

### **NARDOSTACHYS JATAMANSI DC. POTENTIAL HERB WITH CNS EFFECTS**

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#### **ABSTRACT**

*Nardostachys jatamansi* is classified as hypno-sedative in Ayurveda. It is used in treatment of insomnia, hysteria and depressive illness. The plant abounds in sesquiterpenes predominantly; jatamansone and nardostachone. The plant has demonstrated several pharmacological activities including hepatoprotective, cardio protective and hypolipidemic and antifungal. The significant effect is on the central nervous system, as diverse pharmacological actions, ranging from sedative to nootropic have been reported. Animal and clinical research with jatamansone, the active principle of the plant, has justified hypno-sedative claim of Ayurveda. The review summarizes, phytochemical and pharmacological investigations carried out on the plant.

**KEYWORDS:** *Nardostachys jatamansi*; sesquiterpenes, jatamansone, pharmacology

### INTRODUCTION

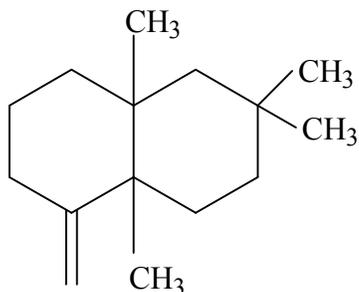
*Nardostachys jatamansi* DC., is important plant of the family Valerianaceae. It is commonly known as Indian spikenard and found in Himalayas. *N. jatamansi* is a perennial herb. Rhizomes occurs in short pieces, has dark grey color and typical smell. Leaves are sessile and ovate. Flowers are dark–pink in color.

In Ayurveda, *N. jatamansi* is used for nervous headache, excitement, menopausal symptoms, flatulence, epilepsy and intestinal colic. In combination with cold water, the oil is considered to be effective against nausea, stomachache, flatulence, liver problems, jaundice and kidney complaints, insomnia and headache. Externally, the oil is added to a steaming bath to treat inflammation of the uterus. The oils are also used in eye compounds and as poison antidotes<sup>1</sup>. Oil is reported to be useful in the treatment of atrial flutter.

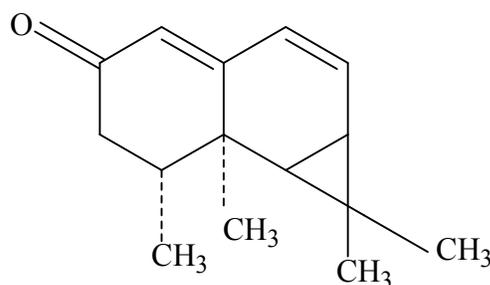
### Phytochemistry

The roots of the plant contain essential oil, rich in sesquiterpenes and coumarins<sup>1</sup>. Jatamansone or valeranone (Fig. 1) is the principal sesquiterpene<sup>2,3</sup>. Other sesquiterpenes include nardostachone (Fig. 2), dihydrojatamansin, jatamansinol, jatamansic acid<sup>4</sup>, jatamansinone, jatamansinol, oroseolol, oroselone, seselin, valeranal, nardostachyin<sup>5</sup>, nardosinone, spirojatamol<sup>6</sup>, jatamol A and B<sup>7</sup>, calarenol<sup>8</sup>, seychellene, seychelane,

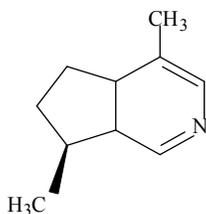
coumarin: jatamansin or xanthogalin<sup>9, 10</sup>. A new sesquiterpene acid, nardin and new pyranocoumarin: 2', 2'-dimethyl-3'-methoxy-3', 4'-dihydropyranocoumarin have been reported<sup>1</sup>. Actinidine, an alkaloid has been reported (Fig 3).



**Fig 1.** Jatamansone



**Fig 2.** Nardostachone



**Fig 3.** Actinidine

## PHARMACOLOGY

### *Gastrointestinal system*

### Hepatoprotective activity

Pretreatment of rats with 800 mg/kg body wt of the 50% ethanolic extract of *N. jatamansi* demonstrated significant hepatoprotective activity against thioacetamide induced hepatotoxicity. Marked reduction in raised levels of serum transaminase and alkaline phosphatase was observed. Pretreatment of the animals with the extract further

resulted in an increase in survival in rats intoxicated with LD90 dose of the hepatotoxic drug <sup>11</sup>.

### *Cardiovascular system*

#### **Cardio protective and hypolipidemic activity**

Rats administered doxorubicin (15 mg/kg (-1), i.p.) showed myocardial damage that was manifested by the elevation of serum marker enzymes (lactate dehydrogenase, creatine phosphokinase, aspartate aminotransaminase and alanine aminotransaminase). The animals showed significant changes in the antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase) and lipid peroxidation levels. Pretreatment with *N. jatamansi* extract significantly prevented these alterations and restored the enzyme activity and lipid peroxides to near normal levels. Restoration of cellular normality accredits the *N. jatamansi* with a cytoprotective role in doxorubicin-induced cardiac damage <sup>12</sup>.

In a study, ethanolic extract of *N. jatamansi* was studied in Wistar albino rats for cardio protective activity against doxorubicin induced myocardial injury. Doxorubicin is inhibitor of fatty oxidation in the heart and results in cardio toxicity. The rats treated with a single dose of doxorubicin (15 mg/kg) intraperitoneally showed an increase in serum and cardiac lipids (cholesterol, triglycerides, free fatty acids and phospholipids), along with a significant rise in serum low density lipoproteins, very low density lipoproteins

and drop in high density lipoproteins levels, resulting in alteration of serum and cardiac lipid metabolizing enzymes.

Pretreatment with an extract of *N.jatamansi* (500 mg/kg) orally for seven days to doxorubicin induced rats showed a significant prevention in the lipid status with the activities of the lipid metabolizing enzymes. Histopathological observations were also in correlation with the biochemical parameters. These findings suggest that the protective and hypolipidemic effect of *N. jatamansi* against doxorubicin induced myocardial injury in rats could possibly be mediated through its anti lipid peroxidative properties<sup>13</sup>.

A 50% ethanolic extract of *Curcuma longa* (tuber) and *N. jatamansi* (whole plant) elevated the HDL-cholesterol/total cholesterol ratio in triton-induced hyperlipidemic rats. There also was a reduction in the ratio of total cholesterol/phospholipids<sup>14</sup>.

### *Nervous system*

Acetyl cholinesterase inhibitory activity of methanolic and successive water extracts of *N.jatamansi* (rhizome), were investigated for acetyl cholinesterase inhibitory activity *in vitro*. Results indicated that methanolic extracts to be more active than water extracts. The IC (50) values obtained for methanolic and successive water extracts of *N.jatamansi* was 47.21µg/ml. These results partly substantiate the traditional use of *N.jatamansi* for improvement of cognition<sup>15</sup>.

### **Anticonvulsant activity**

Ethanol extract of the roots of *N. jatamansi* was studied for its anticonvulsant activity and neurotoxicity, alone and in combination with phenytoin in rats. The results demonstrated a significant increase in the seizure threshold by *N. jatamansi* root extract against maximal electroshock seizure model as indicated by a decrease in the extension/flexion ratio. However, the extract was ineffective against pentylenetetrazole-induced seizures. *N. jatamansi* root extract also showed minimal neurotoxicity against rota rod test at doses that increased the seizure threshold. Further, pretreatment of rats with phenytoin at a dose of 12.5, 25, 50 and 75 mg/kg in combination with 50mg/kg of *N. jatamansi* root extract resulted in a significant increase in the protective index of phenytoin from 3.63 to 13.18. The dose response studies of phenytoin alone and in combination with *N. jatamansi* extract on the serum levels of phenytoin clearly demonstrated the synergistic action of both the drugs <sup>16</sup>.

### **Antidepressant activity**

A 15-day treatment with an alcoholic root extract of *N. jatamansi* caused an overall increase in the levels of central monoamines and inhibitory amino acids, including a change in the levels of serotonin, 5-hydroxyindole acetic acid, gamma-amino butyric acid, and taurine in rat brain <sup>17</sup>.

### Antiparkinson's activity

Rats were treated with 200, 400, and 600 mg/kg body weight of *N. jatamansi* roots for 3 weeks. On day 21, 2 µl of 6-OHDA (12 µg in 0.01% in ascorbic acid-saline) was infused into the right striatum, while the sham-operated group received 2 µl of vehicle. Three weeks after the 6-OHDA injection, the rats were tested for neurobehavioural activity and were sacrificed after 6 weeks for the estimation of lipid peroxidation, reduced glutathione content, the activities of glutathione-S-transferase, glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase, quantification of catecholamines, dopaminergic D2 receptor binding and tyrosine hydroxylase expression. The increase in drug-induced rotations and deficits in locomotor activity and muscular coordination due to 6-OHDA injections were significantly and dose-dependently restored by *N. jatamansi*.

Lesioning was followed by an increased lipid peroxidation and significant depletion of reduced glutathione content in the substantia nigra, which was prevented with *N. jatamansi* pretreatment. The activities of glutathione-dependent enzymes, catalase and superoxide dismutase, in striatum which were reduced significantly by lesioning, were dose-dependently restored by *N. jatamansi*. A significant decrease in the level of dopamine and its metabolites and an increase in the number of dopaminergic D2

receptors in striatum were observed after 6-OHDA injection, and both were significantly recovered following *N. jatamansi* treatment. All of these results were exhibited by an increased density of tyrosine hydroxylase immunoreactive fibers in the ipsilateral striatum of the lesioned rats following treatment with *N. jatamansi*; 6-OHDA injection had induced almost a complete loss of TH-IR fibers. This study indicates that the extract of *N. jatamansi* might be helpful in attenuating Parkinsonism<sup>18</sup>.

### **Neuroprotective activity**

Pretreatment with an alcoholic extract of *N. jatamansi* dosed at 250 mg/kg of for 15 days protected rats against focal ischemia caused by middle cerebral artery occlusion. The protective effect may be associated with improving glutathione content, inhibiting lipid peroxidation, and activity on the Na<sup>+</sup>/K<sup>+</sup> ATPase and catalase enzyme systems<sup>19</sup>.

### **Nootropic activity**

The elevated plus maze and the passive avoidance paradigm were employed to evaluate learning and memory parameters. Three doses (50, 100, and 200 mg/kg, p.o.) of an ethanolic extract of *N. jatamansi* were administered for 8 successive days to both young and aged mice. The 200 mg/kg dose of *N. jatmansi* ethanolic extract significantly improved learning and memory in young mice and also reversed the amnesia induced by diazepam (1 mg/kg, i.p.) and scopolamine (0.4 mg/kg, i.p.).

Furthermore, it also reversed aging-induced amnesia due to natural aging of mice. As scopolamine-induced amnesia was reversed, it is possible that the memory improvement may be because of facilitation of cholinergic transmission in the brain. Hence, *N. jatamansi* might prove to be a useful memory restorative agent in the treatment of dementia seen in elderly persons. The underlying mechanism of action can be attributed to its antioxidant property<sup>20</sup>.

### *Antimicrobial activity*

#### **Antifungal**

*N. jatamansi* essential oil demonstrated fungistatic activity against *Aspergillus flavus*, *Aspergillus niger* and *Fusarium oxysporum*<sup>21</sup>

#### **Jatamansone (valeranone)**

Animal studies done on jatamansone have reported antioestrogenic, antiarrhythmic, antihypertensive, anticonvulsant, sedative and tranquilizing activities<sup>22, 23, 24, 25, 26</sup>. In animal experiments, a limiting effect upon convulsant thresholds and a reduction of motor coordination ability traceable to the sesquiterpene ketone, valeranone

contained in the drug have been demonstrated. Jatamansone is anticonvulsive in effect without exhibiting neuroleptic characteristics<sup>25</sup>.

Some experiments, typical for tranquillizers jatamansone prolonged barbiturate hypnosis, impaired rota rod performance, potentiate the body-temperature lowering activity of reserpine. Jatamansone exhibited anticonvulsant activity against electric shock and gastro protective actions. In toxicological studies on rats and mice an oral LD50 of greater than 3160 mg/kg was found, which suggests the possibility of a therapeutically useful dose ratio<sup>3</sup>.

Preliminary clinical studies with jatamansone reported reduced incidence of aggressiveness, restlessness, stubbornness and insomnia. In a study conducted on hyperkinetic children, jatamansone, D-amphetamine and chlorpromazine were compared for efficacy. Jatamansone and amphetamine significantly improved behavior but amphetamine was better in reducing aggressiveness and restlessness. Children with mental retardation showed little response to any of the drugs. Jatamansone has fewer side effects than D-amphetamine and chlorpromazine<sup>27</sup>.

### **Jatamansin**

The coumarin; jatamansin is efficacious in internal treatment of varicose veins<sup>28</sup>.

### CONCLUSION

*N. jatamansi* is important plant of Ayurvedic materia medica. The plant is major ingredient of Ayurvedic formulations for the treatment of central nervous disorders. Animal investigations and to some extent, clinical trials, have justified the claim of Ayurveda. Keeping in mind the side-effect profile of conventional antipsychotic drugs, *N. jatamansi* seems to be potential candidate for large scale clinical trials.

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