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Review Article

AN OVERVIEW ON THE BIOLOGICAL PERSPECTIVES OF *NARDOSTACHYS JATAMANSI*

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ABSTRACT

Nardostachys jatamansi is a flowering plant of the Valerianaceae family, which is a native plant of the Indian and Nepal Himalaya. It is found from 2200m to 5000m asl. in random forms. It is also called as spikenard, nard, nardin, or muskroot used in the formulation of traditional Ayurvedic medicines as well as modern herbal preparations for curing various ailments. The plant abounds in sesquiterpenes predominantly; jatamansone and nardostachone. *Nardostachys jatamansi* possesses biological properties such as antioxidant, antimicrobial, anticholinesterase, oxidative stress, antidepressant and anti-inflammatory activities. It is also useful in the management of insomnia and CNS disorders. This study has detailed information regarding the various activities and mainly focuses on the pharmacological activity of *Nardostachys jatamansi*.

Keywords: Biological perspectives, *Nardostachys jatamansi*

INTRODUCTION

Plant is a natural and one of the most important sources for medicine. The use of plants to heal or combat diseases is probably as old as humankind. It has been estimated that 14-28% of higher plant species are used medicinally and that 74% of pharmacologically active plant-derived components were discovered after following up ethnomedicinal use of plants [1]. WHO potrayed that about 80% of the world's population believes on the ancient and traditional plant-based treatment for different ailments [2]. The plant extracts from various parts are of great importance in therapeutics as they have been discovered to contain many biological properties [3]. In recent years, scientists have focussed the attention of research towards phytochemicals to cure disorders. Nootropic herbs refer to the medicinal role of various plants/parts for their properties by the active phytochemicals including alkaloids, steroids, saponins, terpenoids, flavonoids, phenolics, etc. [4].

Nardostachys jatamansi (D. Don) DC, a critically endangered rhizome-bearing medicinal plant, is restricted to specialized habitats in high altitudes of the Himalaya, ranging from 3000 to 5000m asl. [5]. *Jatamansi,* botanically equated to *Nardostachys jatamansi*, is an important drug of Ayurveda and used in different traditional systems of medicine such as Ayurveda, Unani, Siddha, etc. [6]. Rhizomes and roots are used as a tranquilizer, laxative, cardiac tonic, for curing vertigo, nervous headache, low and high blood pressure, etc [7]. Hence this present study explores on the various activities and focuses on the basic pharmacological activities namely antioxidant, oxidative stress, anticholinesterase, anti-inflammatory, antidepressant, antimicrobial, phytochemical, neurotoxic, etc.

Antioxidant activity

Chaudhary *et al.*, 2015 evaluated antioxidant activity in breast carcinoma from roots and rhizomes of *N. Jatamansi* [8]. Mathew *et al.*, 2014 studied antioxidant activity of *N. jatamansi* by DPPH scavenging assay with IC50 value<10 g/ml [9]. Mishra *et al.*, 2014 prepared herbal antioxidant face cream from the ethanol extract of *N. jatamansi* and showed IC50 value of 58.39 g/ml [10].

The antioxidant activities of methanol extract of *N. jatamansi* were found to contain only protocatechuic and syringic acids, which was analysed by Panday *et al.*, 2013 [11]. Dugaheh *et al.*, 2013 studied the antioxidant effect of *N. jatamansi,* which inhibited beta-carotene oxidation [12]. The calibration curve of valerenic acid was linear in the range of 2-51 mg/l. The antioxidative potential of a hydroalcohol extract of *N. jatamansi* (NJE) rhizomes were studied by Sharma *et al.*, 2012 that exhibited free radical scavenging, against DPPH and superoxide anions and the extract exhibited high reduction capability and powerful free radical scavenging, especially against DPPH and superoxide anions as well as a moderate effect on NO [13].

The antioxidant potential of the essential oil of *N. jatamansi* DC roots, was able to reduce the stable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) to yellow-colored DPPH-H was studied by Parveen *et al.*, 2012 [14]. Rasheed *et al.*, 2011 investigated the aqueous root extract from *N. jatamansi* for its antioxidant activity and the increased generation of TBARS and reduced GSH were restored to near normal levels [15]. The antioxidant potential of *N. jatamansi* was examined by Kumari *et al.*, 2010 and in-vitro lipid peroxidation was reported due to the presence of phenols, flavonoids, alkaloids [16]. The antioxidant effects of NJE which tended to normalize augmented lipid peroxidation, nitrite, superoxide dismutase activities and catalase level were studied by Lyle *et al.*, 2009 [17]. Lyle *et al.*, 2009 evaluated the antioxidant effect of hydro-ethanol extract (70%) of *N. jatamansi* (NJE) that reversed the stress-induced elevation of LPO and NO levels [18].

Oxidative stress

The volatile oil of NRR (the root and rhizome of *N. jatamansi* DC.), that stimulated the gene expressions of self-defence antioxidant enzymes and activated the phosphorylation of Akt in cultured H9c2 cells was studied by Maiwulanjiang *et al.*, 2014 [19]. The study on a protective role in H_2O_2-induced oxidative stress in C6 glioma cells by extracts from *N. jatamansi* rhizomes was done by Dhuna *et al.*, 2013 which increased the level of antioxidant enzymes and reduced Lipid peroxidation [20]. Lyle *et al.*, 2012 investigated the anti-stress activity of *N. jatamansi* (NJE) on CRS model that significantly mitigated CRS induced altered level of neurotransmitters in different brain regions [21]. The neuroprotective efficacy of antioxidants with the combined treatment with the extract of *N. jatamansi* (N), crocetin (C) and selenium(Se) as sodium selenite performed by Khan *et al.*, 2012 reduced the level of TBARS, and elevated the content of glutathione and activities of enzymes [22]. Suchitra *et al.*, 2012 studied the anxiolytic and protective effect of the ethanolic extract of *N. jatamansi* that caused depletion in lipid peroxidation and elevation in GSH [23]. The modulatory effect of *N. jatamansi* DC on benzoyl peroxide-induced oxidative stress that resulted a reduction in lipid peroxidation and xanthine oxidase activities ($p<0.05$) was investigated by Ali *et al.*, 2005 [24].

Anticholinesterase

Mathew *et al.*, 2014 studied the, methanolic extract of *N. jatamansi* for improving cognitive function for acetylcholinesterase inhibitory activity and showed IC50 values<100 g/ml [25]. The various effects of *N. jatamansi* root ethanol extract (NJE) on the central nervous system was investigated by Karkada *et al.*, 2011 and showed a higher level of AChE activity in the frontal cortex (179% higher) and hippocampus (36% higher) [26]. Mukherjee *et al.*, 2007 studied acetylcholinesterase (AChE) inhibiting activity of *N. jatamansi* and it inhibited 50% of AChE activity at a concentration of 100-150 g/ml [27]. The methanol and water extracts of *N. jatamansi* for acetylcholinesterase (AChE) inhibitory activity in which methanol extract was found to have IC50 value 47.21g/ml was studied by Vinutha *et al.*, 2007 [28].

Anti-inflammatory

Li *et al.*, 2014 studied the methanol extracts of *N. jatamansi* (D. Don) DC (NJ) roots for anti-inflammatory activities, and it downregulated both iNOS and COX-2 expression and mRNA expression of the pro-inflammatory cytokines tumor necrosis TNF, IL-1, and IL-6 was decreased [29]. The anti-inflammatory effects of *N. jatamansi* (NJ) against LPS-induced inflammatory responses was studied by Bae *et al.*, 2014 and inhibited the production of cytokines, LPS-induced activation of c-jun NH2-terminal kinase (JNK) and p38, activation of MAPKs and NF-B [30]. The protective effects of *N. jatamansi* (NJ) that inhibits endotoxin shock by inhibiting the production of IL-1, IL-6, TNF, and IFN, investigated by Bae *et al.*, 2011 [31].

Antidepressant activity

Deepa *et al.*, 2013 investigated the antidepressant effect of *N. jatamansi* ethanol root extract in electron beam irradiated mice, which has shown a significant reduction in the duration of immobility (in seconds) in Forced Swimming Test and Tail Suspension Test [32]. The mechanisms for antidepressant like activity of *N. jatamansi* in mice, studied by Dhingra *et al.*, 2008, found that it decreased the whole brain MAO-A and MAO-B activities as compared to the control [33].

Antimicrobial activity

Chandrasekhar *et al.*, 2013 performed the Bacterial Reverse Mutation Test with *N. jatamansi* plant rhizome powder using *Salmonella typhimurium* tester strains and substantial increase in revertant colony number was not observed in all the *Salmonella typhimurium* tester strains both in the presence and absence of metabolic activation system up to the dose 5.0 mg/plate [34]. Parveen *et al.*, 2011 studied the antibacterial effect of the essential oil of *N. jatamansi* DC roots and among Gram-positive bacteria oil exhibited maximum antibacterial activity against *B. subtilis* followed by *S. aureus* and Gram-negative bacteria only *K. pneumoniae* and *E. aerogenes* were found to be sensitive [35]. The antimicrobial activity of ethanol, ethyl acetate and hexane extracts of *N. jatamansi* roots was studied by Sohail *et al.*, 2007, among which ethanol root extract exhibited maximum antimicrobial activity against all the tested bacteria and fungi, at concentrations of 5, 10 and 20 mg/ml [36].

Neurotoxic

Etebari *et al.*, 2012 evaluated the aqueous and hydro-alcohol extract of *N. jatamansi* and were genotoxic in the concentrations 5 and 10 mg/ml, respectively [37]. Patil *et al.*, 2012 aimed to assess the neuroprotective potential of alcohol extract of roots and rhizomes of *N. jatamansi* (ANJ) and its triterpenes (TNJ) in reserpine-induced orofacial dyskinesia, which significantly inhibited reserpine-induced VCM, TP, and catalepsy, and exhibited elevation in the levels of SOD, CAT, and GSH and inhibition of lipid peroxidation (LPO) [38]. The effect of ethanol extract of the roots of *N. jatamansi* DC on anticonvulsant activity and neurotoxicity was studied by Rao *et al.*, 2005 and treatment resulted in a significant increase in the protective index (PI) of phenytoin from 3.63 to 13.18 [39].

Other activities

Chaudhry *et al.*, 2015 determined MTT assay for NJM, which exhibited the highest antiproliferative activity (IC50: 58.01±6.13 and 23.83±0.69g/ml in MCF-7 and MDA-MB-231 respectively) [40]. Maiwulanjiang *et al.*, 2015 investigated the vascular benefit of Nardostahyos Radix Rhizoma (NRR; the root and rhizome of *N. jatamansi* DC.) and found that the phosphorylation level of Akt kinase is increased, which was partially attenuated by PI3K/Akt inhibitor LY294002 [41]. The interaction between lithium carbonate and *N. jatamansi* extract (NJE) was studied by Kasture *et al.*, 2014 and confirmed that rats receiving lithium carbonate and NJE showed significantly diminished anxiolytic activity [42]. Gowda *et al.*, 2013 investigated the protective effect of *N. jatamansi* root extract (NJE) on the radiation-induced haematological damage in rats that exhibited a time-dependent significant elevation [43]. Thermo-responsive nasal gel of *N. jatamansi* extract that had a mucoadhesive strength of 1524.44 and 1720.44 dyne/cm^2 was formulated and evaluated by Jadhav *et al.*, 2013 [44]. Naveen *et al.*, 2012 investigated the protective effect of *N. jatamansi* root extract and it was found to play an important role in its radioprotective action without any toxicity [45]. Rasheed *et al.*, 2012 investigated anticataleptic effects of hydro-alcohol root extract from *N. jatamansi* that restored the increased generation of TBARS and reduced GSH to near normal levels [46]. The effect of ethanol extract of *N. jatamansi* on the mice exposed to electron beam radiation was studied by Madhu *et al.*, 2012 showed a significant depletion in lipid peroxidation followed by significant elevation in reduced glutathione, total antioxidants, glutathione peroxidase and catalase activity [47]. Gi-Sang *et al.*, 2012 investigated the ability of NJ to ameliorate severe acute pancreatitis (SAP) induced by a choline-deficient diet supplemented with ethionine (CDE) inhibited the secretion of digestive enzymes, cytokine production, and the activation of mitogen-activated protein kinases (MAPKs) [48]. Bae *et al.*, 2012 determined the potential of the fraction of *N. jatamansi* (NJ) to ameliorate the severity of acute pancreatitis (AP) and found that it resulted in the *in vivo* up-regulation of heme oxygenase-1 (HO-1) [49].

Karkada *et al.*, 2012 investigated the potential of *N. jatamansi* extract (NJE) in protecting against chronic stress-induced impairments in spatial learning and memory and found that NJE treated animals, made significantly more correct choices (38%, P<0.001), and fewer reference memory errors (53%, P<0.01) [50]. The inhibitory effects of *N. jatamansi* (NJ) on alcoholic chronic pancreatitis (ACP) was examined by Bae *et al.*, 2012, the treatment increased the pancreatic acinar cell survival and reduced collagen deposition and pancreatic stellate cell (PSC) activation [51]. The anti amnesic activity of methanol extract of *N. jatamansi* DC (MENJ) rhizome was studied by Rezaie *et al.*, 2010 on sleep deprived (SD) amnesic mice, showed a significant improvement in learning and cognition parameters in behavioural tests [52]. Rahman *et al.*, 2010 conducted a comparative study of this plant with chemical drugs, and the herbal extract of *N. jatamansi* with the maximum inhibition was observed at the does of 200 mg/kg of sedative and anxiolytic effect [53]. The anti-diabetogenic mechanism of *N. jatamansi* extract (NJE) was investigated by Song *et al.*, 2010 and found that NJE protected against cytokine-mediated cytotoxicity, and resulted in a significant reduction in cytokine-induced NF-B activation [54]. Bae *et al.*, 2010 investigated the effect of *N. jatamansi* on cerulein-induced Ap and treatment caused reductions in pancreatic edema, neutrophil infiltration, serum amylase and lipase levels, serum cytokine levels, and messenger RNA expressions of inflammatory mediators [55]. Rasheed *et al.*, 2009 analyzed anti-parkinsonism effect by measuring various neurological and behavioral parameters of *N. jatamansi* roots extracted with water (50%) & ethanol (50%) and found that *N. jatamansi* reversed the haloperidol-induced Parkinsonism significantly (p<0.01), when compared to drugs [56]. The effects of strength training and drug (*Jatamansi*) on reducing hand tremor in archers was investigated and compared by Laishram *et al.*, 2008, using One Way ANOVA, left and right arm showed significant differences (F = 5.64, p<0.05; F = 8.97, p<0.001) respectively and Group II showed (F = 12.50, p<0.001; F = 9.23, p<0.001) respectively [57].

The effect of ethanol extract of *N. jatamansi* rhizomes on Wistar albino rats evaluated by Subashini *et al.*, 2007, showed a significant prevention in the lipid status with the activities of the lipid metabolizing enzymes [58]. Subashini *et al.*, 2007 studied the effect of ethanol extract of *N. jatamansi* on the mitochondrial and

lysosomal damage induced by doxorubicin in rats, extract prevented the mitochondrial respiration, lysosomal integrity, membrane bound phosphatases and ultrastructural studies in doxorubicin-induced rats [59]. Joshi *et al.*, 2006 evaluated the potential of *N. jatamansi* as a memory enhancer which significantly improved learning and memory in young mice and reversed the amnesia induced by diazepam (1 mg/kg, i. p.) and scopolamine (0.4 mg/kg, i. p.) [60]. Subashini *et al.*, 2006 evaluated the effect of *N. jatamansi* (rhizomes) and treatment significantly prevented the elevation of serum marker enzymes and restored the enzyme activity and lipid peroxides to near normal levels [61]. Ahmad *et al.*, 2006 evaluated whether ethanol extract of *N. jatamansi* roots (ENj), can slow the neuronal injury in a 6-OHDA-rat model of Parkinson's and found that the activities of glutathione-dependent enzymes, catalase and superoxide dismutase in the striatum, were dose-dependently restored by Enj [62]. The protective effect of *N. jatamansi* (NJ) was studied by Salim *et al.*, 2003 and found that it caused a significant elevation in the level of TBARS, and the activities of Na+K+, ATPase and catalase were also decreased [63]. Ali *et al.*, 2000 evaluated the hepatoprotective activity of 50% ethanolic extract of the rhizomes of *N. jatamansi* and **e**levated levels of serum transaminases (aminotransferases) and alkaline phosphatase, were significantly lowered in *N. jatamansi* pretreated rats [64]. The effect of alcoholic extract of the roots of *N. jatamansi* in male albino Wistar rats studied by Prabhu *et al.*, 1994, resulted in a significant increase in the levels of NE, DA, 5-HT, 5-HIAA, and GABA [65].

Phytochemistry

The phytochemical investigation of $CHCl_3$: MeOH (1:1) extract from the rhizomes of *N. Jatamansi* was studied by Rekha *et al.*, 2013, which led to the isolation of two new sesquiterpenoids named compound 5 and 6 [66]. Jha *et al.*, 2012 studied phytochemical, microbial load estimation of the rhizome in which different extracts showed the difference in the presence of phytochemical constituents but studies showed that all extracts contained valtrate [67]. Mallavadhani *et al.*, 2011 evaluated *N. jatamansi* using Nardin marker and the LOD and LOQ were 3.050 and 9.277ng/ml respectively [68]. *N. jatamansi* DC rhizomes, when subjected to different techniques, led to the isolation of nardal, jatamansic acid, and nardin was studied by Gottumukkala, V. R. *et al.*, 2011 [69]. E-2-methyl, 3-(5,9-dimethylbicyclo[4,3,0]-non-9(1)-en-3-yl)-2-propenal from the hexane extract of the rhizomes of *N. jatamansi* DC was isolated by Venkateswara *et al.*, 2008 [70]. Chatterjee *et al.*, 2005 isolated quiterpene acid, nardin and a new pyranocoumarin from the rhizomes of *N. jatamansi* and characterized as E-2-methyl, 3-(5,9-dimethylbicyclo[4.3.0]-nonen-9-yl)-2-propenoic acid and′,**2′** -dimethy]-3′-methoxy-3′,4′-dihydropyranocoumarin, respectively [71]. Chatterjee *et al.*, 2000 isolated, nardostachysin from the rhizomes of *N. jatamansi*, and were established as the 7',8'-dihydroxy-4'-methylene hexahydrocyclopenta-[c]pyran-1'-one-8'-methyl ester of 7,9-guaiadien-14-oic acid [72].

Two new eudesmanes jatamols, A and R from the roots and rhizomes of *N. Jatamansi* were isolated by Bagchi *et al.*, 1991 [73]. Bagchi *et al.*, 1990 isolated a new sesqui terpenoid 1 from the roots of *N. jatamansi* and it has a novel spiranic sesqui terpenoid skeleton [74]. A new diethenoid, bicyclic ketone, $C_{15}H_{22}O$, named nardostachone, from the roots of *N. jatamansi* D. C was isolated by Sastry *et al.*, 1967 [75]. A new monoethynoid tricyclic tertiary alcohol, $C_{15}H_{24}O$, named calarenol, from the roots of *N. jatamansi.* D. c, was isolated by Sastry *et al.*, 1967 [76]. Shanbhag *et al.*, 1965 isolated several hydrocarbons, a new oxide, alcohols, a poloxygenated crystalline material together with eudesmol, elemol, sitosterol, angelicin and jatamansinol from the oil of the roots of *N. Jatamansi* [77]. Two terpenic coumarins, oroselol and jatamansin, from the oil obtained from the roots of *N. Jatamansi* was isolated by Shanbhag *et al.*, 1964 [78].

Poly herbal formulations

Singh *et al.*, 2015 studied the colouring effect of herbal hair formulations on graying hair. HD-3 formulation, having gudhal, *jatamansi,* kuth, kattha, amla, coffee and henna, was found to act synergistically in hair colouring action [79]. The neuropsycho-pharmacological effect of a polyherbal formulation (PHF) on the learning and memory processes in rats was investigated by Shah *et al.*, 2011 and found a significant decrease in transfer latency as compared to the control group in EPM [80]. Thorat *et al.*, 2009 evaluated polyherbal formulations for hair growing activity and confirmed that hair growth after treatment with oil exhibited a greater number of hair follicles [81]. The immunomodulatory and antioxidant activity of a polyherbal formulation that increased the rate of carbon clearance and the percent neutrophil adhesion to nylon fibres was assessed by Meera *et al.*, 2008 [82]. Kolte *et al.*, 2008 evaluated the efficacy of herbal formulation in subclinical 24 mastitic cows and were found effective in restoring the altered milk constituents in subclinical mastitis with increased milk production [83]. The antidepressant activity of a polyherbal formulation Anximin was investigated by Mishra *et al.*, 2008 and found that it possesses antidepressant activity acting through 5-HT2A receptors [84]. The effects of a polyherbal formulation Abana that reversed the amnesia induced by scopolamine and diazepam, was investigated by Vasudevan *et al.*, 2008 [85]. Dandagi *et al.*, 2008 explored the hepatoprotective activity of a polyherbal formulation, has shown the significant hepat protective effect by reducing the elevated serum enzyme levels [86]. The effect of PHF (Abana) on the radiation-induced mortality in mice was studied by Jagetia *et al.*, 2003 and the LD50 value was found to be 1.8 g/kg body weight [87].

CONCLUSION

Medicinal plants have a promising future as there are about half million plants around the world, and most of them have many biological activities which have not been investigated yet. The rhizomes and roots of the plant have medicinal value and, therefore, have been the focus of chemical studies. *N. jatamansi* is an important plant of Ayurvedic materia medica. The rhizomes of the plant are used in the Ayurvedic system of medicine as a bitter tonic, stimulant, antispasmodic, and to treat hysteria, convulsions, and epilepsy [88]. The root has been medically used to treat insomnia and blood, circulatory, and mental disorders. Some preparations of the plant have been used as a heptatonic, cardiotonic, analgesic, and diuretic in the Unani system of medicine [89].

CONFLICT OF INTERESTS

Declared none

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