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Medicinal Natural Drug of Valerian (Valerina Officinalis): An- Over 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: V. officinalis, Active constituents , Effectiveness, Valerian Extract, Photochemistry, Pharmacology

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INTRODUCTION[1-19]

Valerian is a genus of flowering plants in the Caprifoliaceae family, members of which can be normally called as valerians. The name valerian is derived from Valerio's, the Latin term "valere," which means health or well-being. Valerian consists of the fragments or whole fresh or dried rhizomes, roots, and stolon'. There exist about 200 species in Europe, Asia, and North America. Some of the species are Valeriana officinalis, Valeriana jatamansi, Valeriana wallichii, Valeriana Hardwicke, Valeriana microphyll a, Valeriana long flora, and Valerian quadrangular is, etc. It has been used medicinally for 2000 years. It absolutely was first used as a treatment for brain disorder within the late 16th century. It is habitually used for the treatment of varied nervous disorders , antispasmodic, anthelmintic, diuretic, diaphoretic, and emmenagogue, and hysteria. It has an aromatic stimulant and reported some distinctive indications, as well as its use for rheumatism, low-grade fevers, and aphrodisiac, further as its use in hysteria . Valerian is used as a nervine sedative for the treatment of hysteria, epilepsy and sedative in nervous anxiety . It conjointly used as a cerebral stimulant, analgesic and sedative in nervous irritability, specifically once the condition may be a result of "enfeebled cerebral circulation ." Natural products have upper hand over synthetic drugs because they have fewer side effects and also does not alter physiological and biochemical pathways . Over the years, medicinal plants of the Valeriana genus are shown to treat rheumatism, low-grade fevers, aphrodisiac, nervous disorders, spasmolytic, anthelmintic, diuretic, diaphoretic emmenagogue, and additionally to hysteria. However, the traditional uses of these plants have been recorded primarily in local herbal books or have been passed down orally from one generation to other. The medicinal use of the Valerian, compared pharmacological activities, including antioxidant, antimicrobial, anti-inflammatory, antirheumatic sedative, anxiolytic, tranquilizing, spasmolytic, anticonvulsant, and neuroprotective activities. In this review, an attempt was made to present an overall overview of the ethnopharmacological uses of this Indian traditional medicine, its phytochemical properties and pharmacological activities of V. officinalis, so the gaps and are as requiring further research works of this plant can be highlighted

V officinalis (Valerian)

V officinalis var. latifolia is a perennial herb obtained from the Valeriana genus of the Valerianaceae family found in North America, Europe, and Asia . It is a glabrous or more or less pubescent herb, up to 1.5 m in height. Rootstocks short, sub-erect, hardly thicker than stem, and stoloniferous; stem solitary, erect, and furrowed. V. officinalis has pinnately-separated leaves,

generally with 6–10 pairs of lance-shaped leaflets and bears numerous small white or pink flowers in a dense head of many stalked clusters. These heads bare small (5 mm) tapered seeds, almost hairless at maturity (fig .1).

Taxonomical classification

Kingdom: Plantae

Unranked: Angiosperms

Unranked: Eudicots

Unranked: Asterids

Order: Dipsacales

Family: Caprifoliaceae/Valerianaceae

Genus: Valeriana

Species: Officinalis

Vernacular names

Arabic - Sanballat Web

English -Allheal, English valerian, garden heliotrope, German valerian, great Wild valerian, valerian root

Marathi - Kalavala

Sanskrit -Balahrivera

Tamil - Catamaci, jatamansi, paicavi, takram

Urdu -Balchar, balchhar, bulchar, ikleel-ul-malik, nardin, sumbul-ut-teeb

Common names

English: Valerian, garden heliotrope, common valerian.

Ayurvedic:Tagara, Nata. Baalaka (syn. Udichya, Jala, Barhishtha) is also equated with Valeriana

Folk: Sugandhabaalaa ,Tagger

Figure 1: Morphology of Valeriana officinalis whole plant, (b) aerial parts with flower, flower at an early stage, (d) flower and (e) stem [16,17]

History of Valerian [12,19-24]

Valerian has been used as a medicinal herb since at least the time of ancient Greece and Rome. Hippocrates described its properties, and Galen later prescribed it as a remedy for insomnia medieval Sweden, it was sometimes placed in the wedding clothes of the groom to ward off the "envy" of the elves. Sometimes people put it in a tea. The Greek physician, Dioscorides, apparently recommended valerian root to treat myriad disorders including heart palpitations, digestive problems, epilepsy and urinary tract infections. Valerian was recommended by Galen during the second century as a treatment for insomnia. Valerian plants are as attractive as catnip to cats, and it is rumored that the Pied Pipers secret to clearing the streets of Hamlin was a store of valerian under his cloak.

By the 18th century, valerian was widely used as a sedative and to treat nervous disorders associated with a “restless” digestive tract as well as the “vapors” in women. During World War I, valerian was used to prevent and treat shell shock in frontline troops, and it was used during World War II to help calm civilians subjected to air raids. Valerian was listed as a sleep aid and anxiolytic on the US national formulary until the 1940’s. It fell into disuse as more potent sedative-hypnotic pharmacologic agents became available. Related species have been used in Traditional Chinese Medicine (TCM), Ayurvedic Medicine and African herbal healing practices. V. fauriei is used in Traditional Chinese Medicine and Japanese medicine as a sedative, spasmolytic and antidepressant. V. capensis is used in African traditional medicine as a treatment for epilepsy, hysteria and nervous disorders. In the 1980’s valerian again assumed a place of importance as a widely used nonprescription hypnotic and daytime sedative, particularly in France, Belgium, Switzerland, Britain, Russia and Germany. Over 50 tons of valerians are sold each year in France alone. Adolescents and young adults appear to be particularly attracted to valerian and other herbs that affect the central nervous system. The German Commission E has given Valerian root a positive evaluation for use in states of restlessness. The European Scientific Cooperative on Phytotherapy cites its indications as “tenseness, restlessness and irritability with difficulty in falling asleep”.

The Herbal PDR lists its primary indications as “nervousness and insomnia”, as well as lack of concentration, stress headache, menstrual states of agitation, neuralgia, nervous stomach, and states of angst. It has also been included in herbal remedies for cardiovascular disorders to help reduce hypertension and reduce the effects of stress and tension on the heart. Some health resort

put valerian in whirlpool baths to help reduce pain and enhance sleep for patients with fibromyalgia. Valerian is often used in combination with other sedative herbs such as chamomile, lemon balm, passion flower, valerian was the 10th most popular herbal remedy sold in the United States. For thousands of years, the Chinese, Greeks, Romans, and Indians have used valerian as a mild sedative. The origin of the word "pew" is said to come from the foul odor of the valerian root, which a first century AD Roman physician, Dioscorides, called phu. In the mid-1800s in the United States, the Shakers began growing valerian and other herbs to market to doctors and pharmacists in America and Europe. Valerian is sometimes used. flavor foods and drinks such as root beer

Botany of Valerian Drug [25-26]

The family Valerianaceae comprises 10 genera and about 300 species or the Valeriana genus is of the family Caprifoliaceae and comprises about 200 species. The Valerianaceae are mostly distributed worldwide and consist of herbs, rarely shrubs, with opposite leaves, a sympetalous, spurred corolla, 1–4 stamens, and a tricarpellate, inferior 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 minor edible, medicinal, or essential oil plants.

Toxicology of Valerian Drug [27-33]

Numerous studies have indicated that aqueous and alcoholic extracts of V. officinalis are a little toxic and have high LD50 values. For example, Valera none has LD50 for mice at i.p. administration 580 mg/kg. A unique case of overdose where the patient had ingested almost 25 g of powdered V. officinalis root in capsule form, demonstrated only mild symptoms. hitch included fatigue, abdominal cramps and tremor; all of the symptoms disappeared within 24 hours. The clinical evidence indicates that valerian is a relatively safe substitute for the benzodiazepines as a mild tranquilizer. It was traditionally contraindicated in pregnancy, but until recently there were no studies to warrant this warning. An Australian study on female rats which were orally dosed with a valerian extract daily on either gestation days 1–8 or 8–15 indicated that valerian had no adverse effects on fertility or fetal development. Literature reports have suggested that valerian induces genotoxicity in vitro (ECV304 cells) by a reactive oxygen species-mediated mechanism ; however, there are no reports on its genotoxicity and/or the epigenetic mechanism in vivo . Genotoxicity has been reported for both baldrinal and homobaldrinal, the decomposition products of valtrate and isovaltrate. These compounds showed direct mutagenic effects in vitro in the AMES assay and the

SOS-chromo-test. Studies on the effects of baldrinals on haemopoietic cells in vitro , indicating decreased liver function .

Cultivation of Valerian Drug [34]

Valerian plants are available from some garden centers in the prairies and they can be transplanted into well fertilized moisture-retentive soil. Alternatively, the plants can be grown from seed or propagated by splitting established plants in spring or fall. When growing plants from seed, the beginner should be aware that germination is unpredictable and often slow. The seeds require light for germination and must not be covered. After transplanting the seedlings, the plants require two or three years before harvesting the roots if they are to be used medicinally. Older plants will have a greater mass of root for harvest. However, most people cultivating valerian in gardens tend to grow it for horticultural interest rather than medicinal use.

Phytochemistry of Valerian Drug [24, 35-38]

The roots and rhizomes (underground stems) of valerian are typically used to make supplements, including capsules, tablets, and liquid extracts, as well as teas. The root of the plant is used medicinally and is pressed into fresh juice or freeze-dried to form powder. Valerian contains over 150 chemical constituents; many are physiologically active. There is substantial variation in the chemical constituents in plants from different sources, growing conditions, processing methods and storage conditions. Even in standardized plant extracts sold in Germany, there is some variation in the amount of different chemical constituents that may account for clinical efficacy. Despite these differences, the clinical effects appear to be remarkably consistent across different preparations.

Although the sedative effects of the plant's root have been known for centuries, the exact chemical compounds responsible for its activities have not been identified and agreed upon. There is little correlation between the content of volatile oils and the plant’s clinical effects. Valerian’s effects on the central nervous system have been variously attributed to valepotriates, their breakdown products (baldrinals), valerenic acid, valerenal and valeranone, and other constituents in the essential oil.

Pharmacological Properties Valerian Drug [38-53]

Valerian has been used as a medicinal herb since at least the time of ancient Hippocrates described its properties, and the later prescribed it as a remedy for insomnia. Pharmaceutical application of valerian is due to its sedative, anticonvulsant, antidepressant, antihypertensive, hypnotic effects, antispasmodic and anxiolytic activity. The pharmacological effects of valerian have primarily been attributed to the valepotriates (iridoid esters), volatile oils, monoterpenes, and sesquiterpenes

constituents .Lately, the potential cytoprotective effect of aqueous extract of V. officinal is on human neuroblastoma cells has also been demonstrated. In 1998, valerian was the tenth most popular herbal cure sold in the United States. Now, valerian extracts are available as dietary supplements, which are primarily composed of dried root or extracts from the root, formulated into tablets or soft gelatin capsules are extensively used with an estimated 210 million doses sold annually in the United States and 125 million doses sold annually in Europe.

Cardiovascular activity:

The coronary dilating and antiarrhythmic effects of valerian extract has been demonstrated in rabbits, mice and cats. reported that valepotriates an important component of Valerian, prevented the appearance of acute coronary insufficiency as well as vasopressin-induced arrhythmia, provoked a short-lived increase of coronary blood flow, and had moderate positive inotropic and negative chronotropic effects. In mice, valeranone another bioactive compound found in small quantities in valerian and in larger amounts in its relative, Nardostachys jatamansii, exerted weak hypotensive effects .A significant increase in coronary blood flow, a transient fall in blood pressure and a decrease in heart rate was noticed when cats were intravenously injected with valerian extracts Valerian is included in a German heart tonic to maintain neuro-cardiac stability .In an open, multicenter trial of 2,243 patients with a variety of functional cardiac disorders, an herbal combination (valerian, hawthorn, cereus and camphor) was associated with improvement in 84% of patients, reported significant anticoronaryspastic, ant bronchospastic, antihypertensive activities from ethanolic and aqueous extracts of V. officinalis L. roots in anaesthetized guinea-pigs and were found similar to those exhibited by nifedipine

Anxiolytic activity

Evaluated the pharmacological profile of different extracts derived from V. officinalis L. including two commercially available extracts and the newly developed preparations VAL SE 35E and Phyto fin Valerian 368. Therefore, tests for sedative, anxiolytic, antidepressant as well as for myorelaxant properties were conducted in rodents. The results revealed that none of the valerian extracts displayed sedative or myorelaxant effects when used up to maximum dosages of 500 or 1000 mg/kg body weight. However, pronounced anxiolytic of the 45% methanolic and 35% ethanolic extract as well as of phyotofin Valerian 368 was noticed in the elevated plus maze test in a dose range of 100–500 mg/kg body weight. Additionally, and different from its primary extract (35% ethanolic extract) Phyto fin Valerian 368 showed antidepressant activity in the forced swimming test after subacute treatment. They concluded that anxiolytic and antidepressant activity may contribute to the sleep-enhancing properties of valerian. Further, reported primary anxiolytic

activity of valerian due to the presence of valerenic acid and the enhanced anxiolytic effect of valerenic acid in the presence of GABA. During their experiment rats were administered either ethanol (1ml/kg), diazepam (1mg/kg), valerian root extract (3ml/kg), valerenic acid (3mg/kg), oral solution of valerenic acid and exogenous GABA (75 mg/kg and 3.6 mg/kg, respectively) and assessed for the number of entries and time spent on the open arms of an elevated plus maze. Results showed that there was a significant reduction in anxious behavior when valerian extract or valerenic acid exposed subjects were compared to the ethanol control group.

Sedative/anticonvulsant activity

Evaluated the biological activity of the different root extracts of Valeriana officinalis wherein two fractions (V103 and VI15) were found to potentiate the pentobarbital sleeping time in rats. In mice, intraperitoneal injections of valerenic acid, valerenal and whole herb extracts produced significant sedation, ataxia and anticonvulsant effects. Intraperitoneal injections of 100 mg/kg had sedative effects as strong as barbiturates; doses of 400 mg/kg led to death. In comparison with diazepam and chlorpromazine, valerian extract had weak anticonvulsive properties. Valerian root extract (Valdispert) reduced motility and increased thiopental and pentobarbital-induced sleeping time. Even the aroma of valerian root exerted sedative effects in mice is reported the sedative and sleep enhancing property of hesperidin, a compound isolated from V. officinalis. They also demonstrated the ability of 6 Methylepigenin, another compound from V. officinalis, to potentiate the sleep enhancing property of hesperidin. further reported the presence of the flavone glycoside linarin and its sedative and sleep-enhancing properties that are potentiated by simultaneous administer ration of valerenic acid. An intraperitoneal co-administration of linarin (4 mg/kg) and valerenic acid (5 mg/ kg) had sedative and sleep-enhancing effects as evidenced by the remarkable reduction in the exploration of holes, the time mice spent head dipping and the number of their rearing's as assayed in the hole board test and also produced a striking increase in the sleeping time induced by sodium thiopental whereas the administration of linarin and valerenic acid independently at the above mentioned doses did not increase the sleeping time induced by sodium thiopental.

Gastrointestinal activity

Valerian is traditionally used in the treatment of intestinal spasms, colic, and "nervous stomach". Valerian has a bitter flavor, and bitters have historically been used to enhance appetite and digestion. Valerenic acid, valtrate and valeranone exert spasmolytic effects in guinea pig ileum through direct effects on smooth muscle /Anti dysmenorrheal activity

Valerian seems to be an effective treatment for dysmenorrhea, probably because of its antispasmodic effects. In a double-blind, randomized, placebo-controlled trial, 100 students were randomly assigned to receive valerian (dose 255 mg) 3 times daily for 3 days beginning at the onset of menstruation, for 2 consecutive menstrual cycles. At baseline and during the intervention cycles, the pain severity was evaluated with a visual analog scale and the systemic manifestations were assessed using a multidimensional verbal scale. The pain severity at baseline did not differ significantly between the groups. After the intervention, the pain severity was significantly reduced in both groups, but the extent of the reduction was larger in the valerian group, with the difference between the 2 groups being statistically significant. The total scores of the systemic manifestations associated with dysmenorrhea decreased after the intervention, but there was no significant difference between the groups, with the exception for syncope.

Attention enhancing activity: -

In Germany valerian is sometimes used to treat attention deficit hyperactivity disorder (ADHD) in children. German studies during 1960's reported that valerian could antagonize the hypnotic effects of alcohol, enhancing concentration and coordination. In a randomized, placebo controlled, double-blind study, valepotriates demonstrated a dose-dependent increase in concentration abilities in 24 healthy volunteers. Also, valeropotriates when given in combination with alcohol did not affect blood alcohol levels, sedative effects or effects on driving performance. There are no controlled trials evaluating valerian's use in treating attention deficit hyperactivity disorder (ADHD)

Other neurological activity

Unlike diazepam, valerian did not affect spontaneous ambulation and rearing or approach-avoidance conflict in mice in a water-lick conflict test. On the other hand, valerian and imipramine significantly inhibited immobility induced by a forced swimming test in rats and significantly reversed reserpine-induced hypothermia in mice, leading researchers to conclude that valerian may be a useful antidepressant .Among 80 hospitalized geriatric patients enrolled in a placebo controlled trial for 14 days, those assigned to an aqueous valerian extract had significant improvements in mood and behavioral disturbances as well as sleep Among 121 patients with sleep disturbances enrolled in a controlled trial, those assigned to an alcoholic extract of valerian (600 mg daily for 28 days) had a significant improvement in depression, mood and global functioning as well as sleep; no significant side effects were reported .

Pharmacokinetics of Valerian Drug [(34)]

There are inadequate data on the pharmacokinetics of valerian preparations and their constituent compounds. The pharmacokinetics of valerenic acid were explored in a single-dose study involving six healthy adults who received a 70% ethanol extract of valerian root (drug to extract ratio 5: 1) 600 mg in the morning. For five participants, maximum serum concentrations of valerenic acid occurred between one and two hours after valerian administration and ranged from 0.9 to 2.3 ng/mL; valerenic acid concentrations were measurable for at least five hours after valerian administration. For one subject, maximum concentration occurred at both one and five hours after valerian administration. The mean elimination half-life (t1/2) for valerenic acid was 1.1 hrs. and the mean area under the plasma concentration time curve was 4.80 µg/mL/hr. Further investigation of the pharmacokinetics of valerian is required, including those of different manufacturers' preparations and their constituents.

Mechanism of Action of Valerian Drug [54-55]

Many chemical constituents of valerian have been identified, but it is not known which may be exactly responsible for its sleep-promoting effects in animals and in in vitro studies. It is likely that there is no single active compound and that valerian's effects result from multiple constituents acting independently or synergistically. Two categories of constituents have been proposed as the major source of valerian's sedative effects. The first category comprises the major constituents of its volatile oil including valerenic acid and its derivatives, which have demonstrated sedative properties in animal studies. However, valerian extracts with very little of these components also have sedative properties, making it probable that other components are responsible for these effects or that multiple constituents contribute to them. The second category comprises the iridoids, which include the valepotriates. Valepotriates and their derivatives are active as sedatives in vivo but are unstable and break down during storage or in an aqueous environment, making their activity difficult to assess. A possible mechanism by which a valerian extract may cause sedation is by increasing the amount of GABA, an inhibitory neurotransmitter) available in the synaptic cleft. Results from an in vitro study using synaptosomes suggest that a valerian extract may cause GABA to be released from brain nerve endings and then block GABA from being taken back into nerve cells. In addition, valerenic acid inhibits an enzyme that destroys GABA.

Valerian extracts contain GABA in quantities sufficient to cause a sedative effect, but whether GABA can cross the blood-brain barrier to contribute to valerian's sedative effects is not known. Glutamine is present in aqueous but not in alcohol extracts and may cross the blood-brain barrier and be converted to GABA. Levels of these constituents vary significantly among plants depending on when the plants are harvested, resulting in marked variability in the amounts found

in valerian preparations. The Valerenic acid also appears to inhibit the enzyme system responsible for the central catabolism of GABA, increasing GABA concentration and decreasing CNS activities. There is also some evidence that may suggest valerian containing other constituent such as lignan and GABA, which may be responsible for sedative effects of valerian because of valerian's historical 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. These studies remain inconclusive and all require independent replication. Valerian also contains isovaltrate, which has been shown to be an agonist for adenosine A1 receptor sites. This action may contribute to the herb's sedative effects. Under the US Preventative Services Task Force's (USPSTF) classification system for herbs, valerian was rated as probably safe and effective as a sleep aid, based on evidence from randomized clinical trials. In respect to its spasmolytic properties, it was rated possibly effective and probably safe, based on animal studies.

While valerian appears to be safe and possibly effective, the literature available in the English language evaluating this herb is limited due to small sample size, short study duration, and some inconsistent results. Valerian's long-term safety has yet to be demonstrated, and therefore it should not be recommended for extended use for any indication. Valerian's main attribute may be that it serves as an alternative, with a low incidence of side effects, to synthetic sedative agents. When recommended, patients should be counseled about possible side effects and closely monitored during therapy.

Nutritional and Chemical Constituent Valerian Drug [43,56-80]

Valerian was studied for its mineral content and they reported that valerian root contains 13.1 ppm copper, 75.1 ppm zinc and 16.8 ppm manganese. 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. There is significant variation in the chemical constituents in plants from different sources and growing conditions, processing methods and storage conditions. To guarantee the quality of the drug, producers have standardized production of the plant extracts. 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. Alkaloids (0.01–0.05%), notably terpene alkaloids are present in valerian. The main valerian alkaloids are actinidine, chatinine, Valeria nine, valerine, alpha-methyl pyrryl ketone and naphthyridine methyl ketone. The structures of some valerian alkaloids are shown in Fig 2.

Actinidine (Ia) is a steam-volatile monoterpenoid pyridine alkaloid with a cyclopenta [c] pyridine skeleton present in the essential oil of valerian root and Actinidia polygama (silver vine). Actinidine is compound in valerian, which can attract cats] Biosynthesis of actinidine results from lysine and quinolinic acid as precursors. 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. Alpha-methyl pyrryl ketone was studied in Germany as a central nervous system active compound on 1970.Synthetic naphthyridines similar in structure to natural naphthyridyl methyl ketone were introduced as potential drugs for the treatment of schizophrenia. 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.

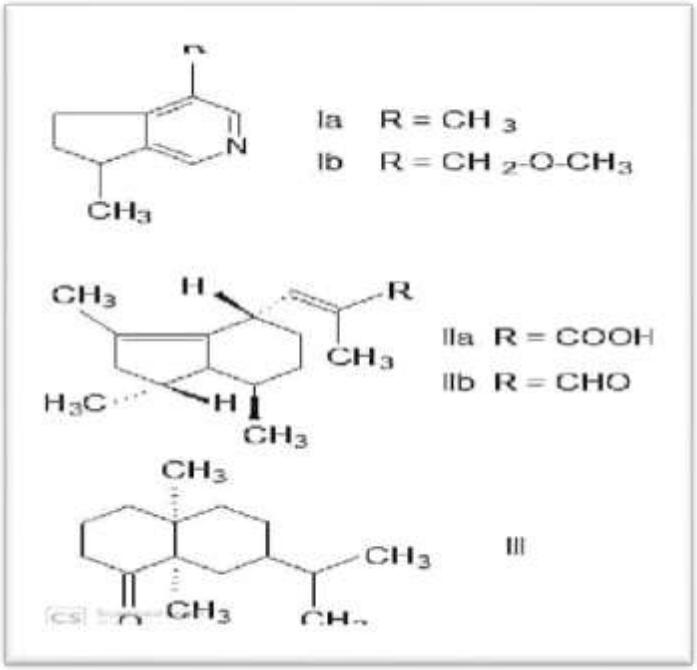

Figure 2: The structures of principal compounds present in volatile essential oil of Valeriana officinalis

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. Terpenes are characterized chemically as monoterpenes and sesquiterpenes. Valeric, isovaleric, valerenic, isovalerenic and acetoxyvalerenic acids, boranyl acetate, boranyl isovalerenate, 1-pinene, 1-comphene, 1borneol, 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 academic patients.

Valerenic acid (IIa) and its aldehyde valerenal (IIb) are monoterpenes which are pharmacologically active compound. 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 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. 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%. Valeranone (III) was tested as a medical drug in hyperkinetic. behavior disorders. 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. Thus, valerian may carry the sedative effects of anesthetics and other medications that act on GABA receptors and use of valerian before surgery may cause a valerianan aesthetic interaction.

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		

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-hydroxy isovaleric and âacetoxy-â-methylvaleric acid. 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 iso valeroxy hydroxy didrovaltrate. 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. 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. The main decomposition products of the valepotriates are the yellow colored baldrinals. Baldrinals are chemically reactive and may subsequently form polymers.

In vitro antioxidant studies

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, pH 7.0) using a Polytron homogenizer 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, pH 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.

General Preparations of Valerian Drug [81]

Valerian fluid extracts and tinctures are sold in alcohol or alcohol-free (glycerite) bases. Powdered valerian is available in capsule or tablet form, and also as a tea. Valerian root has a sharp odor, and to mask the scent valerian is often combined with other calming herbs, including passionflower (Passiflora in carnata), hops (Humulus lupulus), lemon balm (Melissa officinalis), skullcap (Scutellaria lateriflora), and kava (Piper methysticum). Kava has been associated with liver damage, so it is best avoided .

The chief constituent of Valerian is a yellowish-green to brownish-yellow oil which is present in the dried root varying from 0.5- 2% though an average yield rarely exceeds 0.8%. This variation in quantity is partly explained by location: a dry, stony soil, yielding a root richer in oil than one that is moist and fertile. The volatile oils that form the active ingredient are extremely pungent, somewhat reminiscent of well-matured cheese or wet dog. Valerian tea should not be prepared with boiling water, as this may drive off the lighter oils.

Preparations of valerian marketed as dietary supplements are made from its roots, rhizomes (underground stems), and stolon's (horizontal stems). Dried roots are prepared as teas or tinctures, and dried plant materials and extracts are put into capsules or incorporated into tablets. There is no scientific agreement as to the active constituents of valerian, and its activity may result from interactions among multiple constituents rather than any one compound or class of compounds. The content of volatile oils, including valerenic acids; the less volatile sesquiterpenes; or the valepotriates (esters of short-chain fatty acids) is sometimes used to standardize valerian extracts. As with most herbal preparations, many other compounds are also present. Valerian is sometimes combined with other botanicals. Because this fact sheet focuses on valerian as a single ingredient, only clinical studies evaluating valerian as a single agent are included**.**

Efficacy and Safety of Valerian Extracts Drug [82-104]

The clinical relevance of acute as well as chronic sleep disorders is oblivious: epidemiological data show that they affect approximately one-third of the adult population. Treatment is indicated in about 15% of these cases Insomnia, defined as in sufficient quantity or quality of sleep resulting in compromised daytime alertness and activity, is a common condition. It can result in serious adverse consequences, including attention and memory impairment, depression, falls, and perceived reduced quality of life to the most common treatments of insomnia belong drugs, this however bears some problems. Benzodiazepines and imidazopyridines offer only short-term relief, while data on their long-term efficacy are scarce. Both drug classes have significant adverse effects such as serious psychomotor symptoms, behavioral aberrations, memory impairment resulting in injuries, respiratory depression, rebound insomnia, and paradoxical agitation. Especially for benzodiazepines ,the potential for abuse is high. Therefore, the National Institutes of Health consensus conference strongly discouraged chronic treatment of insomnia with benzodiazepine in Sedating antihistamines, such as diphenhydramine, the active ingredient in most over-the-counter sleep aids, are associated with cognitive impairment, daytime drowsiness, and anticholinergic effects. There is no evidence-based data available on their efficacy improving insomnia or prolonging sleep. It therefore was recommended that they should be avoided in the elderly Finally,

antidepressants used for treating insomnia, such as trazodone, can produce dangerous and life-threatening adverse events due to their anticholinergic, cardiovascular, and neurologic actions. Herbal substances improving insomnia, such as valerian, hops, or passion flower, are well-known sleep aids. While marketed as food in the US, they are authorized or registered as medicines in Europe and many other regions, being used in self-medication and holding wide spread appeal, presumably because of their lower co stand higher range of safety when compared to chemically defined pharmaceutical .Among these, the roots of valerian (Valeriana officinalis L.) are the most familiar ones, especially in Europe. They improve the subjective experience of sleep when take nin the evening over a period of one or two weeks the constituents of valerian root include, among others, valepotriates (iridoids) and volatile oil, including monoterpenes and sesquiterpenes (valerenic acids). Commercially available extracts are free from valepotriates. Recommended daily doses of valerian root extracts are about 600mg, usually taken as capsules or tablets. Several controlled clinical trials with various valerian extracts are available, and, a meta-analysis on eighteen randomized placebo-controlled trails was published. Its qualitative results suggest that valerian would be effective for a subjective improvement of insomnia, although its effectiveness could not be demonstrated with quantitative or objective measurements. In a study conducted in cancer patients, an improvement in the primary variable, a sleep quality index based mainly on objective parameters, could not be demonstrated; however, fatigue and sleep problems were significantly improved, The clinical studies available show an excellent short-term tolerability, and from several decades of clinical use within the frame of pharmacovigilance systems no data quest owning its long-term safety have evolved, while prospective data are missing In contrast to classical sedatives, valerian extracts did not impair the ability to drive or to use machines, neither after single nor after repeated doses. Reports of putative adverse reactions are extremely rare and include one case of hepatic symptoms after prolonged treatment and one case of cardiac symptoms after discontinuation of a long-term treatment with very high doses, which were interpreted as a withdrawal reaction in both case reports, outcome was benign, causality was questionable ,and characteristics of the extract preparations were not provided. While the side effect profile therefore is benign, a potential for adverse drug interactions has been claimed by some reviews, while other reviews did not, so that are evaluation not the existing evidence is necessary.

fundamental use of Valerian drug [(105)]

Valerian is a versatile Ayurvedic remedy for a variety of ailments and diseases. It was given during World War I to soldiers suffering from battle shock. It has also been recommended for the relief of menstrual cramps and as a carminative, or preparation that relieves gas in the stomach and

intestines. Lotions made with valerian extract are said to soothe skin rashes and swollen joints. There is some disagreement among researchers about the efficacy of valerian as a tranquilizer and aid to sleep. While a team of Swiss researchers found a valerian/lemon balm combination to be significantly more effective than a placebo in inducing sleep, another group in the United States concluded that valerian is overrated as a sedative. Further research may help to settle the question, but multiple studies that are currently available are inconclusive. Following sections sequentially narrates basic uses of valerian:

Food Use: Valerian is not generally used as a food. Valerian is listed by the Council of Europe as a natural source of food flavoring. Previously, valerian has been listed as GRAS (Generally Recognized as Safe).

Medicinal Use: Valerian is used against sleeping disorders, restlessness and anxiety, and as a muscle relaxant and is often indicated as transition medication when discontinuing benzodiazepines. It has been recommended for epilepsy but that is not supported by research (although valproic acid-an analogue of one of Valerian's constituents, valeric acid is used as an anticonvulsant and mood-stabilizing drug). It has also been reported to cause agitation, headaches and night terrors in some individuals. This may be due to the fact that some people lack a digestive conversion property necessary to effectively break down Valerian. One study found that valerian tends to sedate the agitated person and stimulate the fatigued person, bringing about a balancing effect on the system.

Valerian is used for insomnia and other disorders and can be a useful alternative to benzodiazepine drugs. However more recent research has shown it to be ineffective in this use. A recent article states, "Most studies found no significant differences between valerian and placebo either in healthy individuals or in persons with general sleep disturbance or insomnia." In the United States Valerian is sold as a nutritional supplement. Therapeutic use has increased as dietary supplements have gained in popularity, especially after the Dietary Supplement Health and Education Act was passed in 1994. This law allowed the distribution of many agents as over-the-counter supplements, and therefore allowed them to bypass the regulatory requirements of the Food and Drug Administration (FDA). Under the US Preventative Services Task Force's (USPSTF) classification system for herbs, valerian was rated as probably safe and effective as a sleep aid, based on evidence from randomized clinical trials. In respect to its spasmolytic properties, it was rated possibly effective and probably safe, based on animal studies.

While valerian appears to be safe and possibly effective, the literature available in the English language evaluating this herb is limited due to small sample size, short study duration, and some

inconsistent results. Valerian's long-term safety has yet to be demonstrated, and therefore it should not be recommended for extended use for any indication. Valerian's main attribute may be that it serves as an alternative, with a low incidence of side effects, to synthetic sedative agents. When recommended, patients should be counseled about possible side effects and closely monitored during therapy.

CONCLUSION

This paper provides a systematic overview of the use of valerian for various disorders and it can be concluded that valerian is an herb sold as a dietary supplement throughout the world. It is a common ingredient in products promoted as mild sedatives and sleep aids for nervous tension and insomnia. It has been suggested for several conditions but has been most studied as a treatment for insomnia. Valerian may reduce the length of time it takes to fall asleep and may improve sleep quality with fewer adverse effects than commonly used prescription drugs. The chemical composition of valerian includes sesquiterpenes of the volatile oil (including valeric acid), iridoids (valepotriates), alkaloids, and free amino acids. Although the sesquiterpene components of the volatile oil are believed to be responsible for most of valerian's biologic effects, it is likely that all of the active constituents of valerian.

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