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Nutritional and Medicinal Properties of Valerian *(Valeriana Officinalis)* Herb: A Review

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Abstract

Valerian *(Valeriana officinalis)* belonging to valerianaceae family is a well known herb and medicinal plant that has been widely used all over the world especially in Europe, China and Middle East. It is widely used as a sleep aid and sedative in many parts of the world but is also known to relax smooth muscle, hence used for treating stomach and intestine cramps. Alkaloids, terpenes, organic acids and its derivatives, valepotriates and flavones are the known pharmacologically active compounds found in valerian extract. In general, it is accepted that the valepotriates are the compounds responsible for the sedative activity of the Valerianaceae. The present article aims at reviewing the recent reports on its constituents, traditional use, clinical use and scientific verification of pharmacological actions of valerian.

Keywords: Active constituents; Sedative; Sleep aid; Antioxidant properties; Appetite; Food intake.

Introduction

Valerian *(Valeriana officinalis)* plant root is a herb which is used worldwide over centuries. It belongs to Valerianaceae family. There are 10 genera and about 300 species in the family *Valerianaceae.* The *Valeriana* genus is of the family *Caprifoliaceae* and approximately contains 200 species.[1] The Valerianaceae are typically distributed worldwide and consist of herbs, rarely shrubs, with opposite leaves, a sympetalous, spurred corolla, 1–4 stamens, and a tricarpellate, poorer ovary with 1 functional locule and a single, apical ovule, the fruit is an achene, with a pappuslike calyx in some members. The economic uses include some cultivated ornamentals (e.g. *Centranthus*) and negligible edible, medicinal, or essential oil plants. The plant of *Valeriana officinalis* is native to Europe and Asia and in addition has naturalized in eastern North America. This tall perennial has a preference in moist woodlands; it has been broadly cultivated in northern Europe. Most of the European supply is grown in Holland. Low lying, damp sandy humus with lime fertilizer is the way to cultivate Valerian. It harvests in the late fall and dries. *V. officinalis* is the species which is used in Europe. This genus contains more than 250 species. In traditional Chinese and Japanese medicine *V. fauriei* is used commonly.[2-5] *Valerian capensis* is other species which is used in African traditional medicine[6], *V. edulis* is used in Mexico and *V. wallichii* is used in India.[7]

History of use

The roots of *V. officinalis* known as valerian, since long are taken as sedative medicine in Europe. Valerian is an agent with mild sedative and sleep-promoting properties that is often used as a milder substitute or a possible alternate for stronger synthetic sedatives, such as the benzodiazepines, in the treatment of nervous states and anxiety-induced sleep disturbances.[8] Lesniewicz *et al*,[9] reported that valerian is tranquillizer for people with hyper-excitability and as a smooth-muscle relaxing agent to treat stomach and intestine cramp. Valerian is also a component of many herbal mixtures, which are widely used to treat sleeping disorders.[10] Nowadays, valerian

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extracts are available as dietary supplements, which primarily involve dried root or extracts from the root, formulated into tablets or soft gelatin capsules. Usually each dose contains approximately between 50 mg and 1 gram of dried root or extract. The use of these dietary supplements is widespread, with an estimated 210 and 125 million doses sold annually in the United States and in Europe respectively.[11] Though not supported by research, traditionally it has been recommended for epilepsy.[12] Restlessness, insomnia, nervousness, and tension are the present indications for valerian as reported by Tariq and Pulisetty.[13] It is suggested that the large doses when stopped, as most sleep aids, cause withdrawal symptoms.[14] Cohen and Toro[15] expressed that patients with liver disease are advised not to take valerian. Although it is shown to be a successful remedy for the reduction of anxiety, in some individuals some side effects like headaches and night terrors were reported.[16] He explained the reason may be due to the fact that some people lack a digestive conversion property required to effectively break down valerian. In these individuals, valerian can cause agitation.

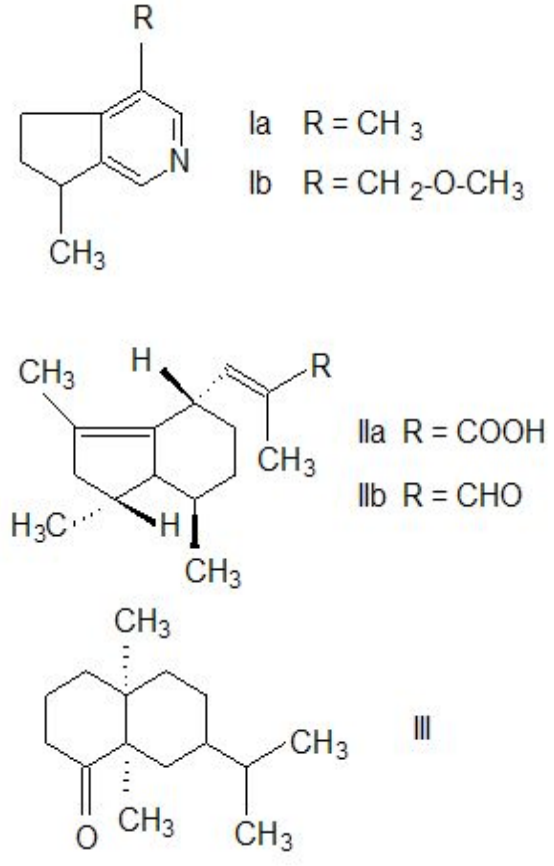
Nutritional and Chemical constituent

Valerian was studied for its mineral content by Adamczyk and Jankiewicz[17] and they reported that valerian root contains 13.1 ppm copper, 75.1 ppm zinc and 16.8 ppm manganese. Adel Pilerood and Prakash[18] analyzed the chemical constituents of valerian as reported in Table 1. More than 150 chemical constituents were found in valerian of which many are physiologically active.[19] There is significant variation in the chemical constituents in plants from different sources and growing conditions, processing methods and storage conditions.[20] To guarantee the quality of the drug, producers have standardized production of the plant extracts.[21] Alkaloids, terpenes, organic acids and its derivatives, valepotriates and flavones are the known pharmacologically active compounds found in valerian extract. In general, it is accepted that the valepotriates are the compounds responsible for the sedative activity of the Valerianaceae.[22] Alkaloids (0.01–0.05%), notably terpene alkaloids are present in valerian.[23] The main valerian alkaloids are actinidine, chatinine, valerianine, valerine, alpha-methyl pyrryl ketone and naphthyridin methyl ketone.[24-26] The structures of some valerian alkaloids are shown in Fig 1.

Actinidine

Actinidine (Ia) is a steam-volatile monoterpenoid pyridine alkaloid with a cyclopenta [c] pyridine skeleton present in the essential oil of valerian root[27] and *Actinidia polygama* (silver vine).[28] Actinidine is compound in valerian, which can attract cats.[22] Biosynthesis of actinidine results from

Figure 1: The structures of principal compounds present in volatile essential oil of *Valeriana officinalis*



lysine and quinolinic acid as precursors.[29] Actinidine is an alkaloid which is psychoactive which interferes with the gamma-aminobutyric acid (GABA)-ergic metabolism; it is an agonist on benzodiazepine receptors and thus revealed an allosteric modulation of the GABA-receptor-proteins.[22]

Waliszewski[30] isolated *Chatinine* from valerian but its biological properties have not been studied. *Alpha-methyl pyrryl ketone* was studied in Germany as a central nervous system active compound on 1970.[31] Synthetic naphthyridinones similar in structure to natural naphthyridyl methyl ketone were introduced as potential drugs for the treatment of schizophrenia.[32-33] Since the pharmacological properties of valerian alkaloids have been studied separately only infrequently, it is difficult to say how these participate in the medical effects of *V. officinalis*.

Organic acids and Terpenes

Organic acids and terpenes are available in the volatile essential oil, which is 0.2–2.8% of the dry weight of the root. The essential oils are not only seen in the subrerranean parts of the plants but also in the aerial parts.[34] Terpenes are characterized chemically as monoterpenes and sesquiterpenes. Valeric, isovaleric, valerenic, isovalerenic and acetoxyvalerenic acids, bornyl acetate, bornyl isovalerenate, 1-pinene, 1-comphene, 1-borneol, terpineol, valeranone and cryptofauronol are most considerable valerian organic compounds. It is suggested that some of the oil components pose sedative properties. Isovaleric acid and bornyl isovalerate are two compounds which are mainly responsible for the characteristic aroma of valerian. Isovaleric acid and 3-methylbutanoic acid do not have significant pharmacological and toxicological properties and only share the drug's odor. However, it was found in 2007 that isovaleric acid decreases ATPase activity in the synaptic membranes of the cerebral cortex and it may be necessary in the pathophysiology of the neurological dysfunction of isovaleric acidemic patients.[35]

Valerenic acid (IIa) and its aldehyde *valerenal* (IIb) are monoterpenes which are pharmacologically active compound. Cavadas et al[36] recommended that valerian acts via GABA mechanisms. Other studies revealed binding of valerian extract to GABA receptors, but the functional effect of the binding was not demonstrated. Data from the study of Yuan *et al*[37] and Trauner *et al*[38] suggest that the pharmacological effects of valerian extract and valerenic acid are mediated through modulation of GABAA receptor function. By passive diffusion valerenic acid is known to penetrate into the central nervous system trans cellular.[39] Dietz *et al*[40] showed that valerenic acid is a partial agonist of the 5HT receptor with the strong binding affinity to the 5-HT (5a) receptor, but only weak binding affinity to the 5-HT(2b) and the serotonin transporter. In a study valerenic acid, acetylvalerenolic acid and valerenal served as inhibitors of NF-êB at a concentration of 100 ìg/ml. Acetylvalerenolic acid reduced NF-êB activity to 4%, while valerenic acid reduced NF-êB activity to 25%.[41] *Valeranone* (III) was tested as a medical drug in hyperkinetic

Table 1: Nutritional composition of Valerian

Constituents	Value	Constituents	Value
Moisture (g)	7.60±0.11	Ash (g)	8.97±0.30
Protein (g)	4.63±0.10	Phosphorous (mg)	328±1.00
Fat (g)	1.17±0.08	Calcium (mg)	829±0.8
Insoluble fiber (%)	77.00±0.20	Iron (mg)	272.0±0.89
Soluble fiber (%)	7.3±0.10	Zinc (mg)	4.80±0.01
Carbohydrate (g) (By difference)	2.24±0.02	Copper (mg)	2.69±0.01
Vitamin C (mg)	44.90±0.40	Manganese (mg)	11.47±0.00
Total carotenoids (mg)	132.7±0.1	Chromium (µg)	249.0±0.01
Anthocyanin (mg)	ND	-	-

[Adapted from Ref. 18.]

behavior disorders.[42] In animal experiments its sedative, tranquilizing and antihypertensive properties was pharmacologically investigated but the activity of valeranone was found to be lesser than those of the standard substances used.[43] Thus, valerian may carry the sedative effects of anaesthetics and other medications that act on GABA receptors, and use of valerian before surgery may cause a valerian-anaesthetic interaction.

Valepotriates

Valepotriates are esterified iridoid-monoterpenes. Their name is derived from the valeriana-epoxy-triester, because these are triesters of polyhydroxycyclopenta-(c)-pyrans with carboxylic acids: acetic, valeric , isovaleric , á-isovaleroxy-isovaleric, â-methylvaleric, â acetoxy-isovaleric, â-hydroxyisovaleric and â-acetoxy-â-methylvaleric acid.[44] It is a major component consisting of 50–80% active compounds. Valepotriates are divided into two classes: monoene and the diene derivatives. The principal diene valepotriates are *valtrate*, *isovaltrate*, *7-desisovaleroyl-7-acetylvaltrate* and *7-homovaltrate*, and the major monoene derivatives are *didrovaltrate* and *isovaleroxyhydroxydidrovaltrate*. The amount of valepotriates varies widely between species. In general the underground parts of plant contain higher amount of valepotriates than the other parts of the plant.[45] Valepotriates are unstable compounds: they are thermolabile and decompose quickly under acidic or alkaline conditions in water, as well as in alcoholic solutions. However in anhydrous methanol, and stored at 20°C, the diene valepotriates were found to be relatively stable. Dissolved in methanol or ethanol, with only a small amount of water and stored at room temperature, gives 90% decomposition within a few weeks.[46] The main decomposition products of the valepotriates are the yellow-coloured baldrinals.[47] Baldrinals are chemically reactive and may subsequently form polymers.[46]

In vitro antioxidant studies

Zheng and Wang[48], studied the antioxidant activity of selected herbs which were grown in the same place with similar conditions to avoid variations of oxygen radical absorbance capacity (ORAC) values because of ecological factors. Herbs (2.0 g) were extracted with 15 ml of phosphate buffer (75 mM, p^H 7.0) using a Polytron homogenizer (Brinkmann Instruments, Inc., Westbury, NY) for 1 min and were then centrifuged at 20000g for 20 min. The supernatant was used for the ORAC and total phenolic compound assay after suitable dilution with phosphate buffer (75 mM, p^H 7.0). They reported the total phenolic content of valerian as 1.78 mg of Gallic acid equivalent (GAE) / g of fresh weight and ORAC as 15.82 µmol of TE / g of fresh weight.

Nutritional and Medicinal properties

The root and rhizome of the valerian plant (*Valeriana officinalis L.*) is used medicinally for its sedative properties with indications including nervous tension, insomnia, anxiety and stress.[49]

One study found that valerian could sedate the agitated person and stimulate the fatigued person, bringing about a balancing effect on the system.[50]

In an *in vivo* and *in vitro* investigation of valepotriates and valeranone on guinea-pig ileum smooth muscle preparations it was found that dihydrovalerate and valeranone were able to relax stimulated smooth muscle preparations with potency comparable to that of papaverine. Moreover, it was shown that these valeriana compounds cause smooth muscle relaxation through a musculotropic action, which is also known to be the case for papaverine.[51]

Hazelhoff[51], in his dissertation, showed that there is a significant reduction in the locomotor activity of mice when the valerian and *V. officinalis* extract was administered. The

effect of a mixture of valepotriates on the elevated plus-maze performance of diazepam withdrawn rats was evaluated by Andreatini and Leite.[52] The rats were chronically (28 days) treated with diazepam (doses increased up to 5.0 mg/kg) and to provide a withdrawal syndrome they were treated with a control solution for 3 days. Chronically vehicle-treated rats were used as control. The abstinent animals treated with the vehicle showed a significant reduction in the percentage of time spent in the open arms when compared with the control animals. Diazepam and valerian 12.0 mg/kg reversed this anxiogenic effect. They did found significant difference in valerian group than the other group.

Mechanism of action

Because of valerian's traditional use as a sedative, anti-convulsant, migraine treatment and pain reliever, most basic science research has been directed at the interaction of valerian constituents with the GABA neurotransmitter receptor system.[38] The mechanism of action of valerian in general and as a mild sedative in particular is not known.[53] Valerian extracts and some of its constituents, mainly valerenic acid, appear to have some affinity for the GABAA receptor, but the exact mechanism of action is not clear. Benke *et al* [54] described a specific binding site on GABAA receptors with nM affinity for two general constituents of valerian namely valerenic acid and valerenol. Both valerenic acid and valerenol increased the response to GABA at multiple types of recombinant GABAA receptors. A point mutation in the beta2 or beta3 subunit of recombinant receptors strongly decreased the drug response. *In vivo*, valerenic acid and valerenol have shown anxiolytic activity with high potencies in the elevated plus maze and the light/dark choice test in wild type mice. In beta3 point-mutated mice the anxiolytic activity of valerenic acid was found to be absent. Thus, neurons expressing beta3 containing GABAA receptors are a main cellular substrate for the anxiolytic action of valerian extracts.[54] Substances such as valerenic acid and its derivatives acetoxyvalerenic acid and hydroxyvalerenic acid have to pass the blood-brain barrier and interact with this receptor in the brain. It was hypothesized that the investigated terpenes from *V. officinalis* can probably only cross through the blood-brain barrier by a still unknown transport system and not transcellularly by passive diffusion.[39]

Effect on appetite

It is also found that valerian increased the food intake and cause weight gain in adult wistar rat.[55] It has been shown that valerian increases release of GABA (gamma aminobutyric acid) and inhibits enzyme induced break down of GABA.[36,56-57] GABA has direct relationship with serotonin the secretion of which inhibits appetite and food intake.[58] It has been found that ghrelin hormone (hunger hormone) increases production and release of GABA[59], the adverse effect may accrue and increase ghrelin production and so improve the appetite. On the other hand Actinidine (Ia) which is a steam-volatile in the essential oil of valerian root[27], is psychoactive which interferes with the gamma-aminobutyric acid (GABA)-ergic metabolism; it is an agonist on benzodiazepine receptors and thus revealed an allosteric modulation of the GABA-receptor-proteins.[22] The mechanism of action needs more study.

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