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Review Article

A COMPREHENSIVE REVIEW ON TAGARA (*Valeriana wallichii*)

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Abstract

Valeriana wallichii (Tagara) is a perennial plant of Valerianeaceae family growing on higher altitude. Rasa, Guna, Vipaka, Veerya, Prabhava and Dosha karma of this plant is well established in Ayurvedic textbooks like Charaka Samhita, Susruta samhita and Bhava prakasha Nighantu etc along with its medicinal properties. Experimental studies proved its activity on anxiety, stress, sleep, depression, performance, alertness, GABBA receptor, Orofacial dyskinesia and blood pressure along with toxicity on liver. Hence an effort was taken to study about the herb.

Key words: *Valeriana wallichii*; Tagara; GABBA; Doshas.

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INTRODUCTION

Valeriana wallichii belongs to Valerianeaceae family, is a hairy perennial herb, growing in temperate Himalayas from Kashmir to Bhutan and Khasia hills up to an altitude of 3,000 m, rhizomes dug in autumn.[1] *Valeriana wallichii* has been used in the Ayurvedic system of medicine for centuries. Traditionally it is also known as Tagara, Nata, Vakra, Kutila, Nahusha, Vinamra, Kuncita, Barhista, Nrpam, Sata, Dadruhasta, Bahram, Parthiva, Rajharshana, Chatra, Deen, Jiwh, Munindhudha,[2] Kalanusarika, Kalanusari, Akrahavam Cheen, Katu, Mahoraga,[3] Karhaat, Swasna, Vishpushka.[4] Acharya Charaka mentioned this plant under Sheeta Prasamana mahakashaya and Tiktaskhandha[5] while Susruta described in Eladi gana.[6] A perennial Leafy slightly hairy, tufted herb, up to 45 cm in height. Rootstalk is thick, horizontal, long petioled, deeply cordate and ovate, usually toothed or sinuate, 2.5-2.75 cm in diameter, cauline leaves only a few, much smaller, entire or pinnate, often crowded stipules nil. Flowers of valerian are often deciduous, white to ting with a pink, in terminal corymbs and unisexual, male and female in different plants.[7] There are two classical varieties of Tagara, they are Tagara and Pindatagara.[8] Their root has been used in the form of powder in a dose of 1-3 g.[1]

The roots of tagara contain Valerianic acid, Valerosidatum (iso-valery) glycoside, Valepotriates (a derivative of iridoid or monoterpene), which is used in sedative and tranquilizer preparation. A sweet smelling essential oil is extracted from the root and dried rhizome of plant. The oil contains sequiterpena, valeriac acid, terpene alcohol, bornyl esters, of formic acid, camphene, terineol and two unidentified alcohol.[9]

The present study aim to collect literature mentioned in ancient textbook backed with recent research evidences. For this known database like pubmed, medline were selected for studies from 1988 to 2010. Mainly clinical and experimental studies on *Valeriana wallichii* in English language were considered.

Pharmacodyanamic Properties

Pharmacodynamic properties (Rasadi gunas) have been mentioned by Ayurvedic acharyas. (Table 1)

Karma (Action)

Medya (brain tonic), Vedanasthapana (analgesic), Aksepahara (anticonvulsant), Dipana (appetizer), Shulprasamana, Hridaya (cardio tonic) and Yakrduttejaka (hepatoprotective), Kaphaghna (mucolytic), Swashara (bronchodilator), Mutrajana (diuretic), Vajikarna (aphoristic), Arttavajanna, Vishagna (antidote), Balya (tonic), Kusta (antileprotic), Jwaragna (antipyretic), Varna Ropana (wound healer).[1]

Roga-haratwa (Thearpeutic indication)

Sandhivatta (osteoarthritis), Agnimandya (appetite depressor), Yakrittasotha (hepatomegaly), Kamla (jaundice), Plihodra (splenomegaly), Jalodara (ascites), Hriddorbalya (cardio tonic), Jirnajawar (chronic fever), Vishamjwara (malaria),[1] Netra Roga (eye disorder), Drstidosha (eye disease), Unamada (insanity),[10] Apasmara (epilepsy), Mastiskavikara (mental disorder), Smiritivinasa (memory loss), Siroroga (headache).[12]

Relevant Classical Reference

- The decoction prepared from haridra (*Curcuma longa* Linn.), vidanga (*Embelia ribes* Burm.), tagara and daruharidra (*Berberis aristata* DC.) is used in the management of Kaphaja premeha.[15]

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Table 1: Pharmacological Properties of *Valeriana wallichii*

S.No	Nighantu	Rasa	Virya	Vipaka	Guna	Doshaghnata	Properties
1	P.N[1]	Tikta, Katu	-	-	-	-	-
2	R.N[10]	Tikta	Sheeta	-	-	-	Pathya
3	S.N[11]	-	-	-	Laghu	Kapha, Pitta	Sugandhi Rasayana
4	D.N[8]	Kashaya	Ushna	-	Snigdha	Tridosha	-
5	B.P.N[12]	Swadu	Ushna	-	Snigdha,Laghu	Tridosha	-
6	K.N[13]	Tikta, Katu, Madhura	Ushna	-	Snigdha,Laghu	Tridosha	-
7	M.P.N[14]	Swadu	Ushna	-	Snigdha,Laghu	Tridosha	-
10	N.A[7]	Madhur, Kashaya Tikta	Ushna	Katu	-	Tridosha	-

(P.N- Priya Nighantu , R.N- Raj Nighantu ,S.N- Sodhala Nighantu , D.N-Dhanwantri Nighantu,B.P.N-Bhava prakasha Nighantu, K.N- Kaiydeva Nighantu , M.P.N-Madan pal Nighantu ,N.A- Nighantu Adarsa)

- An ointment is used in headache, chest and shoulder pain of yakshma patient, prepared from satpuspha (*Anethum sowa*), yasti (*Glycyrrhiza gabra* Linn.), kushta (*Saussura lappa* Linn.), tagar and chandana (*Santalum album* Linn.).[16]
- Used as vishagna, an important constituents in Mritjeevanagada, Mahagandhahastiagada, Masayadi yoga, Kutajadi pradhaman nasaya.[17]

Systemic review of available research literature shows that there are only few experimental and clinical studies which report its therapeutic potential are summarized as follows.

Anxiolytic and Antidepressant Effects

This study evaluates CNS-related effects of different valerian extracts using behavioral paradigms (mice and rats). Following oral administration two commercially available preparations (extraction solvents: 45% methanol m/m and 70% ethanol v/v), a 35% ethanolic v/v extract and a refined extract derived from it (patented special extract phytofin Valerian 368) were tested for sedative (locomotors activity, ether-induced anaesthesia) and anxiolytic (elevated plus maze) activity. Up to maximum dosages of 500 or 1000 mg/kg body weight none of the valerian extracts displayed sedative effects. Neither spontaneous activity was reduced nor was the duration of ether-induced narcosis prolonged. In contrast, results obtained in the elevated plus maze test revealed a pronounced anxiolytic effect of the 45% methanolic and 35% ethanolic extract as well as of phytofin Valerian 368 in a dose range of 100-500 mg/kg bw. Additionally and different from its primary extract (35% ethanolic extract) phytofin Valerian 368 showed antidepressant activity in the forced swimming test after subacute treatment. Myorelaxant effects were not observed in dosages up to 1000 mg/kg body weight. Due to these findings it is proposed that not sedative but anxiolytic and antidepressant activity, which was elaborated particularly in the special extract phytofin Valerian 368, considerably contribute to the sleep-enhancing properties of valerian.[18]

Effect on sleep

A study was conducted on 121 adults with sleep disturbance of at least four weeks duration in which participants were treated with 600 mg of valerian or placebo for four weeks. No improvement was noted initially, however, after two weeks of treatment, significant global improvement was observed in the valerian group but without meaningful

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changes in other measures. After four week, significant improvement was noted on all measures of sleep and mood in favour of valerian.[19]

Effect on performance & alertness

In a double blind study eighty healthy subjects were treated with valerian syrup, tablets containing valerian and hops, flunitrazepam or a placebo. Assessment included self-rating scale of well being and objective of cognitive and psychomotor performance, as well as evaluation of the tolerance. On the morning following treatment, impaired performance was observed in flunitrazepam group only on both subjective and objective ratings, where as those receiving valerian formulation noted feeling better, more alert and active.[20]

Effect on stress

In a double blind study forty healthy volunteers received either 100 mg of valerian extract, 209 mg of propanolol, or a combination of both. In contrast to propanolol, valerian was not associated with reduction in physiological arousal under stress but it did show improvement in anxiety and mood.[21]

Effect on GABAA receptors

1. The modulation of chloride currents through GABAA receptors (IGABA) by Valerian extracts was investigated using the two-microelectrode voltage clamp technique. Apolar extracts induced a significant enhancement of IGABA, whereas polar extracts showed no effect. These results were confirmed by fractionating a highly active ethyl acetate extract: again fractions with high contents of valerenic acid exhibited strong receptor activation. In addition, removal of sesquiterpenic acids from the ethyl acetate extract led to a loss of I (GABA) enhancement. In conclusion, our data show that the extent of GABAA receptor modulation by Valerian extracts is related to the content of valerenic acid.[22]
2. To analyze the molecular basis of VA action GABA (A) receptors with 13 different subunit compositions in Xenopus oocytes and measured I (GABA) using the two-microelectrode voltage-clamp technique. Only channels incorporating beta (2) or beta (3) subunits were stimulated by VA. Replacing beta (2/3) by beta (1) drastically reduced the sensitivity of the resulting GABA (A) channels. The stimulatory effect of VA on alpha (1) beta (2) receptors was substantially reduced by the point mutation beta (2N265S) (known to inhibit loreclezole action). Mutating the corresponding residue of beta (1) [beta (1S290N)] induced VA sensitivity in alpha (1) beta (1S290N) comparable to alpha (1) beta (2) receptors. Modulation of I (GABA) was not significantly dependent on incorporation of alpha (1), alpha (2), alpha (3) or alpha (5) subunits. VA displayed a significantly lower efficiency on channels incorporating alpha (4) subunits. I (GABA) modulation by VA was not gamma subunit dependent and not inhibited by flumazenil (1 microM). VA shifted the GABA concentration-effect curve towards lower GABA concentrations and elicited substantial currents through GABA (A) channels at > or = 30 microM. At higher concentrations (> or = 100 microM), VA and acetoxy-VA inhibit I (GABA). A possible open channel block mechanism is discussed. In summary, VA was identified as a subunit specific allosteric modulator of GABA(A) receptors that is likely to interact with the loreclezole binding pocket.[23]

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Effect on Orofacial Dyskinesia

Chronic treatment with classical neuroleptics in humans can produce a serious side effect, known as tardive dyskinesia (TD). Adult male rats were treated during 12 weeks with haloperidol decanoate (38 mg/kg, i.m., each 28 days) and with Valerian (in the drinking water). Vacuous chewing movements (VCMs), locomotor activity and plus maze performance were evaluated. Haloperidol treatment produced VCM in 40% of the treated rats and the concomitant treatment with Valerian did not alter either prevalence or intensity of VCMs. The treatment with Valerian increased the percentage of the time spent on open arm and the number of entries into open arm in the plus maze test. Furthermore, the treatment with haloperidol and/or Valerian decreased the locomotor activity in the open field test. Haloperidol treatment significantly decreased [(3)H]-dopamine uptake in striatal slices and Valerian was not able to prevent this effect. Taken together, data suggest a mechanism involving the reduction of dopamine transport in the maintenance of chronic VCMs in rats. Furthermore, chronic treatment with Valerian seems not produce any oxidative damage to central nervous system (CNS), but it also seems to be devoid of action to prevent VCM, at least in the dose used in this study.[24]

Liver toxicity

In a case series, four patients taking proprietary product containing multiple ingredient including valerian & skullcap, developed liver changes.[25]

Developmental toxicity

Female rats were orally dosed with a valerian extract in 45% ethanol (supplied by MediHerb) daily on either gestation days (GD) 1-8 or 8-15. On GD 20, rats were sacrificed and fetuses, placentae and ovaries collected. The fetuses were weighed and examined for external malformations. No signs of maternal toxicity were evident. Results indicated that valerian had no adverse effects on fertility or fetal development. Valerian induced toxicity when GD 10.5 embryos were cultured for 26h in rat serum to which 6 microl/ml of the extract was added. The results of the present preliminary study showed that consumption of up to 65 times the human dose of the valerian extract supplied by Mediherb did not have an adverse reproductive outcome in rats. This may be a result of low pH of the extract removing the potentially cytotoxic epoxide moieties. However, consumption of other preparations of valerian, particularly if they contained considerable levels of valepotriates could have a very different outcome.[26]

Antispasmodic and blood pressure lowering effects

Crude extract of *Valeriana wallichii* rhizome (Vw.Cr) and its fractions were studied for possible antispasmodic and blood pressure lowering activities to rationalize some of the folkloric uses. In rabbit jejunum preparations, Vw.Cr (0.1-3.0 mg/mL) caused relaxation of spontaneous contractions. When tested against high K(+) (80 mM)-induced contractions it produced weak inhibitory effect, while caused complete relaxation of the contractions induced by low K(+) (20 mM). In the presence of glibenclamide (3 microM), the inhibitory effect of low K(+) was shifted to the right, similar to that produced by cromakalim while, verapamil caused no differentiation in its inhibitory effect against low and high K(+)-induced contractions. In guinea pig ileum, the plant extract produced similar results as in rabbit jejunum. Intravenous administration of Vw.Cr, produced fall in arterial blood pressure in normotensive anaesthetized rats and this effect was partially blocked by glibenclamide. In rabbit aortic preparations, plant extract also caused selective and glibenclamide-sensitive relaxation of low K(+) (20 mM)-induced

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contractions. Activity-directed fractionation studies revealed that the observed activity was distributed both in the chloroform and aqueous fractions. These results indicate that the antispasmodic and hypotensive effects of *Valeriana wallichii* are mediated possibly through K(ATP) channel activation, which justify its use in gastrointestinal and cardiovascular disorder.[27]

CONCLUSION

Valeriana wallichii (Tagara) is used in Indian traditional system of medicine due to various medicinal properties. Recent researches suggest that it exhibits various properties like anxiolytic activity, anti stress activity, antidepressant activity, antispasmodic activity, hypotensive effect, sleep inducer activity and hepatotoxic activity. These evidences validate the ancient claim of Ayurveda regarding therapeutic potential of *Valeriana wallichii*. But more studies are required for further validation in replication of result.

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