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# Comparative Study of Sedative and Anxiolytic Effects of Herbal Extracts of Hypericum perforatum with Nardostachys jatamansi in Rats

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***Abstract***

***Background*:** Nardostachys and hypericum due to the effects of sedation, anticonvulsant, analgesic and anti-depressants has especial place in traditional medicine. Principal component and the alkaloid extract of valerian and isovalerate, valeric acid and the extract of hypericum is hypersin and hyperforin.

***Materials and Methods*:** We conducted this study, valerian rhizome by chloroform: methanol (70:30) was extracted in order to obtain total extract produced the N-hexane and studied chemically have been took by Gc-Ms. Hydro-alcoholic extract of aerial valerian tea was prepared for study. In order to study the comparative effects of soothing extracts of valerian and hypericum in different groups of female rat extract of valerian with doses of 100 mg/kg, 200 mg/kg, 400 mg/kg, and extracts of hypericum with a dose of 250 mg/kg, 500 mg/kg and DMSO (control) with the same volume of 15 minutes prior to the assessment of sedative and sleep (sleep duration induced with ketamine dose and 40 mg/kg were injected intraperitoneally).

***Results*:** The results indicate a significant increase in sleep time induced by ketamine in the treatment groups with high and low doses of valerian extracts and the hypericum is significant at the 0.01 level.

***Conclusion*:** The results show that the extract of valerian in the dose of 200 mg/kg in compress of dose of hypericum 500 mg/kg contains the significant anesthetic effects.



## Introduction

Today, herbs contain an important part of traditional medicine in many countries. It also has therapeutic value and has a special place in new approaches. In this study attempted to understand what are sedative and anesthetic effects of valerian extracts and Raei flowers. Valerian with the scientific name *Nardostachys jatamansi* belongs to the family of Valerians is known to cat grass [1]. A lot of compounds in the extract of this plant have been identified; most of them can be noted to valproate, iso valproates and didro valproate. The sedative effects of valerian are compared to the volatile oils include valerenal, valerenic acid [2, 3]. In 2001, so crystals suggested in their comparisons that the administration prolonged jatamansi has fewer side effects than benzodiazepines. According to recent studies conducted on brain ischemia, this plant known as GABA agonists gamma amino butyric acid receptor biochemical studies show that the enzyme responsible for valerenic acid catabolism is GABA inhibition and increases GABA concentrations in brain tissue [4]. GABA concentration in brain nuclei of brain activity and thereby reduce the sedative effects [5, 6]. The St. John's wrot or perforatum plant name that is known in Persian as hypericum (Raei) flowers [7]. Chemical compounds in the extract of this plant have been identified that contains of flavonoids and proanthocyanidins, neftodyantron and biflavone and oils and volatile. Recent studies in vitro inhibition of Mono Amino Oxidase (MAO) by compounds in extracts of this plant suggests that its inhibitory effect on MAO-A is more than MAO-B containing of hyperforin in this plant lead to inhibition of resorption of serotonin and dopamine, and norepinephrine [6, 7]. Chronic administration of hypericum extract has significant effect on negative regulation of beta receptors, serotonin receptors adrenergic cortex and upregulated in animal models and Rat. Effects that were seen in vitro is the connection with the use of sigma receptors Hypercin and binding to GABA receptors using flower extracts of Hypericum extracts in the presence as well-producing Interleukin-6 (IL-6) in one study after oral administration of hydro alcoholic extract significant relaxation was observed in rat [8]. The purpose of this study is to know any more sedative effects of valerian extracts of hypericum flowers as compared to the standard depressant drug.

## Materials and Methods

In this research study, 49 Wister rats weighing 200±20 gram of the race with about 12 weeks of age were used for laboratory work. Mice in the animal room and the standard conditions with ambient temperature 21-23ºC and 70% relative humidity and 12 h light-dark cycle and

were kept 12 h light and fed standard rat pellets Ad libitum method (in the animals are provided food to 24) was used and mice were given plenty of water. For providing of the extract from the rhizome of valerian for 500 grams of dried herb and Raei flower extract prepared from dried stems and leaves of Hypericum plant for 1000 gr we powdered it inside the mixture of chloroform: methanol (70:30) and then the mixture soak for at least 24 hours under vacuum pressure inside the rotary machine operator, removing the solvent to crude extracts have been obtained.

The crude extract obtained was dissolved in hot methanol and the lowest temperature in the freezer to -15ºC and brought to the flat rate to fat-free extracts have been obtained. In order to dehydration defat extract, dry dichloromethane solution with the magnesium sulfate and removing the solvent in rotary machine operator under vacuum until purified extracts have been obtained. The resulting amount of valerian extract in order to identifying valproate in N-hexane was riling length of 2 hours till the soluble material to be separate in N-hexane. Then again, throwing the solvent and by the Gc-Ms analysis was distinguished. Photo chemical analysis showed that the soluble material (DNA) is a component of the extract containing more than 15 parts in N-hexane. The majority of them can be the compounds of 9-Aristolen-1-alpha-ol (31%), valerenic acid (26.5%) and valerenal (13%). In order to study the comparative effects of palliative and anesthesia valerian extracts and flower Hypericum rats randomly divided in 7 groups of 7. The first group valerian extracts with a dose of 100 mg/kg intraperitoneally, second group of valerian extract with a dose of 200 mg/kg intraperitoneally, third group valerian extract with a dose of 400 mg/kg intraperitoneally, fourth group Hypericum extract with a dose of 250 mg/kg intraperitoneally, fifth group Hypericum extract with a dose of 500 mg/kg intraperitoneally and to six group (DMSO) was administered intraperitoneally at the same volume and nothing was administered to seven groups. In this section, the aim was to assess the analgesic efficacy of the drug, for this case 30 minutes after administration of this drug, ketamine with dose of 40 mg/kg was administered intraperitoneally in every 7 groups. Immediately after administration of ketamine the periods when the animal loses correction reflex (induction time) and periods when the animal after induction of anesthesia again finds reflex correction (sleeping time) was calculated according to second. Results of these tests using ANOVA and Tukey test were analyzed. SPSS-18 were used for the result.

## Results

According to the diagram with a dose of 200 mg/kg valerian tea has less induction time to Hypericum, and the difference was statistically significant ($p$=0.001) and also according to the chart, valerian with dose of 200 mg/kg has more sleeping time to Hypericum and the difference was statistically significant ($p$=0.001).

According to the chart with dose of 200 mg/kg *N. jatamansi* has less induction time than *H. Perforatum* and statistically the difference of all was significant and $p$<0.01 According to the chart with dose of 200 mg/kg *N. jatamansi* has more sleeping time than *H. Perforatum* and statistically differences were all significant $p$<0.01.

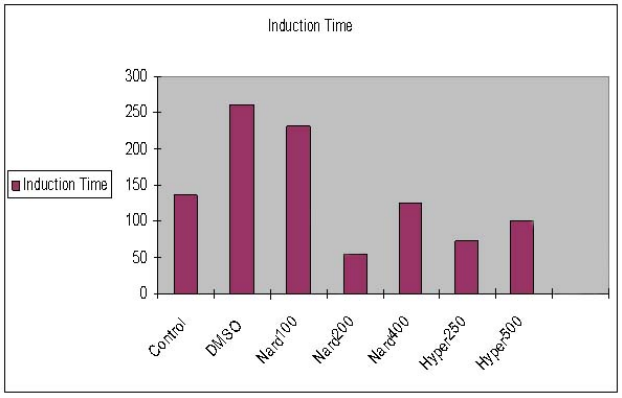


**Figure 1.** Average induction time data in the study groups

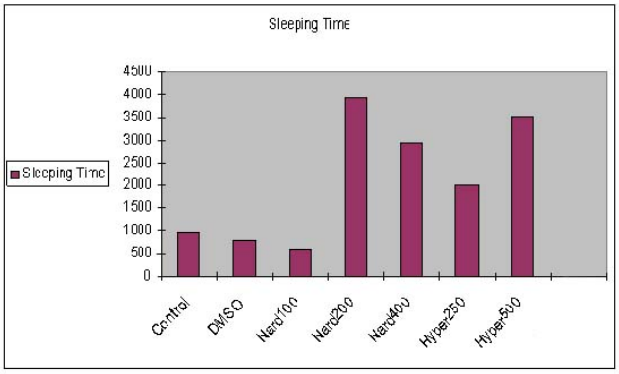


**Figure 2.** Average sleeping time data in the study groups

## Discussion

In this research palliative effect of valerian extracts and flowers in compress with the diazepam was effective and high chemical consumption and the results of this research showed that valerian with dose of 200 mg/kg has less time induction and more sleeping time to diazepam and Raei flower and the difference was statistically significant. With the expending of general admission to herbal drugs, todays have been taken many researchers upon different plants such as Raei flower and valerian, and it can be predictable that because of different affects of chemical drugs the herbals have important and majority roll of chemotherapy.

According to research reported in several valerian compounds isolated and identified, that we can mentioned to major identified compounds such as: 1-9-Aristolen-1-alpha-ol (31%), 2-valerenal (13%), 3-valerenic acid (26%). Also Kumar et al. in their research on the effects of hypericum perforatum therapy in behavioral and biochemical changes caused interdiction available showed

that this plant has relatively little activity in the prevention of these changes [9].

This important finding was that the antidepressant activities of sigma receptors are related to synthetic drugs and are located in the limbic system. Suggested that the sigma receptors, glutamate receptors of N-Methyl D-Aspartate that is very important route for the anti-depressants are considered regulate [10]. Raffa et al. in their research activities in palliative hydroalcoholic extract of hypericum perforatum in rats found that none of the components isolated from the extract have similar activity to hydro-alcoholic extract [11]. Other compounds in this N-hexane fraction, which was separated by gas chromatography and data on crime for them, suggest chemical buildings that even not mentioned [12, 13]. Teufel and Glitz showed an increase (up-regulation) for serotonin receptors after long-term-$HT_1A_5$ and-$HT_2A_5$ extract in rats, similar expression levels of these receptors is a synthetic antidepressant [14]. According to recent studies conducted on brain ischemia, this plant known as gamma-amino-butyric acid (GABA) [15]. *N. jatamansi* is used to treat epilepsy, hysteria, syncope, mental weakness and used as depressant. The ethanol extract of *N. jatamansi* rhizomes used as hepatoprotective agents and considerably increased the seizure threshold in the experimental model of generalized tonic-clonic seizures [16]. *N. jata*mansi has been demonstrated to protect against acute restraint and cold stress induced elevation in plasma corticosterone, increase in adrenal and spleen weights and gastric ulceration. These findings were associated with a reversal of the stress-induced elevation of lipid peroxidase and NO levels and decrease in catalase activity in the brain and therefore the anti-stress effect of *N. jatamansi* was attributed to its anti-oxidant properties. This study provides preliminary evidence for the protective effect of NJE in chronic stress [17]. Donovan results indicate that although a modest increase was observed in the alprazolam $C_{max}$ (the $C_{max}$ is often measured in an effort to show bioequivalence between a generic and innovator drug product)typical doses of valerian are unlikely to produce clinically significant effects on the disposition of medications dependent on the CYP2D6 or CYP3A4 pathways of metabolism [18]. Della Loggia with studies on valerian extract, illustrate that the root and rhizome extract of *N. jatamansi* contains of weakening effects on mouse brain [19]. Hazel Hoff showed that iso valproate rate and valproate rate in the *N. jatamansi* lead to relax the muscle cells [20]. Mihaela 's article suggested that given the long-term *N. jatamansi* has fewer side effects of benzodiazepines [21]. These results confirmed the importance of serotonin in the mechanism of antidepressant action of St. Johns wort. Keahler et al. [6] propose that the mono-amine and glutamate in sculpts synaptic consequently up take inhibition by Hyperforin is the mechanism of antidepressant activity of St. John's wrot (SJW). Rat locus coeruleus an area that is involved in antidepressant action, high levels of catecholamine, serotonin and glutamate found. Raffa, affinity hypericin was investigated for mouse Karin receptors and sigma receptors, which control 49% mouse Karin receptors and 48% observed inhibition sigma receptors. Calapai et al. [4] demonstrated that increased serotonin and 5-hydroxyindoleacetic acid (5-HIAA) in the level of diencephalon and norepinephrine in the brainstem after using of hypericum extract that majority containing of flavonoid, depends to the dose. These findings indicate the importance of flavonoid in antidepressant activity and also possibly the brainstem is a target for the hypericoum's activity. It is concluded that the injection of valerian extract intraperitoneally with dose of 200 mg/kg as pre-anesthetic medication of ketamine (an anesthetic) in compares with Raei flowers of palliative effects, showed significant differences.

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### Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

### Conflict of Interest

The authors declare no conflict of interest.

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