679761.
- ²⁷ Datar, A., Kaur, N., et al. (2010). *Townsend Letter*, 7, 1–4.
- ²⁸ de Paula, L. C., Fonseca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22–30.
- ²⁹ Lamm, S., Sheng, Y., et al. (2001). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 8(4), 267–274.
- 30 Budzinski, J. W., Foster, B. C., et al. (2000). Phytomedicine: International journal of phytotherapy and phytopharmacology, 7(4), 273–282.
- 31 Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126–130.
- 32 Zhou, J., & Zhou, S. (2010). Journal of Ethnopharmacology, 132(1), 15–27.
- 33 Zhou, J. Y., & Zhou, S. W. (2012). Fitoterapia, 83(4), 617-626.



- Antioxidant Support
- Immune Support
- Cardiovascular Support
- Detox Support



INTRODUCTION

Sealantro™ is a blend of chlorella (*Chlorella spp.*), cilantro leaf (*C. sativum*), and Pacific cold-water red seaweed (Chondracanthus chamissoi) extracts.

Chlorella vulgaris is a single-celled algae that belongs to the Chlorellaceae family, and is sometimes referred to as freshwater seaweed. In traditional Chinese health practices, it is considered a gently cleansing, healthful food.*2 *C. vulgaris* contains flavonoids, tannins, triterpenoids, and sulfated polysaccharides, among others.³ As a functional food, its protein content ranges from 55-67%, containing all essential amino acids.4

Coriandrum sativum, also known as Chinese parsley, belongs to the Umbelliferae/ Apiaceae family and is native to the Mediterranean region.⁵ C. sativum is well known as both an herb and a spice. The leaves are referred to as Cilantro, while the seeds as both an nero and a spice. The leaves are referred to as Chairro, while the seeds are referred to as Coriander.⁶ In Chinese health practices, Cilantro is viewed as a healthful and cooling food.⁷ Cilantro (*C. sativum*) contains fiber, B vitamins, vitamin C, carotenoids, and minerals.⁸ The leaves are an abundant source of beta-carotene, with mature leaves containing higher levels.⁸ The majority of the leaf essential oil consists of (E)-2-Decenal.⁵ Cilantro (*C. sativum*) is rich in phenolic compounds and contains phenolcarboxylic acids, coumarins, and flavonoids.⁵

Chondracanthus chamissoi, known commonly as Pacific cold-water red seaweed, belongs to the Gigartinaceae family. It is also known as Sphaerococcus chamissoi, Gigartina chamissoi, and Chondroclonium chamissoi. C. chamissoi contains polysaccharides and carageenans, among other constituents, and its flavonol content may help with antioxidant support.

Sealantro™ is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

ANTIOXIDANT SUPPORT

Chlorella vulgaris may help with antioxidant support.*3,12,13 lt may help to maintain total antioxidant capacity, malondialdehyde levels, and erythrocyte antioxidant function already within the normal range.*

Cilantro (*C. sativum*) may contribute antioxidant support, as measured by DPPH assay and beta-carotene bleaching assay,⁵ and may help to maintain healthy free radical scavenging activity involving hydroxyl and superoxide anion free radicals.*⁵ In preclinical studies, a leaf extract helped to support levels of glutathione, superoxide dismutase, and catalase already within the normal range in a dose-dependent manner, partly attributed to linoleic and linolenic fatty acid content.*¹⁴ In rat studies, Cilantro (*C. sativum*) helped with antioxidant support in both liver cells and plasma;¹⁵ it also helped to maintain SGOT, SGPT, and TBARS already within the normal range.*¹⁶

Red seaweed (*C. chamissoi*) may help with antioxidant support as determined by TRAP, FRAP, and DPPH assays, attributed to the phenolic and flavonoid content.*11

IMMUNE SUPPORT

Chlorella (*C. vulgaris*) may help with immune support.* In studies with mice, it helped to support phagocytic activity, humoral immunity, and cell-mediated immunity already within the normal range.* It also helped to maintain B and T cell proliferation already within the normal range.* In healthy humans, *C. vulgaris* may help to maintain NK cell activity and levels of Th1 cell-induced cytokines already within the normal range.* 19

CARDIOVASCULAR SUPPORT

Chlorella (*C. vulgaris*) may help to maintain blood pressure already within the normal range.*²⁰ It may also help to maintain levels of total cholesterol, triglycerides, VLDL, and apolipoprotein B already within the normal range.*²¹

OTHER USES

Detox Support

Chlorella (*C. wulgaris*) may help to support liver and kidney health.*4,22,23,24 It may also help to support healthy excretion of metals.*4,24,25 In rat studies, it helped to support the healthy excretion of metals both directly and in the form of metallothioneins (MTs), attributed to its chlorophyll and dietary fiber content.*4 Cilantro may also help to support healthy excretion of metals and support kidney health.*26,27 Pacific coldwater red seaweed, in preclinical studies, acted as a biosorbent for metals.*28

SAFETY AND CAUTIONS

Chlorella (*C. vulgaris*) is generally well tolerated. Gastrointestinal complaints such as nausea and diarrhea have been reported, though usually resolved within two weeks.²⁹ Fatigue has also been reported.³⁰ There have been case reports of chlorella causing photosensitivity,³¹ and rare reports of thrombocytopenia which may have been associated with polypharmacy.³² Allergy due to occupational exposure has been reported.³³ Chlorella has significant vitamin K content and may theoretically decrease the effectiveness of warfarin.³⁴ Chlorella may have a high iodine content and caution though the prediction of the property of the content and caution should be used in those who are constituted. should be used in those who are sensitive.³

Cilantro (*C. sativum*) is generally well tolerated. The plant is generally recognized as safe (GRAS) in the U.S.³⁶ There has been one reported case of anaphylaxis following cilantro ingestion.³⁷ Cilantro (*C. sativum*) may have additive effects with antiplatelet medications.³⁸ It may also have additive effects with photosensitizing medications due to the constituent furoisocoumarin coriandrin.³⁹

Pacific red seaweed (C. chamissoi), as a food, is generally well-tolerated. Regarding the potential for drug interactions or adverse effects, little data is available at this

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- $^{1}\ Natural\ Medicines.\ (2021,\ July\ 24).\ Chlorella\ [monograph].\ http://naturalmedicines.therapeuticresearch.com$
- ² Pitchford, P. (2002). *Healing with whole foods* (3rd ed., pp. 232-234). North Atlantic Books.
- ³ Habashy, N. H., Abu Serie, M. M., et al. (2018). *Journal of Functional Foods*, 40, 317-328.
- ⁴ Shim, H. Y., Shin, H. S., et al. (2008). *Journal of Medicinal Food*, 11(3), 479.
- ⁵ Wei, J. N., Liu, Z. H., et al. (2019). Food Chemistry, 286, 260-267.
- ⁶ Natural Medicines. (2021, July 24). Cilantro [monograph]. http://naturalmedicines.therapeuticresearch.com
- 7 Pitchford, P. (2002). Healing with whole foods (3rd ed., p. 62). North Atlantic Books.
- Bhat, S., Kaushal, P., & Sharma, H. K. (2014). African Journal of Plant Science, 8(1), 25-33.
- 9 Guiry, M.D. & Guiry, G.M. (2021). AlgaeBasé. World-wide electronic publication, National University of Ireland, Galway. http://www.algaebase.org; searched on 25 July 2021.
- ¹⁰ Wang, P., Zhao, X., et al. (2012). Carbohydrate Polymers, 89(3), 914–919.
- ¹¹ Miranda-Delgado, A., Montoya, M. J., et al. (2018). Latin American Journal of Aquatic Research, 46(2), 301-313.
- ¹² Okada, H., Yoshida, N., et al. (2017). *The Kurume Medical Journal*, 64(4), 83-90.
- ¹³ Lee, S. H., Kang, H. J., et al. (2010). *Nutrition (Burbank, Los Angeles County, Calif.*), 26(2), 175–183.
- ¹⁴ Park, G., Kim, H.G., et al. (2012). Skin Pharmacology and Physiology, 25, 93-99.
- ¹⁵ de Almeida Melo, E., Bion, F.M., et al. (2003). European Journal of Lipid Science and Technology, 105, 483-487.
- 16 Sreelatha, S., Padma, P. R., & Umadevi, M. (2009). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 47(4), 702–708.
- ¹⁷ Morris, H. J., Carrillo, O., et al. (2007). *Enzyme and Microbial Technology*, 40, 456-460.
- ¹⁸ Cheng, F. C., Lin, A., et al. (2004). *Journal of Medicinal Food*, 7(2), 146–152.
- ¹⁹ Kwak, J. H., Baek, S. H., et al. (2012). *Nutrition Journal*, 11, 53.
- ²⁰ Merchant, R. E., & Andre, C. A. (2001). Alternative Therapies in Health and Medicine, 7(3), 79–91.
- ²¹ Ryu, N. H., Lim, Y., et al. (2014). *Nutrition Journal*, 13, 57.
- ²² Ebrahimi-Mameghani, M., Aliashrafi, S., et al. (2014). Health Promotion Perspectives, 4(1), 107–115.
- ²³ Azocar, J., & Diaz, A. (2013). World Journal of Gastroenterology, 19(7), 1085–1090.
- ²⁴ Zhai, Q., Narbad, A., & Chen, W. (2015). *Nutrients*, 7(1), 552–571.
- ²⁵ Uchikawa, T., Kumamoto, Y., et al. (2011). *The Journal of Toxicological Sciences*, *36*(1), 121–126.
- ²⁶ Aga, M., Iwaki, K., et al. (2001). *Journal of Ethnopharmacology*, 77(2-3), 203–208.
- ²⁷ Omura, Y., & Beckman, S. L. (1995). Acupuncture & Electro-Therapeutics Research, 20(3-4), 195–229.
- ²⁸ Yipmantin, A., Maldonado, H. J., et al. (2011). *Journal of Hazardous Materials*, 185(2-3), 922–929.
- ²⁹ Panahi, Y., Badeli, R., et al. (2015). *Complementary Therapies in Medicine*, 23(4), 598–602.
- 30 Halperin, S. A., Smith, B., et al. (2003). CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne, 169(2), 111–117.
- 31 Jitsukawa, K., Suizu, R., & Hidano, A. (1984). International Journal of Dermatology, 23(4), 263–268.
- ³² Yavasoglu, I., Turgutkaya, A., & Bolaman, Z. (2018). Sao Paulo Medical Journal = Revista Paulista de Medicina, 136(6), 602–603.
- 33 Ng, T. P., Tan, W. C., & Lee, Y. K. (1994). Respiratory Medicine, 88(7), 555–557.
- 34 Ohkawa, S., Yoneda, Y., et al. (1995). Rinsho Shinkeigaku = Clinical Neurology, 35(7), 806–807.
- 35 Norman, J. A., Pickford, C. J., et al. (1988). Food Additives and Contaminants, 5(1), 103–109.
- 36 CFR Code of Federal Regulations Title 21. Accessdata.fda.gov. (2021). Retrieved 24 July 2021, from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=182.10.
- 37 Unkle, D. W., Ricketti, A. J., et al. (2012). Annals of Allergy, Asthma & Immunology: Official publication of the American College of Allergy, Asthma, & Immunology, 109(6), 471–472.
- 38 Suneetha, W. J. & Krishnakantha, T. P. (2008). Pharmaceutical Biology, 43(3), 230-3.
- ³⁹ Ashwood-Smith, M. J., Warrington, P. J., et al. (1989). *Photochemistry and Photobiology*, 50(6), 745–751.

SERRAPEPTASE



APPLICATIONS

- Supports Protein Digestion
- Supports Prebiotic Intestinal Health
- Inflammatory Support
- Antioxidant Support
- Blood Glucose Support
- Cardiovascular Support
- Respiratory Support



INTRODUCTION

Serrapeptase, also known as serratiopeptidase, is a proteolytic enzyme or protease isolated from the silkworm (*Bombyx mori*), which is used by the silkworm to help dissolve its cocoon. It is commonly used for human health support in Europe and Japan. Serrapeptase is a proteolytic enzyme that may help with the digestion of dietary proteins and may also help with clearing normal waste proteins associated with tissue repair.* Additionally, proteolytic enzymes may help to maintain tissue health by supporting plasmin and contributing healthy inflammatory support.*3

Inulin is a prebiotic, a non-digestible dietary fiber that is fermented by colonic microflora.*4 Its scientific name is beta(2-1)fructan.⁵ It is a fructo-oligosaccharide (FOS) found in roots and tubers that may help to support healthy microbiota, specifically *Lactobacillus spp.* and *Bifidobacteria spp.* 6,7 Dietary sources of inulin include various fruits and vegetables as well as herbs such as chicory.4 Our inulin is sourced from Helianthus tuberosus, an edible tuber known as Jerusalem artichoke and a perennial in the Asteraceae/Compositae family.

Serrapeptase may help to digest dietary proteins, facilitating the absorption of their constituent amino acids, and inulin helps support a healthy intestinal microbiome.*6,7,8 Together, they work to support digestion, absorption, and overall intestinal health.* This product is a proprietary blend of serrapeptase (Peptizyme SP) and Inulin. This product is wheat-free, egg-free, and dairy free. It is gluten-free as defined by the U.S. FDA, with less than 20 ppm per S-ELISA testing, and is free from other gluten-containing grains such as barley, oats, rye, and spelt. It is also free of fish, shellfish, tree nuts, and peanuts.

SUPPORTS PROTEIN DIGESTION

Healthy protein digestion and absorption depend on the ability to disassemble dietary proteins into their constituent amino acids. Serrapeptase is a proteolytic enzyme that may help to support healthy digestion and absorption of dietary protein.*1 Serrapeptase may also help to support healthy clearing of normal cellular waste proteins.*1

SUPPORTS PREBIOTIC INTESTINAL HEALTH

Inulin is a dietary fiber that supports digestive health through a variety of mechanisms.* Inulin is indigestible, and therefore, not absorbed. Instead, it is fermented in the large intestine, resulting in short-chain fatty acids (SCFs) that support the growth of both *Lactobacillus spp.* and *Bifidobacteria spp.* with help to maintain gastrointestinal health.*^{6,7,8} Short-chain fatty acids may also help to maintain levels of GLP-1 and ghrelin already within the normal range.*⁹ Inulin may help to provide a sense of fullness and maintain a healthy caloric intake, in addition to supporting normal stool consistency and healthy stool regularity.*¹⁰

INFLAMMATORY SUPPORT

Serrapeptase may help with healthy inflammatory support. Int. It may help to maintain tissue health by supporting plasmin's role in healing, and may help to maintain capillary permeability already within the normal range. Serrapeptase helps to support healthy clearing of normal cellular waste, and may also help to maintain levels of C3, C4, and haptoglobin that are already within the normal range. Are Proteases may help to support physical exercise and exercise recovery. Inulin may help to maintain the levels of lipopolysaccharides (LPS) and cytokines such as TNF-alpha and IL-6 already within the normal range. Set IT may also help to maintain NF-kappaB levels already within the normal range.

OTHER USES

Antioxidant Support

The tubers of H. tuberosus and the inulin derived from them may help to contribute antioxidant support in a dose-dependent manner, as quantified by DPPH scavenging assay to determine free-radical scavenging support.*18,19 Animal studies have shown that inulin may contribute antioxidant support in a dose-dependent manner, with an inverse correlation between inulin and malondialdehyde (MDA) levels.*19

Blood Glucose Support

Because inulin is a non-digestible carbohydrate, it may support a more healthful post-prandial glycemic response.*20,21 It may help to maintain levels of ghrelin and somatostatin already within the normal range, which may in turn support healthier caloric intake and slower gastric emptying.*22 Inulin may help to maintain both fasting and post-prandial blood glucose already within the normal range, in addition to supporting healthy insulin sensitivity.*20,21

Cardiovascular Support

Inulin is fermented to short-chain fatty acids (SCFs) which may help to support normal fat oxidation.*23 Inulin may help to maintain levels of LDL and HDL already within the normal range.*24 According to a meta-analysis of randomized, controlled trials, it may also help to maintain levels of triacylglycerols already within the normal range.*25

Respiratory SupportBecause of its proteolytic functions, serrapeptase may help to maintain normal sputum viscosity. ^{26,27} It may also help to support and maintain healthy tissue of the ears, nose, and throat.¹²

SAFETY AND CAUTIONS

Serrapeptase is generally well tolerated, and has been used in clinical trials for up to four weeks.²⁶ While nausea, epigastric pain, and gastrointestinal discomfort have been reported, rates were similar to those with the placebo.¹⁴ Serrapeptase may have fibrinolytic properties and should not be taken with anticoagulant or antiplatelet medications as it may increase the risk of bleeding.¹⁴ For the same reasons, caution should be used in those with bleeding disorders. Due to the potential of perioperative bleeding, serrapeptase should be avoided for at least two weeks prior to elective surgical procedures.²

Inulin is generally recognized as safe (GRAS) in the U.S. and is usually well tolerated.²⁸ Doses up to 20 g/day have been used for up to three weeks without significant negative effects.³¹ Side effects may include diarrhea, constipation, bloating, and flatulence, which are more significant in doses over 30 grams.²⁹ One serving of serrapeptase (two capsules) includes less than one gram of inulin. As inulin may help to support healthy blood glucose levels already within the normal range, theoretically, it may have additive effects with hypoglycemic medications.^{*20,21}

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

1 Tiwari, M. (2017). Asian Journal of Pharmaceutical Sciences, 12(3), 209-215.
2 Natural Medicines. (2021, June 22). Serrapeptase [monograph]. http://inaturalmedicines.therapeuticresearch.com
3 Chandanwale, A., Langade, D., et al. (2017). Advances in Therapy, 34(1), 180-198.
4 Collado Yurrita, L., San Mauro Martin, I., et al. (2014). Nutricion Hospitalaria, 30(2), 244-252.
5 Roberfroid, M. B. (2005). Introducing inulin-type fructans. The British Journal of Nutrition, 93(Suppl 1), S13-S25.
6 Slavin, J., & Feirtag, J. (2011). Food & Function, 2(1), 72-77.
7 Gibson, G. R., Beatty, E. R., et al. (1995). Gastroenterology, 108(4), 975-982.
8 Ramnani, P., Gaudier, E., et al. (2001). The British Journal of Nutrition, 74(2), 233-240.
9 Delzenne, N. M., Cani, P. D., et al. (2005). The British Journal of Nutrition, 93(1, Suppl.), S157-S161.
10 Micka, A., Siepelmeyer, A., et al. (2017). International Journal of Food Sciences and Nutrition, 68(1), 82-89.
11 Tachibana, M., Mizukoshi, O., et al. (2018). Phot Carl Health, 21(1), 91.
12 Tamimi, Z., Al Habashneh, R., et al. (2021). BMC Oral Health, 21(1), 91.
13 Esch, P. M., Gerngross, H., & Fabian, A. (1989). Fortschritte der Medizin, 107(4), 67-72.
14 Mazzone, A., Catalani, M., et al. (1990). The Journal of International Medical Research, 18(5), 379-388.
15 Miller, P. C., Bailey, S. P., et al. (2004). Journal of Sports Sciences, 22(4), 365-372.
16 Nicolucci, A. C., Hume, M. P., et al. (2017). Gastroenterology, 153(3), 711-722.
17 Kang, Y. M., Lee, K. Y., & An, H. J. (2018). Nutrients, 10(11), 1657.
18 Niziol-Łukaszewska, Z., Furman-Toczek, D., & Zagórska-Dziok, M. (2018). Lipids in Health and Disease, 17(1), 280.
19 Shang, H. M., Zhou, H. Z., et al. (2018). Metabolism, 87, 25-35.
20 Cai, X., Yu, H., et al. (2018). Molecular Nutrition & Metabolism. Physiologie Appliquee, Nutrition et Metabolisme, 35(1), 9-16.
21 van der Beek, C. M., Canfora, E. E., et al. (2018). Metabolism, 87, 25-35.
22 Nationa, A., et al. (2017). European Journal of Clinical Nutrition, 71(1), 9-20.
23 Righen



- Antioxidant Support
- Detox Support
- Liver Detox Support
- Kidney Detox Support
- Intestinal Detox Support



INTRODUCTION

Sparga is a hydro-ethanol extract from the stems of *Asparagus officinalis*, which is also consumed as a garden vegetable. Asparagus has a long history of use, dating back at least as far as ancient Egypt, Greece, and Rome, where it was used for food and medicine. Both Dioscorides and Pliny the Elder discussed the cultivation and preparation of asparagus for food in the 1st century CE.² In the 17th century, asparagus was re-established as a culinary delicacy by Louis XIV, the Sun King, who is credited for its nickname as the "King of Vegetables." 1,3

The word asparagus comes from the Greek *asparagos*, meaning shoot or sprout.⁴ There are almost 300 species of asparagus, worldwide.⁴ *A. officinalis* is native to parts of Africa, Asia, Australia, and Europe.⁴ It belongs to the Asparagaceae family, though was considered part of the Liliaceae family prior to the recent subdivision.⁴ *A. officinalis* is also known as *A. longifolius* and Sparrow Grass.⁵

The macronutrient content of *A. officinalis* primarily includes carbohydrate, along with protein, dietary fiber, and a small amount of fat.⁴ The micronutrient content includes minerals such as potassium (202 mg per 100 g serving), phosphorus, calcium, magnesium, selenium, iron, sodium, zinc, and copper; fat-soluble vitamins such as K, A, and provitamin A carotenoids; water-soluble B vitamins such as folate (52 mcg per 100 g serving), choline, thiamin (B1), riboflavin (B2), niacin (B3), and pyridoxine (B6); and the water-soluble vitamin C.⁶ Asparagus also contains amino acids, predominantly aspartic acid and glutamic acid.⁷

A. officinalis also contains steroidal saponins, flavonoids, alkaloids, fructooligosaccharides, steroidal glycosides, tannins, sulfur compounds, nitrogen compounds, and acetylenic compounds. Specific constituents found in A. officinalis include inulin, asparagusic acid, aldehyde, thiophene, thiazole, ketone vanillin, asparoffins A-D, asparenyol, 1-methoxy-2-hydroxy-4-[5-(4-hydroxyphenoxy)-3-penten-1-ynyl] phenolgobicusion B, and asparanin A, as well as the sulfur compounds glutathione, N-acetylcysteine, and cysteine. 4,8,9

Sparga is made at our U.S. manufacturing facility. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

ANTIOXIDANT SUPPORT

A. officinalis may help to support antioxidant activity per ABTS⁺ and DPPH; superoxide dismutase and erythrocyte hemolysis; and FRAP and CUPRAC assays. Antioxidant support has been attributed to the constituent polyphenols, flavanols, flavonoids, tannins and ascorbic acid. When consumed as a vegetable, boiling may decrease flavonol content by as much as 43%. According to HPLC-MS/MS analysis, specific constituents relevant to antioxidant support include phenolic acid, quercetin-3-rutinoside, quercetin, isorhamnetin, and kaempferol. In mice, ethanol and aqueous extracts of A. officinalis helped to maintain healthy levels of superoxide dismutase (SOD) and total antioxidant capacity (TAC) already within the normal range. While there are currently no human studies with asparagus and antioxidant support, a human study with broccoli sprouts, also containing glutathione, helped to maintain total antioxidant capacity (TAC), oxidative stress index (OSI), and malondialdehyde (MDA) levels already within the normal range.

DETOX SUPPORT

The primary systems involved in detoxification are the liver, kidneys, and intestines. *A. officinalis* may help with healthy detoxification through antioxidant support for the liver and kidneys.* When consumed as a vegetable with dietary fiber, *A. officinalis* may help to maintain healthy bile acid binding for normal intestinal excretion.*

Glutathione is an important endogenous antioxidant for healthy detoxification and may be supported through dietary and supplemental means." In a study examining the glutathione content of sulfur-rich vegetables and fruits, asparagus contained the highest amount of glutathione, followed by avocado and spinach. Asparagus also contained the highest amount of N-acetylcysteine (NAC) and significant levels of cysteine, second only to red pepper. NAC and cysteine are glutathione precursors, with cysteine availability as the rate-limiting step in endogenous glutathione production.* Glutathione helps with antioxidant support, helps to maintain normal detoxification, and helps to support the normal excretion of the body's natural toxins.*

LIVER DETOX SUPPORT

A. officinalis may help with liver detox through antioxidant support.* Its constituent antioxidant glutathione is essential for healthy liver detoxification.* Glutathione may contribute direct antioxidant support or act as a cofactor for antioxidant enzymes.* It may support antioxidant activity for free radicals resulting from Phase 1 liver detoxification, and in Phase 2 liver detoxification, may support the conjugation of Phase 1 intermediates to a water-soluble form for urinary excretion.*

A. officinalis may support normal ethanol metabolism and help to maintain alcohol dehydrogenase and aldehyde dehydrogenase already within the normal range.* Consequently, it may help to support hepatocyte health.*18 In mice, both ethanol and aqueous extracts of A. officinalis helped to support liver health by maintaining serum levels of alanine transaminase (ALT) and aspartate transaminase (AST) already within the normal range.*13 In rats, A. officinalis extract helped to support healthy hepatocytes and maintain levels of AST, ALT, ALP and bilirubin already within the normal range.*19

KIDNEY DETOX SUPPORT

A. officinalis may help with kidney detox support through glutathione antioxidant support.* In Phase 2 liver detoxification, the constituent glutathione supports the conjugation of Phase 1 intermediates, rendering them water soluble and available for renal excretion.* In rats, A. officinalis extract helped to support healthy glomeruli, maintaining levels of urea and creatinine already within the normal range. 19

INTESTINAL DETOX SUPPORT

When consumed as a vegetable, the dietary fiber in *A. officinalis* may help with intestinal detox support through the binding of bile acids.*20,21 Steaming (vs. boiling) supports bile acid binding ability, which may help to maintain healthy excretion through stool.*20,21

SAFETY AND CAUTIONS

Asparagus is widely considered safe in amounts found in foods. In some individuals, asparagus can contribute a distinctive odor to the urine, though not all individuals experience this, nor do all individuals perceive this when it occurs. Some individuals have had allergic reactions to asparagus, both orally and topically, and caution should be used in those with allergies to onions, garlic, and similar members of the Liliaceae family due to the potential for cross-allergenicity. In one small study with a product containing asparagus root and parsley, side effects included gastrointestinal complaints such as nausea, abdominal pain and constipation, as well as kidney pain (15% of patients), gout (2% of patients), and dysuria. It is unknown whether these side effects were due to asparagus root, parsley, or both. It should be noted that NutraMedix Sparga is extracted from asparagus stems, not asparagus root.

In a mouse study with NutraMedix Sparga, performed at the Universidad de Guayaquil in Ecuador, no adverse effects were noted with administration of *A. officinalis* extract at approximately 626 times the human dose, daily, over a 14-day period. Researchers concluded that according to OECD TG 423 guidelines, the product is considered innocuous for humans.²²

Asparagus should be avoided in pregnancy as a related species, *A. pubescens*, has been shown to have contraceptive effects in mice, rats, and rabbits, inhibiting fetal implantation. Asparagus may have additive effects with potassium-wasting diuretic medications such as furosemide/Lasix and hydrochlorothiazide (HCTZ), potentially increasing the risk of hypokalemia. When taken with lithium, asparagus may decrease lithium excretion, resulting in elevated lithium levels.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

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- ¹ Pegiou, E., Mumm, R., et al. (2019). *Metabolites*, 10(1), 17.
- ² Mitchell S. C. (2013). Perspectives in Biology and Medicine, 56(3), 341–351.
- ³ Fan, R., Yuan, F., et al. (2015). *Journal of Food Science and Technology*, 52(5), 2690–2700.
- 4 Iqbal, M., Bibi, Y., et al. (2017). Journal of Plant Biochemistry & Physiology, 5(1), 1-6.
- ⁵ Natural Medicines. (2021, November 6). Asparagus [monograph]. http://naturalmedicines.therapeuticresearch.com
- 5 USDA. (2021). Retrieved 6 November 2021, from https://fdc.nal.usda.gov/fdc-app.html#/food-details/1103335/nutrients.
- ⁷ Słupski, J., Korus, A., et al. (2010). International Journal of Food Science and Technology, 45, 733–739.
- ⁸ Li, X. M., Cai, J. L., et al. (2017). Journal of Asian Natural Products Research, 19(2), 164–171.
- ⁹ Demirkol, O., Adams, C., & Ercal, N. (2004). Journal of Agricultural and Food Chemistry, 52(26), 8151–8154.
- 10 Khorasani, A., Sani, W., et al. (2010). African Journal of Biotechnology, 9(49), 8460-8466.
- 11 Lee, J. W., Lee, J. H., et al. (2014). Plant Foods for Human Nutrition (Dordrecht, Netherlands), 69(2), 175–181.
- ¹² Makris, D. P., & Rossiter, J. T. (2001). Journal of Agricultural and Food Chemistry, 49(7), 3216–3222.
- ¹³ Zhu, X., Zhang, W., et al. (2010). Journal of the Science of Food and Agriculture, 90 (7), 1129–1135
- ¹⁴ Bahadoran, Z., Mirmiran, P., et al. (2011). European Journal of Clinical Nutrition, 65(8), 972–977.
- ¹⁵ Pizzorno J. (2014). Integrative Medicine (Encinitas, Calif.), 13(1), 8–12.
- ¹⁶ Forman, H. J., Zhang, H., & Rinna, A. (2009). *Molecular Aspects of Medicine*, 30(1-2), 1–12.
- ¹⁷ Minich, D. M., & Brown, B. I. (2019). *Nutrients*, 17(9), 2073.
- ¹⁸ Kim, B. Y., Cui, Z. G., et al. (2009). *Journal of Food Science*, 74(7), H204–H208.
- ¹⁹ Poormoosavi, S. M., Najafzadehvarzi, H., et al. (2018). *Toxicology Reports*, *5*, 427–433.
- ²⁰ Kahlon, T. S., Chiu, M.-C. M., & Chapman, M. H. (2007b). *Nutrition Research*, *27*, 750-755.
- ²¹ Kahlon, T. S., Chapman, M. H., & Smith, G. E. (2007a). *Food Chemistry*, 103, 676-680.
- ²² Allende, S. (2009). NutraMedix Laboratories, LLC, Florida, USA. Universidad de Guayaquil, Ecuador. Faculty of Clinical Sciences.
- ²³ Nwafor, P. A., Okwuasaba, F. K., & Onoruvwe, O. O. (1998). *Journal of Ethnopharmacology*, 62(2), 117–122.



- Cardiovascular and Metabolic Support
- Microbial Support
- Inflammatory Response Support
- Antioxidant Support



INTRODUCTION

Stevia is a hydro-ethanol extract from Stevia leaf (Stevia rebaudiana). S. rebaudiana, formerly known as Eupatorium rebaudiana, is part of the Asteraceae/Compositae family, native to Brazil and Paraguay, and used as a dietary supplement as well as a sweetener. The constituents responsible for the sweet taste are steviol glycosides, including stevioside, rebaudiosides A-F, steviolbioside, isosteviol, and dulcoside A, of which stevioside and rebaudioside A are the most abundant.^{2,3} Steviol glycosides are approximately 250-300 times sweeter than sucrose. S. rebaudiana also contains phytosterols such as stigmasterol, beta-sitosterol, and campesterol,² as well as flavonoids, diterpenes, triterpenes, vitamins, and minerals.^{2,3}

Stevia is made at our U.S. manufacturing facility and because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

CARDIOVASCULAR AND METABOLIC SUPPORT

Stevioside within *S. rebaudiana* may help to maintain healthy blood pressure levels already within the normal range.*4 Blood pressure support from steviol glycosides may be related to alterations in glomerular filtration rate and transport of water and salt in renal tubules, supporting normal sodium and potassium excretion.*5 Stevioside may support normal vasodilation through changes in Ca²⁺ ion inflow to vascular smooth muscle, and may help to maintain blood pressure levels already within the normal range.*6

Stevioside within *S. rebaudiana* may help to maintain cholesterol levels already within the normal range.*7 It may help to maintain total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL), and the LDL/HDL ratio within the normal range. It may also help to maintain HDL levels already within a healthy range, *8.9 as well as maintain an atherogenic index already within a healthy range.*9 Additionally, Stevia may help to support hepatic cellular health.*10

S. rebaudiana may help to maintain a healthy energy intake and support satiety.*11,12 Colonic microbiota convert steviol glycosides into steviol glucuronides, which are then excreted into the urine.¹³ In a human study comparing Stevia to control without dietary restrictions, a 24-hour diet recall was used to track calories, carbohydrates, protein, fat, and fiber. The Stevia group was found to have a higher protein intake, lower carbohydrate intake, and lower overall calorie intake, compared to control. In animal studies, isosteviol from *S. rebaudiana* has shown support of a healthy body weight.*14

S. rebaudiana may help with blood glucose support, helping to maintain both fasting and postprandial glucose levels already within the normal range.*9,15 Steviol may help to decrease the intestinal absorption of glucose.*16 Steviol glycosides such as stevioside and rebaudioside A may help to support pancreatic health and maintain both insulin and glucagon levels already within the normal range.*9,17,18 S. rebaudiana extract may also help to maintain healthy insulin sensitivity in 3T3-L1 adipocytes.*19 Lastly, S. rebaudiana may help to support healthy glycogen levels in both liver and muscles.*20

MICROBIAL SUPPORT

S. rebaudiana leaf extract may help with diverse types of microbial support, including a variety of morphological forms.*21,22,23 It may also help with mycelial support.

OTHER USES

Inflammatory Response Support

S. rebaudiana may help with healthy inflammatory response support.*24
Stevioside and its metabolite steviol may assist with cytokine support, helping to maintain healthy levels of TNF-alpha, IL-1-beta, IL-6, and NF-kappaB already within the normal range.*24 It may also help to maintain levels of cytokine-governing lipopolysaccharides already within the normal range.*1

Antioxidant Support
Polyphenols and flavonoids in *S. rebaudiana* leaves may contribute antioxidant support to help with normal oxidative stress.*26,27 *S. rebaudiana* may help to maintain superoxide dismutase (SOD) levels already within the normal range, contributing antioxidant support.*14

SAFETY AND CAUTIONS

S. rebaudiana is generally well tolerated. Nausea and dizziness have been known to occur, though at a similar rate to placebo, and usually resolves after the first week of use.4 While one study found S. rebaudiana to weakly inhibit CYP3A4 and CYP2C9,²⁷ another concluded that there were only minor or no changes to CYP activity or expression, and thus unlikely to cause cytochrome P450 interactions with pharmaceuticals.²⁸ S. rebaudiana may theoretically increase lithium levels due to increased diuresis and decreased lithium excretion.²⁹ S. rebaudiana may theoretically have additive effects when taken concurrently with antidiabetic or antihypertensive medications.²⁹

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

Marcinek, K. & Krejpcio, Z. (2016). Journal für Verbraucherschutz und Lebensmittelsicherheit, 11, 3-8.

Goyal, S. K., Samsher, & Goyal, R. K. (2010). International Journal of Food Sciences and Mutrition, 61(1), 1-10.

Montazi-Borojeni, A. A., Esmaeili, S. A., et al. (2017). Current Pharmaceutical Design, 23(11), 1616–1622.

Chan, P., Tomlinson, B., et al. (2000). British Journal of Clinical Pharmacology, 50(3), 215–220.

Melis M. S. (1997). Phytomedicine: International journal of phytotherapy and phytopharmacology, 3(4), 349–352.

Lee, C. N., Wong, K. L., et al. (2001). Planta Medica, 67(9), 796–799.

Adischustrus S. Internacy, Let 14 (2002). Food Technology & Pistochoology, 50(1), 11,66. Lee, C. N., Wolfg, N. L., et al. (2001). Palnia Metuca, 67(9), 790–799.

A disakwattana, S., Intrawangso, J., et al. (2012). Food Technology & Biotechnology, 50(1), 11-16.

8 Ahmad, U., Ahmad, R. S., et al. (2018). Lipids in Health and Disease, 17(1), 175.

9 Ritu, M., & Nandini, J. (2016). Journal of the Science of Food and Agriculture, 96(12), 4231–4234.

10 Holvoet, P., Rull, A., et al. (2015). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 77, 22–33.

11 Farhat, G., Berset, V., & Moore, L. (2019). Nutrients, 17(12), 3036.

12 Chematelia M. S. Care de Alexand, The Journal of Watering 18(16), 18(16). 12 Stamataki, N. S., Scott, C., et al. (2020). *The Journal of Nutrition*, 150(5), 1126–1134. ¹³ Gu, W., Rebsdorf, A., et al. (2019). Endocrinology, Diabetes & Metabolism, 2(4), e00093. 14 Nordentoft, I., Jeppesen, P. B., et al. (2008). *Diabetes, Obesity & Metabolism*, 10(10), 939–949. ¹⁵ Gregersen, S., Jeppesen, P. B., et al. (2004). Metabolism: Clinical and Experimental, 53(1), 73–76. 16 Toskulkao, C., Sutheerawatananon, M., et al. (1995). Journal of Nutritional Science and Vitaminology, 41(1), 105–113. 10Skulkau, L., Suricci awatananini, m., L. a. (1973).

18 Jeppesen, P. B., Dyrskog, S. E., et al. (2017). *Nature Communications*, 8, 14733.

18 Jeppesen, P. B., Dyrskog, S. E., et al. (2006). *The Review of Diabetic Studies: RDS*, 3(4), 189–199. 19 Mohd-Radzman, N. H., Ismail, W. I., et al. (2013). Evidence-Based Complementary and Alternative Medicine: eCAM, 2013, 938081. 20 Aghajanyan, A., Movsisyan, Z., & Trchounian, A. (2017). BioMed Research International, 2017, 9251358. 20 Aghajanyan, A., Movsisyan, Z., & Trchounian, Ä. (2017). BioMed Research International, 2017, 9251358.
21 Theophilus, P. A., Victoria, M. J., et al. (2015). European Journal of Microbiology & Immunology, 5(4), 268–280.
22 Preethi, D., Sridhar, T. M., et al. (2011). Journal of Ecobiotechnology, 3(7), 05-10.
23 Kedik, S. A., Yartsev, E. I., & Stanishevskaya, I. E. (2009). Pharmaceutical Chemistry Journal, 43(4), 198–199.
24 Boonkaewwan, C., & Burodom, A. (2013). Journal of the Science of Food and Agriculture, 93(15), 3820–3825.
25 Marcinek, K., & Kreipcio, Z. (2015). Acta Scientiarum Polonorum. Technologia Alimentaria, 14(2), 145–152.
26 El-Mesallamy, A., Mahmoud, S. A., et al. (2018). Acta Scientiarum Polonorum. Technologia Alimentaria, 17(3), 289–297.
27 Dusek, J., Carazo, A., et al. (2017). Food and Chemical Toxicology: An international journal published for the British Industrial Biological Research Association, 109 (Pt 1), 130–142.
28 Thøgersen, R., Petrat-Melin, B., et al. (2018). Food Chemistry, 258, 245–253.
29 Natural Medicines. (2021, March 27). Stevia [monograph]. http://naturalmedicines.therapeuticresearch.com.



Inflammatory Response Support



INTRODUCTION

Takuna is an extract from the bark of *Cecropia strigosa*, which belongs to the Urticaceae family. It is also known as *Cecropia bicolor*, *Cecropia multiflora*, *Cecropia rugosa*, *Ambaiba bicolor*, and *Ambaiba strigosa*, though Latin binomials other than *Cecropia strigosa* are considered obsolete. The natural habitat ranges from the Amazonian region to the Andes,³ and in Peru, it is commonly known as Tacona blanco.4 The traditional ethnobotanical use of C. strigosa is for gastrointestinal support.*4 Many other species of Cecropia have a strong history of ethnobotanical use. 5,6,7,8,9

Takuna is made at our U.S. manufacturing facility. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

INFLAMMATORY RESPONSE SUPPORT

In a study with mice, NutraMedix Takuna was found to support a healthy inflammatory response.*10

SAFETY AND CAUTIONS

C. strigosa and related species have been traditionally used by native South American peoples for some time. Despite this, information on interactions and adverse events is sparse. Currently, there are no known cautions or interactions, though this may change with additional research and new knowledge. In a study with mice, no toxic effects were found when used in accordance with OECD TG 423 guidelines.¹¹

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

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- 1 Cecropia strigosa Trécul The Plant List. Theplantlist.org. (2021). Retrieved 11 December 2021, from http://www.theplantlist.org/tpl1.1/record/kew-2707147.
- ² Cecropia strigosa. Mindat.org. (2021). Retrieved 18 December 2021, from https://www.mindat.org/taxon-4013364.html.
 ³ Berg, C. C. (2002). An account on the Cecropia species (Cecropiaceae) of Peru/Sinopsis de las especies peruanas de Cecropia (Cecropiaceae). Caldasia, 24(2), 229-238. Retrieved from https://revistas.unal.edu.co/index.php/cal/article/
- Grandtner, M. M., & Chevrette, J. (2013). C. In Dictionary of South American trees. nomenclature, taxonomy and ecology (Vol. C, p. 114). essay, Academic Press.
- ⁵ Rivera-Mondragón, A., Ortíz, O. O., et al. (2021). Planta Medica, 87, 764-779.
- Botsaris, A. S. (2007). Journal of Ethnobiology and Ethnomedicine, 3, 18
- 7 Sarris, J., McIntyre, É., & Camfield, D. A. (2013). CNS Drugs, 27, 207-219.
- 8 Lans, C., Harper, T., et al. (2001). BMC Complementary and Alternative Medicine, 1, 10.
- Paniagua Zambrana, N. Y., Bussmann, R. W., et al. (2017). Journal of Ethnobiology and Ethnomedicine, 13(1), 57.
- 10 Allende, S. (2007). NutraMedix Laboratories, LLC, Florida. University of Guayaquil Faculty of Chemical Sciences, Guayaquil, Ecuador. 11 Allende, S. (2006). NutraMedix Laboratories, LLC, Florida. University of Guayaquil Faculty of Chemical Sciences, Guayaquil, Ecuador.

VITALMEDIX ®



APPLICATIONS

- Immune System Support
- Inflammatory Response Support
- Blood Sugar Support
- Athletic Support



INTRODUCTION

VitalMedix is a proprietary blend of hydro-ethanol extracts from *moringa* leaf (*Moringa oleifera*) and Cat's Claw bark (*Uncaria tomentosa*) which is also known as Samento. *M. oleifera* contains micronutrients such as calcium, iron, potassium, vitamin A and carotenoids, in addition to polyphenols such as phenolic acids and flavonoids, glucosinolates, isothiocyanates, tannins and saponins.^{1,2} The main polyphenols are quercetin, myrecytin, and kaempferol.² *M. oleifera* may help with immune system support,³ healthy inflammatory response support,⁴ blood glucose support,^{5,6} and athletic support.*^{7,8} Samento is extracted from the rare pentacyclic chemotype of *U. tomentosa*, which is TOA-free, with levels in trace amounts or undetectable. This pentacyclic oxindole alkaloid (POA)-predominant, tetracyclic oxindole alkaloid (TOA)-free form of *U. tomentosa* may help with healthy inflammatory response support and immune system support.*^{9,10}

VitalMedix is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. VitalMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

IMMUNE SYSTEM SUPPORT

Both *M. oleifera* and *U. tomentosa* may help to support a healthy immune response and maintain immune system homeostasis.*3,11 *M. oleifera* may help to support a healthy antibody response and to maintain neutrophils already within the normal range.*3 *U. tomentosa* may help to maintain neutrophil function as well as Th1 and Th2 levels already within the normal range.*11,12,13 It should be noted that only TOA-free *U. tomentosa* (such as Samento) may help with immune support.*9

INFLAMMATORY RESPONSE SUPPORT

M. oleifera may help to support a healthy inflammatory response.*4,14 In animal studies, it has been shown to help maintain IL-6, TNF-alpha, IL-1-beta, IFN-gamma and NF-kappaB already within the normal range.*15,16,17 *U. tomentosa* (pentacyclic chemotype) may also help to maintain and support a healthy inflammatory response.*10,18 *U. tomentosa* may help to support NF-kappaB levels already within the normal range in a dose-dependent manner,18,20 thus supporting both TNF-alpha and IL-1-beta within the normal range.*21

BLOOD SUGAR SUPPORT

Both *M. oleifera* and *U. tomentosa* may help with blood sugar support.*5,6,21,22,23 *M. oleifera* may help to inhibit the enzyme alpha-amylase, delaying the breakdown of polysaccharides.⁵ It may also support healthy insulin secretion and maintain healthy glucose levels already within the normal range.*5,6 *U. tomentosa* may help to inhibit the enzyme alpha-glucosidase, delaying the absorption of saccharides, and may help to support healthy insulin sensitivity.*11,23,24

ATHLETIC SUPPORT

M. oleifera may help with athletic support, which is attributed to its polyphenol content.*7 It may help to delay the buildup of lactic acid and maintain the efficient metabolism of both glucose and lipids.*7,8,25

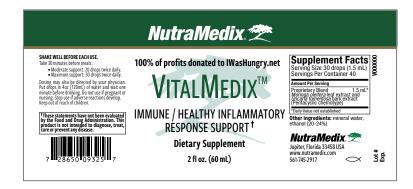
SAFETY AND CAUTIONS

M. oleifera is generally well-tolerated.²⁶ *M. oleifera* may have additive effects when taken with antidiabetic drugs^{27,28} or antihypertensive drugs.²⁹ *M. oleifera* may decrease the effectiveness of T4-containing drugs as it may inhibit the conversion of T4 to T3.³⁰ There has been one case report of Stevens-Johnson syndrome following the ingestion of food containing *M. oleifera* leaves.³¹ *M. oleifera* may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4.³²

U. tomentosa is generally well tolerated. Gastrointestinal effects such as nausea, constipation, and diarrhea have been reported, though generally not at greater rates than with placebo.³³ *U. tomentosa* may inhibit P450 CYP3A4 enzymes and therefore may slow the metabolism of drugs metabolized by CYP3A4.³⁴ *U. tomentosa* should be avoided in those taking immunosuppressants, as it may interfere with immunosuppressant therapy.³⁵ *U. tomentosa* may have additive effects with anticoagulants, generally attributed to the TOAs rhynchophylline and isorhynchophylline,³⁶ as well as additive effects with antihypertensive drugs, generally attributed to the TOAs rhynchophylline.^{37,38} As a reminder, Samento is TOA-free, with levels in trace amounts or undetectable.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

¹ Fahey, J. W. (2005). Trees for Life Journal, 1, 5. ² Vergara-Jimenez, M., Almatrafi, M. M., & Fernandez, M. L. (2017). Antioxidants (Basel, Switzerland), 6(4), 91. ³ Sudha, P., Asdaq, S. M., et al. (2010). *Indian Journal of Physiology and Pharmacology*, 54(2), 133–140. ⁴ Xiao, X., Wang, J., et al. (2020). Frontiers in Pharmacology, 11, 566783. ⁵ Leone, A., Bertoli, S., et al. (2018). *Nutrients*, 10(10), 1494. Anthanont, P., Lumlerdkij, N., et al. (2016). Journal of the Medical Association of Thailand = Chotmaihet Thangphaet, 99(3), 308–313. ⁷ Stohs, S. J., Kaats, G. R., & Preuss, H. G. (2016). *Phytotherapy Research: PTR*, 30(4), 681–688. ⁸ Lamou, B., Taiwe, G. S., et al. (2016). Oxidative Medicine and Cellular Longevity, 2016, 3517824. ⁹ Batiha, G. E.-S., Magdy Beshbishy, A., et al. (2020). *Applied Sciences*, 10(8), 2668. ¹⁰ Liang, J. H., Wang, C., et al. (2020). *Fitoterapia*, 147, 104772. ¹¹ Domingues, A., Sartori, A., et al. (2011). *Phytotherapy Research: PTR*, 25(8), 1229–1235. ¹² Montserrat-de la Paz, S., Fernandez-Arche, A., et al. (2016). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, *23*(2), 141–148. ¹³ Núñez, C., Lozada-Requena, I., et al. (2015). *Revista Peruana de Medicina Experimental y Salud Publica*, *32*(4), 643–651. ¹⁴ Kou, X., Li, B., et al. (2018). *Nutrients*, 10(3), 343. ¹⁵ Bamagous, G. A., Al Ghamdi, S. S., et al. (2018). *Asian Pacific Journal of Tropical Biomedicine*, 8(6), 320-327.
¹⁶ Almatrafi, M. M., Vergara-Jimenez, M., et al. (2017). *International Journal of Molecular Sciences*, 18(7), 1330. ¹⁷ Abdel-Daim, M. M., Khalil, S. R., et al. (2020). *Nutrients*, 12(4), 1031. ¹⁸ Mur, E., Hartig, F., et al. (2002). *The Journal of Rheumatology*, 29(4), 678–681. 19 Sandoval-Chacón, M., Thompson, J. H., et al. (1998). Alimentary Pharmacology & Therapeutics, 12(12), 1279–1289. ²⁰ Allen-Hall, L., Arnason, J. T., et al. (2010). *Journal of Ethnopharmacology*, 127(3), 685–693. ²¹ Mbikay M. (2012). Frontiers in Pharmacology, 3, 24. ²² Villarruel-López, A., López-de la Mora, D. A., et al. (2018). BMC Complementary and Alternative Medicine, 18(1), 127. ²³ Araujo, L., Feitosa, K. B., et al. (2018). *Scientific Reports*, 8(1), 11013.

²⁴ Arauj, L. C. C., Furig, I. C., et al. (2017). *Journal of Diabetes & Metabolism*, 8, 10(Suppl). ²⁵ Stohs, S. J., & Badmaev, V. (2016). *Phytotherapy Research: PTR*, 30(5), 732–740. ²⁶ Agrawal, B., & Mehta, A. (2008). *Indian Journal of Pharmacology*, 40(1), 28–31. ²⁷ Kar, A., Choudhary, B. K., & Bandyopadhyay, N. G. (2003). Journal of Ethnopharmacology, 84(1), 105–108. ²⁸ Jaiswal, D., Rai, P. K., et al. (2009). *Journal of Ethnopharmacology*, 123(3), 392. ²⁹ Sun, M. C., Ruhomally, Z. B., et al. (2020). *Journal of the American College of Nutrition*, 39(1), 54–62. ³⁰ Tahiliani, P., & Kar, A. (2000). *Pharmacological Research*, *41*(3), 319–323.
³¹ Witharana, E., Wijetunga, W., & Wijesinghe, S. (2018). *The Ceylon Medical Journal*, *63*(4), 188–189. ³² Monera, T. G., Wolfe, A. R., et al. (2008). *Journal of Infection in Developing Countries*, 2(5), 379–383. 33 de Paula, L. C., Fonseca, F., et al. (2015). Journal of Alternative and Complementary Medicine (New York, N.Y.), 21(1), 22–30.

34 Budzinski, J. W., Foster, B. C., et al. (2000). Phytomedicine: International journal of phytotherapy and phytopharmacology, 7(4), 273–282. 35 Lamm, S., Sheng, Y., & Pero, R. W. (2001). Phytomedicine: International journal of phytotherapy and phytopharmacology, 8(4), 267–274.

³⁶ Chen, C. X., Jin, R. M., et al. (1992). Zhongguo yao li xue bao = Acta Pharmacologica Sinica, 13(2), 126–130.

³⁷ Zhou, J., & Zhou, S. (2010). *Journal of Ethnopharmacology*, *132*(1), 15–27. ³⁸ Zhou, J. Y., & Zhou, S. W. (2012). *Fitoterapia*, *83*(4), 617–626.

- Immune Support
- Antioxidant Support
- Cardiovascular Support
- Vitamin Support



INTRODUCTION

Vitamin C (ascorbic acid) is a water-soluble vitamin that may help with immune support, antioxidant support, and cardiovascular support.*1 The word a/scorbic comes from the Greek prefix a, meaning not, and the Latin scorbutus, or scurvy. Scurvy was relatively common, particularly in sailors, until the mid 1700s when James Lind discovered that citrus fruits were effective in treating the disease. Scurvy continued to be a problem until prevention with vitamin C-rich citrus fruits became a widely-accepted practice.²

Fortunately, vitamin C deficiency is extremely rare in the United States. Unlike many other mammals, humans are unable to synthesize vitamin C and must obtain it from dietary or supplemental sources. Significant dietary sources of vitamin C include fruits such as grapefruit, oranges, kiwifruit and strawberries, as well as vegetables such as bell peppers, broccoli, and brussels sprouts.³

The chemical structure of vitamin C was discovered in the 1930s by Hungarian researcher Albert Szent-Györgyi. While observing how cells used nutrients, he isolated a hydrogen carrier with the properties of both sugar and acid that would later become known as ascorbic acid. His discovery of the antioxidant properties of vitamin C became the foundation for future research, and Szent-Györgyi would eventually earn a Nobel prize for his work.*4

Linus Pauling also played a significant role in the study and use of vitamin C. In the 1960s, Pauling became fascinated with nutritional chemistry and pioneered the field of orthomolecular medicine. He correctly postulated, amidst disagreement and even ridicule from peers, that factors such as environmental stress, biochemical individuality, and disease might increase the need for certain micronutrients such as vitamin C.*5 While not all of his theories were correct, studies show that there is a role for vitamin C in the support of immune and cardiovascular health.*6

Vitamin C plays a vital role in many biological processes.* It helps to maintain

cytochrome P450 electron transport already within the normal range.*8 Vitamin C is a cofactor for dopamine-beta-hydroxylase which converts dopamine to epinephrine, and for alpha-amidating monooxygenase enzymes which help to form neuropeptides. It is needed for collagen synthesis, myelin synthesis, and the function of neurons, glial cells, and neurotransmitter receptors.¹ Additionally, it helps to support healthy iron absorption.*9 Vitamin C's role in collagen synthesis supports the integumentary and musculoskeletal systems, and its role in antioxidant support may help to maintain both immune and cardiovascular health.*67

NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers. Our Vitamin C is free of gluten, sugar, soy, and dairy. It is also free of GMOs, mold, and yeast.

IMMUNE SUPPORT

Vitamin C participates in several mechanisms of immune support.*10 At the most basic level, it helps to maintain epithelial barriers by supporting collagen synthesis, which contributes to healthy skin and mucous membranes.*1 Vitamin C may support innate immunity by accumulating within neutrophils, where it may enhance chemotaxis and phagocytosis, in addition to generating reactive oxygen species (ROS) for microbial support.*¹¹ It may support adaptive immunity by promoting the differentiation and proliferation of cellular T and humoral B cells.*¹¹

Vitamin C may support upper respiratory health in various age groups, particularly during the winter season.*7,12,13,14 Normal vitamin C levels support healthy immunity and may be helpful for both pre-illness and intra-illness support.*12,14 As adaptive immunity slows with age, it is reasonable to consider vitamin C support for the elder demographic, particularly in cases of known deficiency.^{15,16,17}

ANTIOXIDANT SUPPORT

Vitamin C may support antioxidant function, due to its role as an electron donor, and has the ability to scavenge both reactive oxygen species (ROS) and reactive nitrogen species (RNS).*1,18 Unopposed oxidative stress in the cardiovascular system may result in endothelial cell apoptosis, inflammation and cell adhesion; decreased availability of nitric oxide (NO); and oxidative LDL modification.* Vitamin C may act as a free radical scavenger to help mitigate oxidative stress, support normal NO synthesis, and protect neutrophils from ROS during phagocytosis. 18,19

OTHER USES

Cardiovascular Support

Plasma vitamin C concentration may help to support cardiovascular health and may contribute cardiovascular-specific antioxidant support.*3,6 Vitamin C may help to maintain healthy endothelial function, which is attributed to its antioxidant support.*2 A meta-analysis of 29 randomized, controlled trials found that vitamin C may help to maintain healthy systolic and diastolic blood pressure already within the normal range.*2 A meta-analysis of 13 randomized, controlled trials found that it may help maintain LDL cholesterol and triglycerides already within the normal range.*2 A meta-analysis of 15 randomized, controlled trials found that vitamin C may help to maintain a normal heart rhythm.*23

Vitamin Support

As vitamin C cannot be synthesized by humans, dietary and/or supplemental intake is essential. The dietary reference intake (DRI) to prevent overt deficiency is 75 mg/day in women and 90 mg/day in men. Higher amounts may be needed for optimal support, and doses of 2,000 mg/day have been used safely in multiple trials.* This product contains 1,000 mg vitamin C (ascorbic acid) per capsule, and a serving of two capsules contains 2,222% of the daily value.

SAFETY AND CAUTIONS

Vitamin C is generally well-tolerated. At doses over 2,000 mg/day, heartburn, abdominal cramps, osmotic diarrhea, or gastrointestinal upset can occur. Severe side effects are rare, and often limited to specific populations. In postmenopausal women with diabetes, vitamin C in amounts greater than 300 mg/day may increase cardiovascular risk, though not in women without diabetes, nor in equivalent

amounts found in food. Vitamin C in amounts greater than 500 mg/day may increase the risk of carotid thickening in men, though not in equivalent amounts found in foods. In those with a history of kidney stones, vitamin C may increase the risk of stone formation. It may also increase aluminum absorption in those with renal failure, and may increase the absorption of levothyroxine. Vitamin C may theoretically decrease the effectiveness of alkylating agents, antitumor antibiotics, indinavir and warfarin, though information about the warfarin interaction is conflicting. High doses of vitamin C may also cause dose-dependent side effects such as headache, fatigue, somnolence, or insomnia.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



- 1 Institute of Medicine. (2000). Dietary Reference Intakes for vitamin C, vitamin E, selenium, and carotenoids. Washington, DC: National Academy Press. Available at: http://www.nap.edu/books/0309069351/html/.
- ² Carpenter K. J. (2012). *Annals of Nutrition & Metabolism*, 61(3), 259–264.
 ³ ODS. (2021). Office of Dietary Supplements Vitamin C. Retrieved 26 August 2021, from https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/#h3
- 4 ACS. (2021). Albert Szent-Gyorgyi Vitamin C Landmark American Chemical Society. Retrieved 27 August 2021, from https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/szentgyorgyi.html
- Linus Pauling Institute. (2021). Linus Pauling biography. Retrieved 27 August 2021, from https://lpi.oregonstate.edu/about/linus-pauling-biography Van Guilder, G. P., Hoetzer, G. L., et al. (2008). *The Journal of Physiology*, 586(14), 3525–3535.
- 7 Johnston, C. S., Barkyoumb, G. M., & Schumacher, S. S. (2014). *Nutrients*, 6(7), 2572–2583.
- van Heeswijk, R. P., Cooper, C. L., et al. (2005). *Pharmacotherapy*, 25(12), 1725–1728.
- ⁹ Lynch, S. R., & Cook, J. D. (1980). Annals of the New York Academy of Sciences, 355, 32–44.
- 10 Jacob, R. A., & Sotoudeh, G. (2002). Nutrition in Clinical Care: An official publication of Tufts University, 5(2), 66–74.
- ¹¹ Carr, A. C., & Maggini, S. (2017). *Nutrients*, *9*(11), 1211.
- ¹² Ran, L., Zhao, W., et al. (2018). *BioMed Research International*, 2018, 1837634.
- ¹³ Sasazuki, S., Sasaki, S., et al. (2006). European Journal of Clinical Nutrition, 60(1), 9–17.
- 14 Anderson, T. W., Reid, D. B., & Beaton, G. H. (1972). Canadian Medical Association Journal, 107(6), 503–508.
- 15 Delafuente, J. C., Prendergast, J. M., & Modigh, A. (1986). International Journal of Immunopharmacology, 8(2), 205–211.
- ¹⁶ Kennes, B., Dumont, I., et al. (1983). *Gerontology*, 29(5), 305–310.

 ¹⁷ Starke, J., Schneiber, H., et al. (2011). *Clinical Nutrition (Edinys)*, Scotland), 30(2), 194–201.

 ¹⁸ Li, Y., & Schelihorr, H. E. (2007). *The Journal of Nutrition* (1981), 171–2184.
- ¹⁹ Wintergerst, E. S., Maggini, S., & Hornig, D. H. (2006). *Annals of Nutrition & Metabolism*, 50(2), 85–94.
- ²⁰ Hornig, B., Arakawa, N., et al. (1998). *Circulation*, *97*(4), 363–368.

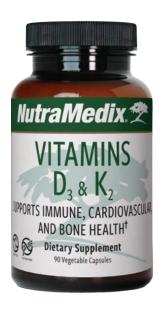
 ²¹ Juraschek, S. P., Guallar, E., et al. (2012). *The American Journal of Clinical Nutrition*, *95*(5), 1079–1088.
- ²² McRae M. P. (2008). Journal of Chiropractic Medicine, 7(2), 48–58.
- ²³ Hemilä, H., & Suonsyrjä, T. (2017). *BMC Cardiovascular Disorders*, 17(1), 49. ²⁴ Hathcock, J. N., Azzi, A., et al, M. G. (2005). *The American Journal of Clinical Nutrition*, 81(4), 736–745.
- Lee, D. H., Folsom, A. R., et al. (2004). The American Journal of Clinical Nutrition, 80(5), 1194–1200.
 Dwyer, J. H., Merz, N. B., et al. (2001). Circulation, 103, 1365d.
- ²⁷ Taylor, E. N., Stampfer, M. J., & Curhan, G. C. (2004). Journal of the American Society of Nephrology: JASN, 15(12), 3225–3232.
- 28 Domingo, J. L., Gomez, M., et al. (1991). Lancet (London, England), 338(8780), 1467.
- ²⁹ Skelin, M., Lucijanić, T., et al. (2017). *Clinical Therapeutics*, *39*(2), 378–403.
- ³⁰ Natural Medicines. (2021, August 26). Vitamin C [monograph]. http://naturalmedicines.therapeuticresearch.com

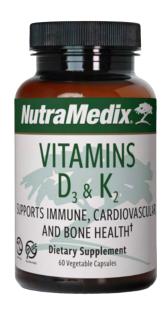
VITAMINS D₃ & K₂



APPLICATIONS

- Immune System Support
- Cardiovascular Support
- Bone Health Support
- Neurological Support
- Vitamin Support





INTRODUCTION

Vitamin D is a fat-soluble vitamin that may be synthesized in the body through a multi-step process. UVB rays convert 7-dehydro-cholesterol in the skin to pre-vitamin D3, which is converted to D3 (cholecalciferol). Cholecalciferol is hydroxylated to calcidiol (25(OH)D) in the liver, and then to calcitriol (1,25(OH)2D) in the kidneys, at which time it is biologically active. The amount of vitamin D produced depends on several factors including latitude, season, skin exposure, skin color, and liver and

While outright vitamin D deficiency is rare, low vitamin D status may affect up to 75% of U.S. adults.³ In supplement form, vitamin D is available as cholecalciferol (D3) or ergocalciferol (D2). D3 is more effective than D2 at maintaining vitamin D levels already within the normal range.⁴⁴ The DRI for Vitamin D is 15 mcg/day (600 IU) for ages 1-70 and 20 mcg/day (800 IU) for ages 70 and older,² as the ability to synthesize vitamin D declines with age.² Significant dietary sources of vitamin D include rainbow trout, sockeye salmon, eggs, and beef liver. Foods such as cow's milk and alternative plant milks are often fortified with vitamin D. Mushrooms, when treated with UV light, are a vegetarian source of vitamin D.⁵

Vitamin K is a fat-soluble vitamin that can be synthesized by colonic bacteria in the form of menaquinones (K2). Vitamin K encompasses a group of compounds with the chemical structure 2-methyl-1,4-naphthoquinone.⁶ Deficiency is rare in adults, and when present, is usually from malabsorption, as occurs in celiac disease, in ulcerative colitis, or from bariatric surgery. The adult DRI for Vitamin K is 90 mcg/day in women and 120 mcg/day in men. 9

Food sources of vitamin K1 include leafy green vegetables and soybeans, while food sources of vitamin K2 include dairy, fermented foods and animal foods.^{5,8} As a dietary supplement, Vitamin K is available as K1 or K2, the latter of which is preferred due to better absorption and bioavailability.^{*9,10} Of the K2 menaquinones, MK-4 and MK-7 are the most commonly available. While both are well-absorbed, the

MK-7 form is preferred due to a longer half-life.*7,12

Together, D3 and K2 have synergistic roles in both bone and cardiovascular health.* Vitamin D supports the production of vitamin-K-dependent proteins such as osteocalcin and matrix Gla protein, while vitamin K allows for their carboxylation and function.^{13,14} Studies suggest that their concurrent use may be more effective than either alone.*13

IMMUNE SYSTEM SUPPORT

Vitamin D receptors and 1-alpha hydroxylase, the enzyme that converts calcidiol to active calcitriol, are found on a variety of immune cells.^{15,16} In innate immunity, vitamin D helps support healthy monocyte function; in adaptive immunity, vitamin D may help to support immune tolerance and homeostasis.*16,17,18 Vitamin D may help maintain cytokines already within the normal range, and may additionally help to maintain dendritic cell function and T cell function already within the normal range*19 Vitamin D 5000 IU may help with immune support, particularly during the winter season.*20 Other amounts have also been protective.*21

CARDIOVASCULAR SUPPORT

Vitamin D levels are associated with cardiovascular health.*²² Vitamin D may help to support heart health by maintaining insulin sensitivity, blood glucose, and blood lipids already within the normal range. ²³ It may also help with homeostatic support of the renin-angiotensin-aldosterone system (RAAS).*²⁴ Vitamin K is needed for the gamma-carboxylation of matrix Gla protein, which is important for vascular health.*²⁵

BONE HEALTH SUPPORT

Vitamin D helps with bone support by facilitating the absorption of dietary calcium and regulating calcium and phosphorus.*²⁶ Vitamin D also helps to maintain PTH already within the normal range, maintaining the calcium in bones and supporting normal bone density.*²⁷ Vitamin K is needed for the gamma-carboxylation of osteocalcin, which is important for normal bone mineralization.*^{28,29,30} Vitamin D3 at 5,000 IU per day may help to maintain normal z scores (p<0.001) and may help with postmenopausal bone support.*31

Vitamin K2, both alone and with D3, helps to support bone health in early postmenopausal women (p<0.005), as evidenced by the maintenance of serum undercarboyalated osteocalcin (ucOC) already within the normal range.*32 Vitamins K2 and D3 together may help to maintain intact osteocalcin (OC) and bone alkaline phosphatase (BAP), serum markers of bone formation, already within the normal range (p<0.05), though K2 alone did not show these benefits.*32

OTHER USES

Neurological Support

Vitamin D receptors have been found in neurons and glial cells, and vitamin D may help with neurological support.*33,34 Vitamin D has many roles in the nervous system, including the regulation of neurotransmitter synthesis.*33 It may help microglia to maintain levels of cytokines, Il-6, Il-12, and TNF-alpha already within the normal range.*35 Vitamin D may support healthy cognition and help to maintain A-beta-related biomarkers already within the normal range.*36 Vitamin K may help to support healthy proliferation, differentiation, and lifespan of brain cells through its role in sphingolinid metabolism, which may help to support healthy cognition.*37 in sphingolipid metabolism, which may help to support healthy cognition."

Vitamin Support

This product includes 125 mcg (5000 IU) of vitamin D3 as cholecalciferol, which is 625% of the Dietary Reference Intake (DRI). This product also includes 150 mcg of vitamin K2 as Menaquinone-7, which is 125% of the DRI. 2.9

SAFETY AND CAUTIONS

Vitamin D is generally well tolerated. Numerous studies have used a dose of 5,000 IU/day safely and without adverse effects. 38,39 Long-term, high-dose vitamin D may result in hypercalcemia, azotemia, or anemia. 40 Possible side effects of vitamin D toxicity include hypertension, 40 pancreatitis, 40 elevated INR, 41 osteoporosis, 40 or

kidney stones.⁴² Vitamin D may increase the absorption and toxicity of aluminum in patients with kidney failure.⁴³ Vitamin D may induce CYP3A4 enzymes, which may decrease absorption of CYP3A4 substrates such as atorvastatin.⁴⁰ Taken concurrently with thiazide diuretics, Vitamin D may increase the risk for hypercalcemia,⁴⁴ which may decrease the effectiveness of anti-arrhythmics.⁴⁵

Vitamin K is generally well tolerated. Side effects may include nausea, stomach upset, and diarrhea. This supplement should not be taken with warfarin, as Vitamin K antagonizes the anticoagulant effects.

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

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<sup>1</sup> Bikle, D. D. (2014). Chemistry & Biology, 21(3), 319–329.
<sup>2</sup> Institute of Medicine. (2011). Dietary Reference Intakes for calcium and vitamin D. Washington, DC: The National Academies Press.
Binkley, N., Ramamurthy, R., & Krueger, D. (2010). Endocrinology and Metabolism Clinics of North America, 39(2), 287-contents.
4 Martineau, A. R., Thummel, K. E., et al. (2019). The Journal of Clinical Endocrinology and Metabolism, 104(12), 5831–5839.
5. Office of Dietary Supplements. (2021). Office of Dietary Supplements - Vitamin D. Ods.od.nih.gov. Retrieved 18 August 2021, from https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/
<sup>6</sup> Booth S. L. (2012). Food & Nutrition Research, 56, 10.3402/fnr.v56io.5505.
7 Office of Dietary Supplements. (2021). Office of Dietary Supplements - Vitamin K. Ods.od.nih.gov. Retrieved 18 August 2021, from https://ods.od.nih.gov/factsheets/vitaminK-HealthProfessional/.
   Sherf-Dagan, S., Goldenshluger, A., et al. (2019). Surgery for Obesity and Related Diseases, 15(8), 1402-1413.
9 Institute of Medicine. (2001). Panel on Micronutrients. Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington (DC): National Academies Press
(US). Available from: https://www.ncbi.nlm.nih.gov/books/NBK222310/
10 Shearer, M. J., Bach, A., & Kohlmeier, M. (1996). The Journal of Nutrition, 126(4 Suppl), 11815–6S.
11 Halder, M., Petsophonsakul, P., et al. (2019). International Journal of Molecular Sciences, 20(4), 896.
<sup>12</sup> Schurgers, L. J., Teunissen, K. J., et al. (2007). Blood, 109(8), 3279–3283.
13 van Ballegooijen, A. J., Pilz, S., et al. (2017). International Journal of Endocrinology, 2017, 7454376.
<sup>14</sup> Kidd P. M. (2010). Alternative Medicine Review: A journal of clinical therapeutic, 15(3), 199–222.
<sup>15</sup> Prietl, B., Treiber, G., et al. (2013). Nutrients, 5(7), 2502–2521.
<sup>16</sup> Siddiqui, M., Manansala, J. S., et al. (2020). Nutrients, 12(9), 2879.
17 Szymczak, I., & Pawliczak, R. (2016). Scandinavian Journal of Immunology, 83(2), 83–91.
18 Mpandzou, G., Aït Ben Haddou, E., et al. (2016). Revue Neurologique, 172(2), 109–122.
19 lijima, H., Shinzaki, S., & Takehara, T. (2012). Current Opinion in Clinical Nutrition and Metabolic Care, 15(6), 635–640.
<sup>20</sup> Jung, H. C., Seo, M. W., et al. (2018). International Journal of Environmental Research and Public Health, 15(9), 2003.
<sup>21</sup> Martineau, A. R., Jolliffe, D. A., et al. (2017). BMJ (Clinical research ed.), 356, i6583.
<sup>22</sup> Judd, S. E., & Tangpricha, V. (2009). The American Journal of the Medical Sciences, 338(1), 40–44.
<sup>23</sup> Podzolkov, V. I., Pokrovskaya, A. E., & Panasenko, O. I. (2018). Terapevticheskii Arkhiv, 90(9), 144–150.
<sup>24</sup> Giménez, V., Sanz, R. L., et al. (2020). Current Protein & Peptide Science, 21(10), 948–954.
<sup>25</sup> El Asmar, M. S., Naoum, J. J., & Arbid, E. J. (2014). Oman Medical Journal, 29(3), 172–177.
<sup>26</sup> Charoenngam, N., & Holick, M. F. (2020). Nutrients, 12(7), 2097.
<sup>27</sup> Khundmiri, S. J., Murray, R. D., & Lederer, E. (2016). Comprehensive Physiology, 6(2), 561–601.
28 Kodama, Y., Okamoto, Y., et al. (2017). Brain & Development, 39(10), 846–850.
<sup>29</sup> Zoch, M. L., Clemens, T. L., & Riddle, R. C. (2016). Bone, 82, 42–49.
30 Wen, L., Chen, J., et al. (2018). Molecular Medicine Reports, 18(1), 3-15.
31 Mocanu, V., Stitt, P. A., et al. (2009). The American Journal of Clinical Nutrition, 89(4), 1132–1137.
32 Yasui, T., Miyatani, Y., et al. (2006). Gynecological Endocrinology: The official journal of the International Society of Gynecological Endocrinology, 22(8), 455–459.
33 Moretti, R., Morelli, M. E., & Caruso, P. (2018). International Journal of Molecular Sciences, 19(8), 2245.
34 Di Somma, C., Scarano, E., et al. (2017). International Journal of Molecular Sciences, 18(11), 2482.
35 Boontanrart, M., Hall, S. D., et al. (2016). Journal of Neuroimmunology, 292 (2016), 126-136.
<sup>36</sup> Jia, J., Hu, J., et al. (2019). Journal of Neurology, Neurosurgery, and Psychiatry, 90(12), 1347–1352.
37 Alisi, L., Cao, R., et al. (2019). Frontiers in Neurology, 10, 239.
38 Bhargava, P., Fitzgerald, K. C., et al. (2017). JCI insight, 2(19), e95302.
39 Han, Q., Li, X., et al. (2019). Journal of the International Society of Sports Nutrition, 16(1), 55.
40 Natural Medicines. (2022, January 31). Vitamin D [monograph]. http://naturalmedicines.therapeuticresearch.com
41 Carlton, S., Clopton, D., & Cappuzzo, K. A. (2010). The Consultant Pharmacist: The journal of the American Society of Consultant Pharmacists, 25(3), 171–177.

42 Letavernier, E., & Daudon, M. (2018). Nutrients, 10(3), 366.
43 Demontis, R., Leflon, A., et al. (1986). Clinical Nephrology, 26(3), 146–149.
44 Jones, G. (2008). The American Journal of Clinical Nutrition, 88(2), 5825–586S.
45 Bar-Or, D., & Gasiel, Y. (1981). British Medical Journal (Clinical research ed.), 282(6276), 1585–1586.
```

46 Natural Medicines. (2021, August 19). Vitamin K [monograph]. http://naturalmedicines.therapeuticresearch.com

47 Crowther, M. A., Ageno, W., et al. (2009). *Annals of Internal Medicine*, 150(5), 293–300.



- Immune System Support
- Skin Support
- Antioxidant Support
- Gastrointestinal Support



INTRODUCTION

Zinc is an essential trace mineral and a cofactor in many biological processes, including catalytic reactions, intracellular signaling, and DNA and protein synthesis. It is an integral part of normal immune function, healthy skin, and normal wound healing.* Zinc may provide antioxidant support, help to maintain healthy mitochondrial function, and help to support epithelial barrier function and gut permeability already within the normal range.* The molecular formula for zinc bisglycinate is $C_4H_{12}N_2O_5Zn.^3$

Zinc supplements are widely available and consist of chelates bound to organic acids, chelates bound to amino acids, and non-chelates bound to inorganic acids. Zinc chelates are generally more bioavailable as they are less likely to interact with food, drugs, or components of the intestinal lumen.*4 Zinc chelates bound to organic acids include zinc aspartate, zinc methionine, zinc monomethionine, and zinc bisglycinate. Zinc chelates bound to amino acids include zinc acetate, zinc citrate, zinc gluconate, zinc orotate, and zinc picolinate. Zinc non-chelates bound to inorganic acids include zinc sulfate and zinc oxide.⁴

NutraMedix Zinc is in the form of zinc bisglycinate, a chelate consisting of two glycines bound to a zinc cation (Zn²¹). Zinc bisglycinate is highly bioavailable, having a low molecular weight which facilitates passage through the cell membrane.*5,6 In a randomized crossover single-dose trial, zinc bisglycinate was significantly more bioavailable (+43.44%) than zinc gluconate (p<0.05).*5 In a subsequent double-blind placebo-controlled trial, 30 healthy women ages 18-24 were assigned to 60 mg/day for six weeks of either zinc bisglycinate or zinc gluconate. Zinc bisglycinate was again found more bioavailable than zinc gluconate.

The recommended dietary allowance (RDA) of zinc for ages 19 and older is 8 mg/day for women and 11 mg/day for men. Zinc deficiency, while relatively rare in high-resource nations, can be caused by low zinc intake, high phytate intake, or long-term use of proton pump inhibitors. It can also can occur in individuals

undergoing hemodialysis.*9 Zinc deficiency is estimated to affect 17% of the world's population, due to inadequate nutrition, severe illness, or alcoholism.¹0 Signs of zinc deficiency include delayed growth and maturation, impaired cognition, and depressed immunity, among others.¹1

Zinc is most abundant in animal foods, though can be found in plant foods and fortified foods as well. Good sources of zinc include seafood such as oysters, lobster, and crab; meats such as beef, chicken, and pork; nuts such as cashews and almonds; and pumpkin seeds. Oysters are, by far, the richest dietary source of zinc. Fortified sources include breakfast cereals, which are fortified with 25% of the daily value (DV).¹²

Vegetarian and vegan diets can decrease zinc absorption due to the high phytic acid content of whole grains and legumes. However, there is currently insufficient evidence showing a higher incidence of zinc deficiency in vegetarians, compared to omnivores. While zinc from animal foods is more easily absorbed, soaking grains and legumes overnight may help to increase the bioavailability of zinc by activating phytase to break down phytic acid. 15,16

NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers. Our Zinc is free of gluten, sugar, soy, and dairy. It is also free of GMOs, mold, and yeast.

IMMUNE SYSTEM SUPPORT

Zinc may help with healthy immune system support.*17,18 Normal zinc levels help to support the natural killer (NK) cells of innate immunity as well as the T and B cells of adaptive immunity, maintaining them already within the normal range.*19 Zinc deficiency may contribute to immune dysregulation, decreased lymphocytes, decreased NK cells, and increased monocyte toxicity.*19 Normal zinc levels are necessary for healthy hematopoiesis, normal cell differentiation, and healthy cell cycle function.*19 Both deficiency and excess can negatively impact the immune system, and zinc homeostasis is needed for correct functioning of both innate and adaptive immunity.19 One systematic review and meta-analysis found that zinc helped to support upper respiratory health (p=0.0004).*20

SKIN SUPPORT

Zinc may help with skin support.* Zinc is prevalent in the epidermis, the majority of which is located in the stratum spinosum. Zinc homeostasis is maintained by zinc transporters (ZnTs); Zrt-, Irt-like proteins (ZIPs); and metallothioneins. Zinc leaves the cells through ZnTs and enters the cells through ZIPs.²¹ Zinc helps to maintain MHC class II expression already within the normal range in dendritic cells, and helps to maintain normal mast cell function.*²¹ Zinc deficiency can contribute to rough skin, and supplemental zinc may help to maintain healthy skin. Additionally, zinc may help to support normal wound healing.*^{21,22}

ANTIOXIDANT SUPPORT

Healthy zinc levels may help with antioxidant support, while both deficiency and excess can contribute to oxidative stress.* Zinc is unable to participate in redox reactions, as its valence shell is full. Instead, its antioxidant activity is attributed to effects on copper/zinc-superoxide dismutase and the upregulation of metallothionein, among other mechanisms.* Zinc's antioxidant effects may involve proteins such as NF-kappaB, PPARs, and Nrf2.* In a randomized, double-blind, placebo-controlled trial, zinc helped to support premenstrual physical health (p=0.03) and mental health (p=0.006) already within the normal range, compared to placebo. Zinc also helped to maintain brain-derived neurotrophic factor (BDNF) already within the normal range (p=0.01) and total antioxidant capacity (TAC) already within the normal range (p<0.001).*

OTHER USES

Gastrointestinal Support

Zinc may support gastrointestinal health.*24 Zinc and gastrointestinal epithelial cells have a reciprocal relationship; zinc is needed for a healthy epithelium, and a healthy epithelium is needed for the absorption of dietary or supplemental zinc.* Zinc may help to support healthy gastrointestinal epithelial barrier function at tight junctions and may help to maintain healthy gastrointestinal permeability already within the

normal range.* It may also help to maintain a healthy lactulose/mannitol ratio already within the normal range (p<0.03).*25

SAFETY AND CAUTIONS

Zinc is generally well tolerated, with side effects more prevalent at higher doses. Common side effects may include gastrointestinal symptoms such as cramps, nausea, vomiting, and diarrhea, the latter two of which are dose-dependent. Serious side effects are rare. There have been two cases of liver deterioration in patients with Wilson's disease. In doses of 100-300 mg/day, copper deficiency may result, leading to anemia, neutropenia, impaired immunity, and worsened LDL/HDL ratio. Tinc bisglycinate at 60 mg/day for six weeks showed no change in erythrocyte superoxide dismutase, a marker of copper deficiency. High-dose zinc (>100 mg/day) may increase the risk of prostate cancer, though a meta-analysis did not find this relationship to be statistically significant. Serve Zinc overdose has resulted in interstitial nephritis and acute renal tubular necrosis.

Zinc may interfere with the therapeutic effects of cisplatin.³¹ Zinc may decrease the levels and clinical effects of ritonavir,³² cephalexin,³³ quinolone antibiotics,³⁴ tetracycline antibiotics,³⁵ and penicillamine.³⁶

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



REFERENCES

35 Neuvonen P. J. (1976). *Drugs*, 11(1), 45–54.

³⁶ Mery, C., Delrieu, F., et al. (1976). Scandinavian Journal of Rheumatology, 5(4), 241–247.

```
<sup>1</sup> Lee, S. R. (2018). Oxidative Medicine and Cellular Longevity, 2018, 9156285.
<sup>2</sup> Michielan, A., & D'Incà, R. (2015). Mediators of Inflammation, 2015, 628157.
3 PubChem. (2021). Zinc bis(glycinate) monohydrate. Retrieved 2 September 2021, from https://pubchem.ncbi.nlm.nih.gov/compound/Zinc-bis_glycinate_-monohydrate#section=InChl-Key
4 Stargrove, M., Treasure, J., & McKee, D. (2007). Herb, nutrient, and drug interactions (pp. 556-582). Mosby|Elsevier.
5 Gandia, P., Bour, D., et al. (2007). International Journal for Vitamin and Nutrition Research. Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung. Journal International de Vitaminologie et de Nutrition, 77(4), 243–248.
<sup>6</sup> DiSilvestro, R. A., Koch, E., & Rakes, L. (2015). Biological Trace Element Research, 168(1), 11–14.
Institute of Medicine (U.S.). (2002). Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academies Press.
8 Skrovanek, S., DiGuilio, K., et al. (2014). World Journal of Gastrointestinal Pathophysiology, 5(4), 496–513.
9 Berger, M. M., Shenkin, A., et al. (2004). The American Journal of Clinical Nutrition, 80(2), 410-416.
<sup>10</sup> Wessells, K. R., & Brown, K. H. (2012). PloS One, 7(11), e50568.
<sup>11</sup> Prasad, A. S., & Bao, B. (2019). Antioxidants (Basel, Switzerland), 8(6), 164.
12 ODS. (2022). Office of Dietary Supplements - Zinc. Retrieved 31 January 2022, from https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/
13 Hunt J. R. (2002). Nutrition Reviews, 60(5 Pt 1), 127–134.
<sup>14</sup> Foster, M., & Samman, S. (2015). Advances in Food and Nutrition Research, 74, 93–131.

    Brown, D. D. (2018). Journal of Dance Medicine & Science, 22(1), 44–53.
    Gupta, R. K., Gangoliya, S. S., & Singh, N. K. (2015). Journal of Food Science and Technology, 52(2), 676–684.

<sup>17</sup> Rerksuppaphol, S., & Rerksuppaphol, L. (2013). Paediatrics and International Child Health, 33(3), 145–150.
18 Rerksuppaphol, L., & Rerksuppaphol, S. (2020). Journal of Tropical Pediatrics, 66(4), 419–427.
<sup>19</sup> Wessels, I., Maywald, M., & Rink, L. (2017). Nutrients, 9(12), 1286.
<sup>20</sup> Abioye, A. I., Bromage, S., & Fawzi, W. (2021). BMJ Global Health, 6(1), e003176.
<sup>21</sup> Ogawa, Y., Kinoshita, M., et al. (2018). Nutrients, 10(2), 199.
<sup>22</sup> Sharquie, K. E., Najim, R. A., & Al-Salman, H. N. (2006). International Journal of Dermatology, 45(7), 857–861.

<sup>23</sup> Jafari, F., Amani, R., & Tarrahi, M. J. (2020). Biological Trace Element Research, 194(1), 89–95.
<sup>24</sup> Rerksuppaphol, L., & Rerksuppaphol, S. (2020). Paediatrics and International Child Health, 40(2), 105–110.
25 Ryan, K. N., Stephenson, K. B., et al. (2014). Clinical Gastroenterology and Hepatology. The official clinical practice journal of the American Gastroenterological Association, 12(9), 1507–13.et.
<sup>26</sup> Natural Medicines. (2021, September 1). Zinc [monograph]. http://naturalmedicines.therapeuticresearch.com
<sup>27</sup> Fosmire G. J. (1990). The American Journal of Clinical Nutrition, 51(2), 225–227.
<sup>28</sup> Leitzmann, M. F., Stampfer, M. J., et al. (2003). Journal of the National Cancer Institute, 95(13), 1004–1007.
<sup>29</sup> Mahmoud, A. M., Al-Alem, U., et al. (2016). Plos One, 11(11), e0165956.
30 Barceloux D. G. (1999). Journal of Toxicology: Clinical toxicology, 37(2), 279–292.
31 Kondo, Y., Yamagata, K., et al. (2003). The Journal of Urology, 170 (6 Pt 1), 2467–2470.
32 Jalloh, M. A., Gregory, P. J., et al. (2017). International Journal of STD & AIDS, 28(1), 4–15.
33 Ding, Y., Jia, Y. Y., et al. (2012). British Journal of Clinical Pharmacology, 73(3), 422-427.
34 Polk, R. E., Healy, D. P., et al. (1989). Antimicrobial Agents and Chemotherapy, 33(11), 1841–1844.
```