



Ingredients and Pharmaceuticals Uses of Valerian

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ABSTRACT

Introduction: Valerian plant contains effective material from volatile and essential oil including terpenes, aldehydes, ketones and phenyl propane derivatives which have little solubility in water. Stable and unstable compounds of this plant play a role in sedative effects and for this reason, their roots and rhizome extract are used as medical plant. Today, there are standard medicines in the form of tablet, drop and syrup which are consumed based on effective materials with recommended dose. Basically, valerian has no side effects and FDA considers no limitation for its use in foods.

Review on literature: studies on plant morphology and physiology shows that all three varieties of Valerian have short cylindrical rhizomes which used part in medicines and extracting its extract was done with similar methods in old and new medicine. Studies about pharmaceutical effects of this plant on human showed that it has considerable effect in reducing number of seizures in patients suffering from treatment-resistant epilepsy. It has similar therapeutic effects in reducing primary dysmenorrhea because of anti-convulsion effects. In rats, sedative and anti-anxiety effects of valerian were higher than Diazepam. Anti-convulsion effect of hydro-alcohol extract of roots and rhizome of valerian in mouse showed that this extract has not optimal therapeutic effect on clinical signs of major epilepsy but it prevents clinical signs of minor epilepsy. Valerian extract reduces number of vomiting caused by Copper Sulfate and epica in chicken and its effect on ileum of guinea pig depending on dose reduces contraction and their similar effects on testing liver and kidney of rat.

Discussion and conclusion: extract of valerian root and rhizome is identified as a pharmaceutics plant in old and new medicine. It is used as decoction in old medicine and today, it is used as tablet, syrup and drop. Studies of various researchers about effects of this herbal extract has verified it as an effective sedative for nervous system and muscles even comparing with chemical drugs like Mefnamic acid and Diazepam and it can be a good alternative for some sedatives.

KEYWORDS: Valerian; pharmaceutical plant; pharmaceutical uses; effective ingredients

INTRODUCTION

Today, pharmaceutical plants are important economic plants which are used in raw or processed form in traditional or modern medicine [19]. Valerian known as cat-grass is one of known pharmaceutics plants. Effective ingredients of valerian are essential or volatile oils. These materials are volatile and aromatic and contain terpenes, aldehydes, Ketones and esters (more than 90%) or derivatives of phenyl propane and ethanol but they slightly solve in water [16]. This plant has iridoid compounds which are permanent and decompose to other polymers. Its other ingredients include Sterizo-valerianic acid, valerianic acid, bornil acetate, valerianic. Stable and instable compounds have a role in sedation and soporific effects. This plant has used in treating mental pressures, fatigue, excessive intellectual work, chronic insomnia and it is used as a sedative. This plant is used in treating muscular cramps, irritated intestine syndrome, timpanists, neural headaches and anxiety. Anatoly valerian extract has anti-dandruff feature [23]. Valerian extract is prepared from rhizome and dried roots of valerian. Valeric acid in valerian extract by limiting GABA-Y-Amino butyric acid catabolizing enzymes increases its concentration. Increase in GABA concentration reduces neuron reactions and as a result, decreases anxiety and causes sedation [22]. Standard medicines in the form of tablet, drop and syrup from this plant are available which are used based on effective material with recommended value on drug label. Valerian use in pharmaceutics was without side effects and FDA has placed in foods. Its toxic effect is not determined yet but there is a report of its overdose as 20 times of pharmaceutical dose.

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LITERATURE REVIEW

Studies about valerian as a pharmaceuticals plant are typically based on three axes: a) studies about plant structure, pharmaceutical ingredients and extraction method; b) studies on effects of plant extract on animals like fish, guinea pig, mouse, chicken and etc; c) studies about effects of plant extract on human and comparing it with synthetic medicines.

A. morphology and ingredients

Valerian is a plant from valerian genus with scientific name *Valeriana officinalis* which is a permanent plant with large roots and short stem. Its stem has corners and its leaves are in opposite direction with comb cut [19]. It has three varieties called minor, *lotifolia* and *media*. Root has a short cylindrical rhizome. Different and cylindrical branches exit from rhizome with 1-15cm length and 2-5mm diameter. External parts of root are bright brown and its internal part is white. Different parts of plant used in pharmaceutical are root, rhizome and dried stolon [12]. This plant is sensitive to high salinity [19]. Using plants in therapy originates from long time ago. The skill of treating with plants has been developed in all nations and is now preserved, more or less, as traditional or popular therapy, commonly named popular medicine. *Valeriana officinalis*, which has been successfully used in traditional therapy, is accepted and represents an important medicinal raw material in contemporary medicine. Considering that clinical effects are not due to single chemical component, numerous scientists have concluded that a combination of valerian ingredients is responsible for its action. Dried root and rhizoma of *Valeriana officinalis* L in forms of different pharmaceutical formulations achieve antioxidative, cytoprotective and neuroprotective activity. Pharmaceutical preparations made of valerian root and rhizoma have multiple roles in treating disorders at the level of cardiovascular gastrointestinal and central nervous systems [2]. Valerian (*Valeriana officinalis* L.) is an important medicinal plant that is widely exploited for its roots and rhizomes which contain valepotriates and valerenic acids (with putative pharmacological activities). Thus root proliferation of valerian is very important. Some researchers were tiered to establish a practical tissue culture method for rapid and large-scale induction of *V. officinalis* L. roots with high capacity for production of valerian phytomedicine. Explants derived from leaves, petioles and root segments (both basal and apical) of four months aged plantlets were cultured on MS basal medium supplemented with different concentrations (0.625-5 μ M) of auxin and cytokinin hormones. Then accumulation of valerenic acids and valepotriates in developed root cultures was studied to find the best yielding conditions. Maximum valerenic acids (0.84%) and valepotriates contents (7.41%) were quantified in roots developed on petiole explants and in roots formed on root basal segments in medium supplemented with 1.25 μ M and 0.625 μ M indole-3-acetic acid respectively. These values were significantly ($P < 0.05$) higher than those in roots from basal and apical root segments without plant growth regulators as control. The highest average number (29.00) of directly formed roots developed on leaf explants in media supplemented with 5 μ M α -naphthalene acetic acid. Also maximum number of indirectly developed roots (30.05) was observed on root apical segments in media containing 2.5 μ M α -naphthalene acetic acid. These results suggest that besides the applied plant growth regulators the type of primary explant is also relevant for biosynthetic capacity of these metabolites in root cultures [20]. The essential oils isolated from roots of 24-month-old field grown valerian (*Valeriana sisymbriifolium*) and hairy root cultures were analysed by GC and GC-mass spectrometry. Transformed root cultures of valerian were established by inoculation of sterile plantlets grown with *Agrobacterium rhizogenes* strain R1601 [6]. Qualitative and quantitative differences were found between the essential oils from the non-transformed roots and those from the hairy roots. There are some major differences in the hairy root culture and field grown valerian essential oils especially in valeranone, valerenal, valerenyl acetate, valerenic acid and valerenol compounds. The essential oils from the plant roots were obtained in a yield of 13.2% bornyl -Pinene 7.50 compared with that from acetate valerenal 12.7% transformed root culture identified as kessyl alcohol (10.10%) and kessyl acetate (9.90%) as the main constituents. Inoculation with *Agrobacterium rhizogenes* strain R1601 was found to be an effective means of inducing hairy root formation on *Valeriana sisymbriifolium* [5]. A dichloromethane extract of the roots of *Valeriana sisymbriifolia* Vahl. afforded a new valepotriate, I- α -aceisovaltrate and a new valepotriatehydrine, acetoxidesiovaleroxy-1- α -acetoxo-isovaleroxy isovaltratehydrine together with a known compound, valtrate. Structural assignments of the compounds were based on spectroscopic methods (UV, IR, MS, 1 H-NMR and 13 C-NMR). [1] The paper presents results concerning ultrasonically assisted extraction of bioactive compounds from roots of valerian. Pulsed ultrasonic field was applied. The investigation was accomplished by varying irradiation time and sonic power. The results were compared with classical (silent) extraction. The study included evaluation of the coefficient of rehydration, yield of extraction, dry matter content in extract and residue, and unit energy consumption. The utilization of pulsed ultrasound was proved to be a more efficient technique than the classical method for extraction of bioactive components from dried valerian roots [8].

Another study conducted in the research farm of institute of medicinal plants through a factorial experiment based on a randomized complete blocks design with three replications. The bio-fertilizers using had a significant effect on the most of studied quantity and quality parameters. Although the bio-fertilizers using had a negative effect on the amount of valernic acid, because of the increasing of root dry weight, it led to a significant rising on yield of valerianic acid per hectare [15].

B. Studies on human

In studies on patients suffering from resistive to treatment epilepsy, which is known as a therapeutic problem for patients and physicians and because valerian has used as an anti-anxiety, insomnia and anti-convulsion treatment, in a study on 13 patients suffering from epilepsy, it becomes clear that full extract of valerian plant has acceptable effect on epilepsy but it is recommended that more studies conducted in future [10]. In a clinical study in three blinded random design on 210 individuals of Arak Medical Sciences University, samples were randomly placed on ginger (250mg capsule), valerian (350mg) and placebo (250mg), intensity of premenstrual pain was measured using Wong-Baker tool. Findings showed that there was significant difference in pain intensity between control and study group and obtained results showed that ginger and valerian are effective in reducing primary dysmenorrheal but valerian effect is more tangible [2].

In a clinical study for comparing therapeutic effect of valerian root and mefenamic acid on improving premenstrual pain in two colleges of Hamedan (in two 54 subjects group), results did not show significant difference after two months. Therefore, this study shows that valerian can be used instead of mefenamic acid [9]. In a clinical double-blinded study on 100 students of Zanzan Azan University in 2008-2009 which investigated effect of valerian root on intensity of dysmenorrheal, subjects were placed into two study and control group. Study group received capsule 255mg valerian root and control group received capsules containing starch. Results showed that valerian can reduce dysmenorrheal pain which seems that it is because of anti-contraction effects [14]. Anxiety is danger feeling in an individual who has threatened by a danger. Anxiety is related with vain and different factors are involved in it. In a study, some coated tablets of moldavic calamint aerial organs and valerian root with percolation method using ethanol 70% was extracted and after concentration in vacuum device, these concentrates entered in calcic tri-phosphat absorbing bed and tablets were prepared by spray method and used as sedative [20].

C. Studies on animals

In a study on gold fish, regarding wide scale application of analgesia in them in aquacultures and problems of medicines, relying on benefits of valerian 2-3-4mg/l valerian along with other plants was prepared and tested on 4 groups of golden fish with same weight and length. Results showed that among four plants valerian, moldavic calamint, poppy and corn-poppy, two latter had no effects and valerian has best effects in analgesia [21].

In a research for comparing sedative and anti-anxiety effects of valerian and diazepam on rat, first its rhizome was extracted with chloroform: methanol (70: 30) and then was undergone phyto-chemical methods to prepare total fraction of n-hexane by GC-MS. Selecting two female groups of Vistar rat, valerian extract was infused to one group with doses 100-200-400 mg/kg and diazepam to other group with dose 1.2mg. Pharmaceutics results showed that valerian extract with highest response in dose 400mg/kg has better sedative and anti-anxiety effects [19]. In a study about anti-convulsion effect of hydro-alcohol extract of valerian in mouse and its relation with nitric oxide, effect of valerian extract in phantilen tetrazole and electroshock was studied. Results showed that extract had no effect in electroshock model but extract can be useful in preventing symptoms of minor epilepsy which is a part of anti-convulsion mechanism of plant in relation with nitric oxide; therefore, it has no effect on major epilepsy [10]. In a study about anti-nausea effect of valerian extract in chicken with the aim of documenting existing reports in traditional medicine which has recommended valerian in treating intestine and colic spasms and neural states as a sedative, effect of aqueous-alcohol extract of valerian with CuS (600mg/kg) and Epica (600mg/kg) was studied. Results showed that infusing intra-chest extract in doses 7, 28 and 49mg/kg has considerable effect in preventing nausea which decreases number of vomiting 65.70 and 79.88%, respectively which is considerable and traditional medicine reports confirm it [6].

In a study about effect of valerian extract on contraction of ileum in guinea pig, after killing 5 male pig, 6 parts of ileum with 2-3cm length were cut and placed in normal tirod and carbogen gas in 37 C and intestine contractions were recorded in physiographic. After that valerine extract was added in different concentration to tissue bath and contractions were recorded. 7 responses of each tissue were gathered. Findings showed that valerian root extract with concentration 50, 250, 150, 100 and 500mg/ml reduced contraction of ileum in guinea pig which percent of reduction was 34.5%, 36.07, 47.53, 56.42 and 76.22%, respectively. This study showed that valerian extract reduces ileum contraction in guinea pig in dose-dependent form [3].

In a study on effect of hydro-alcohol valerian extract on number and sizes of neurons in core Rafe -Mangos in adult rat in Yasuj Medical Sciences University in 2009, 40 Vista rats were used with 170-250g weight and they were randomly assigned in 4 groups including one control and three study groups. Hydro-alcohol valerian extract was given to study rats with doses 300, 400 and 600 mg/kg and distilled water was given to control group. After one month histological changes in neurons were studied with optical microscope. Findings showed no significant difference between numbers of cores in study group but mean diameter of neurons were changes. Nucleus of study group was brighter than control group. Therefore, this extract had no effect on number of

neurons but has effects on their size which shows increase in serotonin [18]. In a research on effect of valerian and *Echium amocnum* on liver and kidney function in rat, percolated extract of these plants with doses 100 and 200 mg/kg were orally given to rats for 7 days and in day 8, blood samples were prepared and biochemical studies were done and results were compared with control group. Results showed that change in AST and ALT enzymes and ALK p showed significant difference with control group and infusing ALK p to control group showed same result. Kidney function test including BUN and keratinin showed no increase after oral infusion with dose 100mg/kg. This research showed that extract of *Echium amocnum* has higher toxic effect for liver which is considerable in higher doses [23].

The effects of feeding levels of *Valeriana officinalis* on the performance, behavior and physiologic parameters of Japanese quails (*Coturnix coturnix japonica*) in the laying periods were evaluated. In the laying period, 192 quails were distributed in a randomized block design according to four nutrition plans (control, 250, 500 and 750mg of valerian/kg of ration) with eight replicates and six birds per cage. Performance (feed intake, egg production, feed conversion per dozen eggs, feed conversion per egg kg, egg weight and viability), behavior (body injury, tonic immobility and focal observation) and physiological parameters (heterophil/lymphocyte ratio and corticosterone blood plasma) were evaluated. The tested valeriana levels did not affect the performance, behavior or physiological parameters of Japanese quails in the laying phases [13]. In this study, the anticonvulsant activity of methanolic extract of the valerian were investigated in mice. The results indicated that valerian extract may be effective on generalized tonic, clonic and tonic-clonic seizures and the dose of 50 mg/kg was enough to produce effective concentration for anticonvulsive activity of the extract in mice [7].

DISCUSSION AND CONCLUSION

Valerian is a pharmaceutical plant which had various uses in traditional medicine. Today, it is available in different forms like tablet, syrup and etc. results of studies on human and animals indicate positive effects of valerian root and rhizome extract and in cases that studies were comparison with an industrial drug like Diazepam or mephnamic acid, its higher efficacy was confirmed and because there is no side effects, it seems that results show that this plant was widely used in traditional medicine and today, is used widely in new forms and can be suitable alternative for industrial drugs with similar effects. It is suggested that clinical researchers study effects of this plant on certain groups like children.

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