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A PHYTOPHARMACOLOGICAL REVIEW ON N. JATAMANSI

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ABSTRACT

Some researchers suggest that two-thirds of the world's plant species have medicinal value; in particular, manymedicinal plants have very rich contents of chemicals. Nardostachys jatamansi [Family Valerianaceae] is a perennial herb found in Alpine Himalayas. N. jatamansi is used for long period in various chronic diseases therapeutically. Aim of the current review is to search literature for the pharmacological properties, safety/toxicity studies, pharmacognostic studies and phytochemical investigation of N. jatamansi. The compiled data may be helpful for the researchers to focus on the priority areas of research yet to be discovered. Complete information about the plant has been collected from various books, journals etc. Journals of the last 20 years were searched. Particulars of pharmacological activities, phytochemical isolation, toxicity studies etc. were extracted from the published reports focusing on the safety profile of the plant. Safety of the whole plant is concluded in the review.

Keywords: Phytochemical, Pharmacological, N. jatamansi, Sesquiterpenes

INTRODUCTION

Nardostachys jatamansi [N. jatamansi] also called nard, nardin Spikenard and muskroot, is a flowering plant of the Valerian family that grows in Nepal, China and India. The plant grows to about 10-60cm in height and has pink, bell-shaped flowers. It is found in the altitude of about 17000ft **[1]**. In Ayurveda *N. jatamansi* is used for Madhya [Brain tonic], Rasayana [Rejuvenative to themind], Nidrajnana [Promotes sleep], Manasrogaghna [Alleviatesmental diseases], Pachana [Digestive], Kasaswasahara [Alleviates coughs and breathing difficulties], Kushtaghna [Stops

skin diseases and itching], Daha prashamana [Stops burning sensations], Varnya [Benefits complexion] and Romasanjanana [Promotes hair growth]**[2, 3]**. It is also 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, stomach-ache, flatulence, liver problems, jaundice and kidney complaints, insomnia and headache. Externally, *N. jatamansi* rhizomes [underground stems] can be crushed and distilled into intensely Aromatic amber-colour essential oil which is very thick in consistency, the oil is added to asteaming bath to treat inflammation of the uterus. The oils are also used in eye compounds and as poison antidotes. *N. jatamansi* oil is used as a perfume, incense, a sedative and an herbal medicine to fight against insomnia, birth difficulties, and other minor ailments**[4]**.

Botanical classification [5]

Kingdom	Plantae
Order	**Dipsacales**
Family	**Valerianaceae**
Genus	**Nardostachys**
Species	***N. Jatamansi***

Common Name [1, 6]

Language	Vernacular Name
Sanskrit	Jatamansi, Bhytajata, Tapaswini
English	Musk-root, Indian spikenard, Indian nard
French	Nard Indian
German	AchteNarde
Hindi	Jatamansi, Bal-chir
Punjabi	Jatamansi
Bengali	Jatamansi
Gujarati	Jatamasi
Marathi	Jatamavshi

Phytochemistry

The roots of the plant contain essential oil, rich in sesquiterpenes and coumarins**[4]**. Jatamansone or valeranone is the principal sesquiterpene**[7, 8]**. Other sesquiterpenes include nardostachone, dihydrojatamansin, jatamansinol, jatamansic acid**[9]**, jatamansinone, jatamansinol, oroseolol, oroselone, seselin, valeranal, nardostachyin**[10]**,nardosinone, spirojatamol**[11]**, jatamol A and B**[12]**, calarenol **[13]**, seychellene, seychelane, coumarin, jatamansin or xanthogalin [14]**[15]**. A new sesquiterpene acid, nardin and new pyranocoumarin: 2, 2-dimethyl-3-methoxy-3, 4 dihydropyranocoumarin have been reported. An alkaloid actinidine has also has been reported [4].

Pharmacological activity

Hepatoprotective activity

Pre-treatment of rats with800mg/kg, p.o of the 50% ethanolic extract of therhizomes of *N. jatamansi*significantly lowered the elevated levels of serum transaminases [aminotransferases] and alkalinephosphatase in thioacetamide treated group of animals. The hepatoprotectiveactivity was shown by the normalization of variousserum enzymes elevated in response to thioacetamide-induced liver damage. The investigation provides biochemical evidence to validate the useof *N. jatamansi* as a component of some hepatotonicpreparations used by Unani [Greco-Arab] physicians **[16]**.

Cardio protective activity

Doxorubicin [15 mg/kg, i.p.] administered rats showed myocardial damage that was demonstrated by the elevation of serum marker enzymes [lactate dehydrogenase, creatine phosphokinase, and aspartate amino transaminase and alanine amino transaminase]. The animals showed significant changes in the antioxidant enzymes [superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase] and lipid peroxidation levels. Pre-treatment with *N. jatamansi* extract significantly prevented and restored the antioxidant enzyme activity and lipid peroxides to near normal levels. Restoration of cellular normality accredits the *N. jatamansi* with a cyto-protective role in doxorubicin-induced cardiac damage **[17]**.

Hypolipidemic activity

Ethanolic extract of *N. jatamansi* was studied in Wistar albino rats for cardio protective activity against doxorubicin induced myocardial injury. The rats treated with a single dose of doxorubicin [15 mg/kg] intra-peritoneally 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.

Pre-treatment 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. Histo-pathological 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 **[18]**.

Treatment of rats with 50% ethanolic extract of *Curcuma longa* [tuber] and *N. jatamansi* [whole plant] elevated the HDL-cholesterol/total cholesterol ratio in triton induced hyper lipidemic rats. It also reduced the ratio of total cholesterol/phospholipids **[19]**.

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] value obtained for methanolic and successive water extracts of *N. jatamansi* was 47.21mg/ml. These result partly substantiated the traditional use of *N. Jatamansi* for improvement of cognition **[20]**.

In another study the effect of acute and sub-chronic administration of an alcoholic extract of the roots of *N. jatamansi* on nor-epinephrine [NE], dopamine [DA], serotonin [5-HT], 5- hydroxyl indoleacetic acid [5-HIAA], gamma-amino butyric acid [GABA] and taurine were studied in male albino Wistar rats. The acute oral administration of the extract did not change the level of NE and DA but resulted in a significant increase in the level of 5-HT and 5-HIAA. A significant increase in the level of GABA and taurine was observed in the drug-treated groups when compared to the controls. A 15-day treatment resulted in a significant increase in the levels of NE, DA, 5-HT, 5-HIAA and GABA. These data indicated that the alcoholic extract of the roots of N. jatamansi caused an overall increase in the levels of central monoamines and inhibitory amino acids **[21]**.

Anticonvulsant activity

Ethanolic extract of the roots of *N. jatamansi* was studied for its anticonvulsant activity. 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 pentylene tetrazole induced seizures. Further, pre-treatment 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 **[22]**.

Antidepressant activity

The antidepressant activity of methanolic extract of *N. jatamansi* by forced swim test, tail suspension test and locomotor activity in inbred male Swiss were determined. The efficacy of the extract [200 and 400 mg/kg, p.o] was compared with the standard drug imipramine [10mg/kg, p.o] on normal and sleep deprived mice. Drugs were administered for 10 days in normal mice groups and the other groups were subjected to 24 hours sleep deprivation by using multiple platforms on 9th day and last dose was given 1 hour before experiment on 10th day. Duration of immobility was noted in both themodels. *N. jatamansi* [200 and 400 mg/kg, p.o] produced significant [P<0.001] antidepressant like effect in normal and sleep deprived mice in both TST and FST and their efficacies were found to be comparable to imipramine [10 mg/kg, p.o]. It did not show any significant change in locomotor functions of mice as compared to normal control. However, it significantly [P<0.01] improves the locomotor activity in case of sleep deprivation which is comparable to normal control. This finding suggests that *N. jatamansi* has dose dependent antidepressant activity and can also be used in patients suffering from depression due to sleep disturbances **[23]**.

In another study the ethanolic extract [100, 200 and 400 mg/kg, p.o] of *N. jatamansi* administered for 14 successive days to Swiss young albino mice [either sex] produced significant antidepressant like effect in both tail suspension and forced swim tests. The efficacy of the extract was found to be comparable to imipramine [15 mg/kg, p.o] and sertraline [20 mg/kg, p.o]. Ethanolic extract [200 mg/kg, p.o] did not show any significant change on locomotor activity of mice as compared to control; hence it did not produce any motor effects. Further, the extract decreased the whole brain MAO-A and MAO-B activities as compared to control, thus increased the levels of monoamines. The antidepressant effect of the extract was also significantly reversed by pre-treatment of animals with baclofen [GABA agonist]; when tested in tail suspension test. The result suggested that the antidepressant-like effect of the extract may also be due to interaction with GABA receptors resulting in decrease in the levels of GABA in mouse brain. Thus, the extract may have potential therapeutic value for the management of mental depression so finally it may be concluded from reported articles that the antidepressant activity of *N. jatamansi*due to interaction with GABA receptors and decrease in the levels of GABA [24].

Antiparkinson 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 neurobehavioral 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 catecholamine's, 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* pre-treatment. 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 immune reactive fibres 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 fibres. This study indicates that the extract of *N. jatamansi* might be helpful in attenuating Parkinsonism **[25].**

Neuroprotective activity

The protective effect of N. jatamansi on neurobehavioral activities, thiobarbituricacid reactive substance [TBARS], reduced glutathione [GSH], thiol group, catalase and sodium potassium-ATPase activities was studied in middle cerebral artery [MCA] occlusion model of acute cerebral ischemia in rats. The right MCA of male Wistar rats was occluded for 2 h using intraluminal 4-0 monofilament and reperfusion was allowed for 22 h. MCA occlusion caused significant depletion in the contents of glutathione and thiol group and a significant elevation in the level of TBARS. The activities of Na [+] K [+] ATPase and catalase were decreased significantly by MCA occlusion. The neuro behavioral activities [spontaneous

motor activity and motor coordination] were also decreased significantly in MCA occlusion group. All the alternations induced by ischemia were significantly attenuated by 15 days pre-treatment of *N. jatamansi* [250 mg/kg p.o] and correlated well with histopathology by decreasing the neuronal cell death following MCA occlusion and reperfusion. The study provides first evidence of effectiveness of *N. jatamansi* in focal ischemia most probably by virtue of its antioxidant property **[26]**.

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. jatamansi* 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. **[27]**

Antifungal Activity

N. jatamansi essential oil demonstrated fungi static activity against Aspergillus flavus, Aspergillus niger and Fusarium oxysporum **[28]**.

Anti oxidant activity

The anti-stress effect of hydro-ethanolic extract [70%] of N. jatamansi was evaluated in reference to its antioxidant property. Wistar rats were divided into four groups: naïve, stressed and T-200 and T-500 stressed with oral pre-treatment of *N. jatamansi* extract 200 and 500 mg/kg, respectively. Restraint of rats in metallic chambers for 4 h at 4°C was followed by sacrifice and assessment of stress-induced alterations in biochemical parameters, incidence and severity of ulcers. The In-vitro antioxidant activity of *N. jatamansi* was studied by measuring the free radical scavenging activity. *N. jatamansi* showed potent antioxidant activity and significantly reversed the stress-induced elevation of LPO and NO levels and decrease in catalase activity in the brain. The findings suggest that the *N. jatamansi* possesses significant anti-stress activity, which may be due to its antioxidant activity [26**, 29**].

Anticancer activity

The roots of *N. jatamansi*a well-known traditional medicinal plant was explored for *in vitro* ant proliferative potential against two neuro blastoma human cancer cell lines *viz*., IMR-32 and SK-N-SH using SRB assay. Three extract *viz*., 95% alcoholic [ACE], 50% hydro-alcoholic [HAE] and aqueous [AQE] extracts and four fractions *viz*., hexane [HXF], chloroform [CHF], butanol [BTF] and aqueous [AQF] were evaluated. 95% alcoholic extract had showed significant and dose-dependent inhibitory effect on proliferation of both the cell lines of neuroblastoma. The percent growth inhibition was found to be 71% against IMR-32 and 85% against SK-N-SH at 100µg/ml respectively. On fractionation the n-hexane [HXF] fraction was found to be more potential in comparison to the rest of the other three fractions. It showed growth inhibition of 54% and 91% against IMR-32 and 45% and 82% against SKN-SH at 30µg/ml and 100µg/ml against neuroblastoma cancer cell lines respectively. Our results suggested that the 95% alcoholic extract and its n-hexane fraction of *N. jatamansi* had strong *in-vitro* cytotoxic effect against neuroblastoma cancer cell lines. Hence, active compounds are non-polar in nature. In conclusion the roots of N. jatamansi showed cytotoxic effect to human neuroblastoma cells in culture [29].

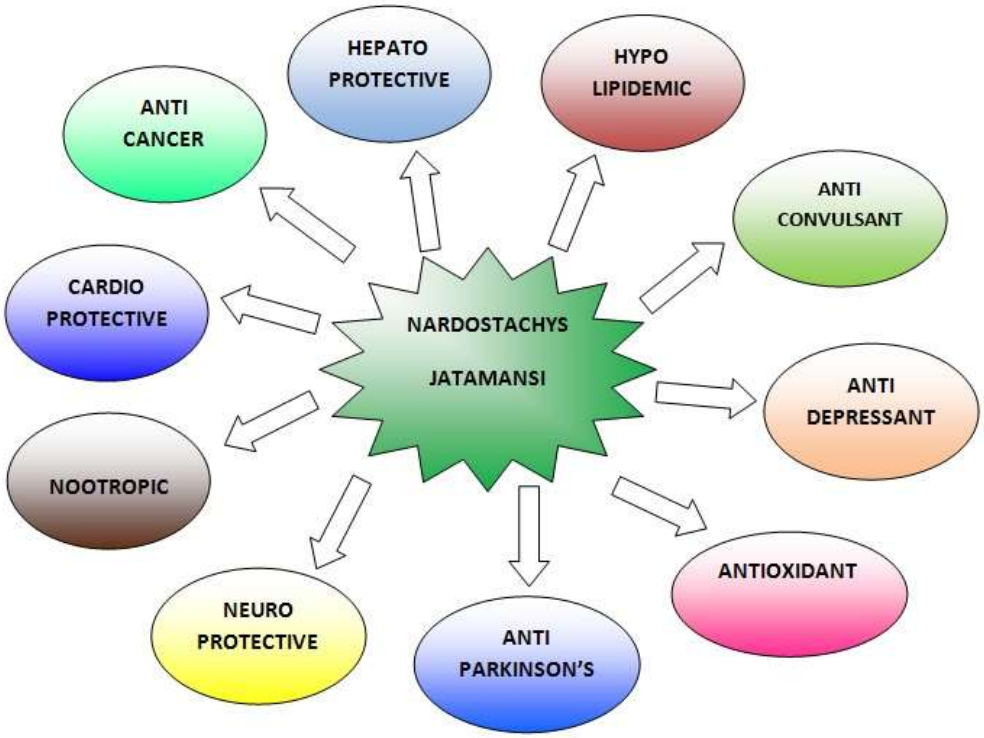

Fig 1: Different Activities shown by *N. jatamansi*

Conclusion:

*N. jatamansi*is an important medicinal plant mentioned in Ayurveda and Unani system used for treatment of various diseases. The different studies done on animals provide a significant effect of the different activities mentioned in traditional treatise. *N. jatamansi* also have many properties with no animal study which provide the researchers to do research on those activities to serve the humanity.

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