Melatonin

An Antioxidant in Edible Plants

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ABSTRACT: Melatonin, a molecule with antioxidant properties that is widely distributed in the animal kingdom, has now been shown to exist in the plant kingdom, including edible plants. Our findings show that melatonin is not only an endogenously produced antioxidant, but that it is also consumed in the diet. Since melatonin concentrations in the blood correlate with the total antioxidant status of this fluid, it is likely that dietary melatonin could be important in protecting against oxidative damage.

KEYWORDS: melatonin; antioxidant; free radicals; oxidative damage; edible plants

INTRODUCTION

Melatonin, *N*-acetyl-5-methoxytryptamine, has long been known to be a secretory product of the vertebrate pineal gland. This product, which is synthesized in and secreted from the pineal gland in a circadian manner with highest values at night, is related to the regulation of other 24 hour cycles, mediates annual reproductive changes in seasonal breeding animals, and has oncostatic actions.

Besides these functions, melatonin was recently discovered to be a free radical scavenger[1,2] and antioxidant.[2–4] As to its direct interactions, melatonin has been shown to detoxify the hydroxyl radical (·OH), hydrogen peroxide (H_2O_2), peroxynitrite anion ($ONOO^-$), nitric oxide (·ON) and hypochlorous acid (HOCl). The resulting products which are produced when melatonin reacts with these toxic agents are listed in TABLE 1.

In addition to these actions, melatonin, possibly via receptor-mediated mechanisms, has been shown to have indirect antioxidative actions as well. Thus, the indole promotes the activity of several enzymes which metabolically remove toxic reactants; these enzymes include superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase. Also, melatonin inhibits the potentially proxidative enzyme, nitric oxide synthase.[2–4] Both the direct scavenging actions of melatonin as well as its indirect effects on the enzymes that metabolize toxic reactants are induced with both physiological and pharmacological levels of melatonin.

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TABLE 1. A summary of the free radicals and other reactive species reported to be directly scavenged by melatonin along with the products that are formed as a consequence of these interactions

Reactant scavenged	Product identified
$^1O_2$	N^1-Acetyl-N^2-formyl-5-methoxytryptamine
H_2O_2	N^1-Acetyl-N^2-formyl-5-methoxytryptamine
·OH	Cyclic 3-hydroxymelatonin
HOCl	2-Hydroxymelatonin
·NO	*N*-Nitrosomelatonin
$ONOO^-$/ONOOH	6-Hydroxymelatonin; cyclic 2-hydroymelatonin; cyclic 3-hydroxymelatonin; 1-nitromelatonin; 1-hydroxymelatonin

NOTES: $^1O_2$, singlet oxygen; H_2O_2, hydrogen peroxide; ·OH, hydroxyl radical; HOCl, hypochlorous acid; ·NO, nitric oxide; $ONOO^-$, peroxynitrite anion; $ONOO^-$, peroxynitrous acid.

MELATONIN IN EDIBLE PLANTS

The existence of melatonin in plants was initially theorized after the indole was found in algae, species that have characteristics of both the plant and animal kingdoms.[5] This discovery was followed by identification of melatonin in a variety of different plants, including mono- and dicotyledonous angiosperms. The highest melatonin levels reported in plants to date are those measured in so-called medicinal plants,[6] i.e., fever few and St. John's wort; in these plants melatonin concentrations are in the range of μg/g tissue. In the seeds of a number of plants and in the cherry fruit, melatonin levels are in the ng/g tissue range (TABLE 2).[7]

Several facts have come to light since melatonin was discovered in plants: (a), the indole is found in roots, stems, leaves, fruits and seeds; (b), in different plants, the concentrations of melatonin vary widely; (c), and melatonin in unequally distributed within a given plant. While melatonin has been found in a wide variety of plant tissues, few foodstuffs have been examined as to their melatonin levels.[8]

CONCLUDING REMARKS

Melatonin, consumed in the diet, is absorbed by the gut and significantly alters circulating levels of the indole. Since the concentration of melatonin in the blood correlates positively with the total antioxidant status of this fluid,[9] the implication is that consuming foodstuffs containing melatonin would increase the antioxidative capacity of the organism. Melatonin readily crosses both the placenta and blood-brain barrier and gets into every cell and, so far as is known, into all subcellular compartments including the mitochondria.[2–4] Melatonin's presence in mitochondria may be of special importance since these organelles are a major source of free radicals and oxidative damage.

TABLE 2. Melatonin concentrations in a some of the plant products that have been analyzed

Common name	Scientific name	Melatonin concentration (ng/g)
Milk thistle seed	*Silybum marianum*	2
Tart cherry fruit (Balaton)	*Prunus cerasus*	2
Poppy seed	*Popaver somniferum*	6
Anise seed	*Pimpinela anisum*	7
Coriander seed	*Coriandrum sativum*	7
Celery seed	*Apium graveolens*	7
Flax seed	*Linum usitatissimum*	12
Green cardamom seed	*Elettaria cardamomum*	15
Tart cherry fruit (Montmorency)	*Prunus cerasus*	15
Alfalfa seed	*Medicago sativum*	16
Fennel seed	*Foeniculum vulgare*	28
Sunflower seed	*Helianthus annuus*	29
Fenugreek seed	*Trigonella foenum-graecum*	43
Wolf berry seed	*Lycium barbarum*	103
Black mustard seed	*Brassuca nigra*	129
White mustard seed	*Brassica hirta*	189
St. John's wort, leaf	*Hypericum perforatum*	1,750
Fever few, gold leaf	*Tanacetum parthenium*	1,920
Fever few, green leaf	*Tanacetum parthenium*	2,450
St. John's wort, flower	*Hypericum perforatum*	4,390
Huang-qin	*Scutellaria biacalensis*	7,110

NOTES: Clearly, the amount of melatonin plants contain varies widely, and melatonin within a given plant is not uniformly distributed.

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REFERENCES

1. TAN, D.X., L.D. CHEN, B. POEGGELER, *et al*. 1993. Melatonin: a potent, endogenous hydroxyl radical scavenger. Endocrine J. **1:** 57–60.
2. TAN, D.X., L.C. MANCHESTER, R.J. REITER, *et al*. 2000. Significance of melatonin in antioxidative defense system. Biol. Signals Recept. **9:** 137–159.
3. REITER, R.J., D.X. TAN, C. OSUNA & E. GITTO. 2000. Actions of melatonin in the reduction of oxidative stress. J. Biomed. Sci. **7:** 444–458.

4. REITER, R.J., D.X. TAN, D. ACUÑA-CASTROVIEJO, *et al*. 2000. Melatonin: mechanisms and actions as an antioxidant. Curr. Top. Biophys **24:** 171–183.
5. POEGGELER, B. & R. HARDELAND. 1994. Detection and quantification of melatonin in a dinoflagellate, Gonyaulax polyedra: solutions to the problem of methoxyindole destruction in non-vertebrate material. J. Pineal Res. **17:** 1–10.
6. MURCH, S.J., C.B. SIMMONS & P.K. SAXENA. 1997. Melatonin in fever few and other medicinal plants. Lancet **350:** 1598–1599.
7. MANCHESTER, L.C., D.X. TAN, R.J. REITER, *et al*. 2000. High levels of melatonin in the seeds of edible plants: possible function in germ tissue protection. Life Sci. **67:** 3023–3029.
8. REITER, R.J. 1999. Phytochemicals: melatonin. *In* Encyclopedia of Food Science and Technology. F.J. Frances, Ed.: 1918–1922. John Wiley. New York.
9. BENOT, S., R. GOBERNA, R.J. REITER, *et al*. 1999. Physiological levels of melatonin contribute to the antioxidant capacity of human serum. J. Pineal Res. **27:** 59–64.