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Potentiating effect of N. Jatamansi root extract by evaluating anti-depression and anxiolytic activity in rats

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Abstract
Depression is considered as affective disorder characterized by change in mood, lack of interest in the surrounding. It is one of the mental health problems of people all over the world. Depression is a multifaceted condition characterised by episodes of mood disturbances alongside other symptoms such as anhedonia, psychomotor complaints, feelings of guilt and suicidal tendencies, all of which can range in severity. Anxiety and fear can be defined as response of subject to real or potential threats that may impair his/her homeostasis that can significantly mark function and quality of life. Some of depressive disorder overlap those of anxiety disorders, including severe phobias, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder. Anxiety-related disorders such as patient's nervousness, obsessive compulsive disorder and post-traumatic stress are foremost causes of infirmity in the world. Antidepressant and anxiolytic drug are the drug use for treatment of depression and anxiety but there are several side effect of these drug were observed like dry mouth, mental confusion, weakness and sedation. So, we evaluate the anti-depressant and anti-anxiety effect of N. Jatamansi root extract in rats by dose dependent manner. The behavior assessment observed by force swim test, locomotor activity, tail suspension test and elevated plus maze for depression and anxiety experimentation. The drug given 150mg/kg and 300mg/kg by oral route. The study observed that the ethanolic root extract reduced depression and anxiety generated by force swim test, tail suspension method, actophotometer and elevated plus maze.

Keywords: N. Jatamansi, depression, anxiety, obsessive compulsive disorder

Introduction
Depression and anxiety are two of the commonest psychiatric disorders worldwide (Ebmeier *et al*., 2006; Kessler *et al*., 2012, Silvia M *et al*., 2019) [11, 23, 44]. Depression is one of the main mental health problems of people all over the world, and it is connected with many disabilities (Ren S *et al*., 2015, Govindarajan VS *et al*., 1982, Mohammad S *et al*., 2015) [38, 17, 18, 30]. Depression is a multifaceted condition characterised by episodes of mood disturbances alongside other symptoms such as anhedonia, psychomotor complaints, feelings of guilt and suicidal tendencies, all of which can range in severity (Ebmeier *et al*., 2006, Silvia M *et al*., 2019) [11, 44]. It may range from a very mild condition, bordering on normality, to severe psychotic depression accompanied by hallucinations and delusions (Rang HP *et al*., 2008, Mithun S *et al*., 2011) [37, 29]. Major depression is distinguish by feelings of enormous sadness and despair, mental slowing and loss of concentration, pessimistic worry, lack of pleasure, self-deprecation, and variable agitation or hostility. Somatic changes also occur, particularly in severe, vital, or melancholic depression. These comprise insomnia or hypersomnia, altered eating motif, with starvation and slimming or sometimes overeating; decreased vitality and libido; and disruption of the normal circadian and ultradian tempo of activity, body reversal, and many endocrine functions (Tondo L *et al*., 2003, Mithun S *et al*., 2011) [46, 29]. The primary clinical reflexion of major depression are significant depression of mood and impairment of function.

Some features of depressive disorder overlap those of the anxiety disorders, including panicagoraphobia syndrome, severe phobias, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder (American Psychiatric Association., 2000, Mithun S *et al*., 2011) [3, 29]. World Health Organisation, depression affects over 350 million individuals and is the global leading cause of disability (Smith, 2014; Greenberg *et al*., 2015, Silvia M *et al*., 2019) [45, 20, 44]. Anxiety-related disorders such as patient's nervousness, obsessive compulsive disorder and post-traumatic stress are the

foremost causes of infirmity in the world (Barua CC *et al*., 2012) [8]. Currently, the most common approved medicines for anxiety disorders are benzodiazepines. Nevertheless, the medical uses of benzodiazepines are restricted by their side effects such as psychomotor destruction, potentiating activity of other sedatives and reliance liability (Latha K *et al*., 2015, Mohammad S *et al*., 2015) [26, 30]. It is a persistent illness that changes thoughts, mood and behavior of any person and has been expected to affect up to 21% population of the earth (Govindarajan VS *et al*., 1982) [17, 18]. Synthetic drugs taken as antidepressant in proper dosages are regularly connected with their anticipated reactions like powerlessness in driving abilities, dry mouth, sexual brokenness and blockage and most of patients are hesitant to take this type of treatment (Govindarajan VS *et al* 1982) [17, 18]. Consequently, natural plants may be potential sources of novel antidepressant drugs and the usage of plant extracts and their phytoconstituents may act as refined means in the management of depression and anxiety (Mohammad S *et al*., 2015) [30].

Nardostachys Jatamansi (Family *Valerianaceae*) is widely used in several Asian countries as a bitter tonic, a stimulant and an antispasmodic, as well to treat epilepsy, hysteria, coria, palpitation and convulsion, also have been used to treat syncope an mental weakness (Bagchi *et al*., 1991, Gi-sang B *et al*., 2011) [6]. Various sesquiterpenes, such as jatamansic acid, jatamansone, lignance, and neoligance are present in the roots of plants (Aora RB *et al*., 1965, chatterji A *et al*., 1997, Gi-sang B *et al*., 2011) [5, 10]. The species has very prolong history of use as medicine in ayurvedic, Homeopathic, ethno medicine and Indian System of Medicine (ISM) to modern medicinal industry which is dispense in the Himalaya from Pakistan, India (Jammu and Kashmir, Himachal Pradesh, Uttarakhand, and Sikkim) to Nepal, Tibet and China (Nayar MP *et al*., 1988) [31]. It is acquire from wild and cultivated plant in Britain. The Netherlands, Belgium, France, Germany, Eastern Europe and Japan. Polyploidy occurs in *V. officinalis*and there are diploid, tetraploid, and octaploid type (Evans WC *et al*., 2008, Purnima *et al*., 2015) [13, 33, 34]. Sesquiterpenes and coumarins are present in considerable amount in the roots of *Jatamansi* plant mainly responsible for its essential oil (Chatterjee B *et al*., 2005) [9]. It has protective effect in epilepsy, cerebral ischemia, liver damage (Ali S *et al*., 2007 [2], Anonymous. The Wealth of India; vol2., 20010. Alcoholic extract of NJ are protective against thiacetamide-induced liver damage in rats (Bagchi *et al*., 1991, Gi-sang B *et al*., 2011) [6]. In Ayurveda, *N. Jatamansi* is used for 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 problem, jaundice and kideney complaints, insomnia and headache. Externally, it is used as oil in steaming bath to treat inflammation of the uterus. (Alam F *et al*., 2016) [14, 15]. It has ben also used as herbal combination with other herb to evaluate depressant activity (Indurwade and Biyani 2000, Vidya S *et al*., 2015) [22, 48]. The bimonthly treatment with an alcoholic root extract of *N. Jatamansi* caused an overall increase in the level of central monoamines and inhibitory amino acid, including a change in the level of serotonin, 5-hydroxyindole acetic acid, gamma-amino butyric acid and taurine in rat brain gives antidepressant action (Shastry Sd *et al*., 1967, Firoj A *et al*., 2016) [42, 14, 15]. For evaluating potentiating of N. Jatamansi we performed antidepressant and anxiolytic activity of extract.

Materials and Method

Materials

a. Procurement of experimental animals: The albino rats (Wister strain) of either sex weighing 150-200g, bred in the animal house of 'Kamla Nehru College of Pharmacy', Butibori, were procured. The animal were housed in polypropylene cages at a temperature of 25±2°C with relative humidity of 40-56% and 12 hrs.light dark cycle. Animal were fed with a balanced diet and water ad libitum during the complete experiments. All animal experiment were approve by the Institutional Animal Ethical Committee of Kamla Nehru College of Pharmacy, Butibori, Nagpur.

b. Plant material collection and authentication: The *N. Jatamansi* root were collected from Nagpur district, Maharashtra, India. The plant was identified an authenticated by "Post graduate" Teaching Department of Botany, Rashtrasant Tukadoji Maharaj, Nagpur University, Nagpur.

c. Drugs and Chemicals: Chemicals required for extraction and animal study was procured from institutional store. Distill water was used throughout the studies. The drugs and chemicals are listed below.

Table 1: Drugs and Chemical

Drugs and Chemical	Source/Supplier
Diazepam	Watson laboratories. Inc, Corona.
Imipramine	West-ward Pharmaceuticals corporation.
Ethanol	Chagshu Hongsheng Fine Chemicals Corporation Ltd.

Methods

1. **Drying and size reduction of *N. Jatamansi* roots:** The dried roots of N. Jatamansi roots were dried in shed and powdered to #22 mesh size, stored in airtight container till further use (Purushottam K *et al*., 2016)
2. **Soxhlet extraction of N. Jatamansi root:** The dried root of N. Jatamansi was coarsely powdered. 50gm of the powder was wrapped in a filter paper and put into a thimble with 500ml 0f 95% ethanol in a round bottom flask and subjected to Soxhlation for 6-8 hours. Dark brown solution of extract with alcohol was collected. Dark brown paste like extract was obtained after evaporation of alcohol (Purushottam K *et al*., 2016).
3. **Dose preparation and administration of extracts:** The ethanolic extract of *N. Jatamansi* root was found to be non-toxic up to the dose of 200mg/kg and did not cause any death, therefore it is considered as safe. The biological evaluation was carried out at 150mg/kg and 300mg/kg dose level. The extract was concentrated on water bath at at a temperature not exceeding 60 °C. The % Yield of the extract was 6%. Ethanolic extract of N. Jatamansi was administered at a dose of 150mg/kg and 300mg/kg orally (Purushottam k *et al*., 2016).

Sr. No.	Solvent	Extraction Process	% Yield
1	Ethanol (90%)	Soxhlation	6%

Results:

Anti-depressant activity

1. **Forced Swim test:** The FST is the most widely used Pharmacological model for assessing antidepressant activity. The occurence of immobility when the rodent

are put down in an inescapable cylinder of water through back the cessation of persistent escape directed behavior. The apparatus consisted of a clear Plexiglas cylinder (20cm high x 20cmdiameter) filled to 15 cm depth with water during test session the immobility time was recorded for 5 min, when the mice makes no further attempts to escape and make only movement to keeps it's above the water the water (Satish Rao *et al*., 2013) [43].

2. **Tail Suspension Test:** The TST is the second method used for assessing the depressive state. A cord of about 50 cm in length was stretched between two metal tripods at a height of 70 cm tape. After the initial period of vigorous motor activity the mice became still and the immobility time was measured with a stopwatch, for a total duration of 5minute. Mice were considered immobile when the hung passively and completely motionless (Satish Rao *et al*., 2013) [43].
3. **Locomotors activity:** The locomotor activity was measured by using actophotometer. The actophotometer consisted of a square area (30x30x25cm) with wire mesh bottom, in which the animal moves six light photocells were place in the outer periphery of the bottom such a way that a single mouse can obstruct only one beam. The movement of the animal interrupt a beam of light falling on photocell, at which a count was recorded and display digitally. The locomotor activity was measured for a period of 10 minute. Technically its principle is that, a photocell is activated when the rays of light falling on the photocell are cut off by animal crossing the beam of light. As the photocell activated, a count is recorded. The photocells are connected to an electronic automatic counting device which count the number of 'cut off'.
4. **Elevated plus maze:** EPM test is the commonly used behavioral paradigm to assess the anxiolytic behavior in rodents. Briefly, the apparatus consisted of two open arms (5x5cm) and two closed arm (30x5x15cm) that extended from a common central platform (5x5cm). The entire maze was elevated to a height of 60 cm from the floor level (Lister, 1987). Testing was conducted in a quiet room that was illuminated only by a dim light. Each mouse was placed individually at the center of elevated plus maze with its head facing toward an open arm and its behavior was observed for a period of 5 minute using any maze software. During the test period, the number of entries into open arm, closed arm and time spent in each arm and percentage of time spent on the open arms was determined.

Observations

Anti-depressant activity

Table 2: Force swim test

Sr. No.	Body weight (gm)	Drug	Dose (mg/kg)	Immobility time (Sec)	% Decrease in immobility
Vehicle (Control)					
Mean SEM	178.2	Control	-	20.5	100
Treated (Standard)					
Mean SEM	178	Imipramine	2	9.5	46.34
Treated (N. Jatamansi)					
Mean SEM	180.5	N. Jatamansi	150	12.75	62.19
Mean SEM	184.25	N. Jatamansi	300	10.7	48.78

Table 3: Tail Suspension method

Sr. No.	Body Weight (gm)	Drug	Dose (mg)	Immobility Time (Sec)	% Decrease in Immobility
Vehicle (Conrtol)					
Mean SEM	177.5	Control	Saline	74	100
Treated (standard)					
Mean SEM	178	Imipramine	10	46	62.16
Treated (N. Jatamansi)					
Mean SEM	180.5	N. Jatamansi	150	63.25	85.47
Mean SEM	182.75	N. Jatamansi	300	50.25	67.90

Table 4: Locomotor activity

Sr. NO.	Body Weight (gm)	Drug	Dose (mg/kg)	Before Treatment	After Treatment	% Changes
Treated (Standard)						
1	178	Imipramine	10	41	61	173.17
2	175	Imipramine	10	68	88	129.41
3	174	Imipramine	10	52	72	138.46
4	184	Imipramine	10	69	89	128.98
Treated (N. Jatamansi)						
1	176	N. Jatamansi	150	42	48	114.28
2	183	N. Jatamansi	150	44	51	115.90
3	186	N. Jatamansi	150	69	74	107.24
4	177	N. Jatamansi	150	41	44	107.31
1	179	N. Jatamansi	300	40	69	172.05
2	181	N. Jatamansi	300	66	85	128.78
3	192	N. Jatamansi	300	50	60	120
4	185	N. Jatamansi	300	68	86	126.47

Anxiolytic Activity

Table 5: Elevated plus Maze (EPM)

Sr. No.		Number of Entries		Time spent (sec)		% Preference to open arm
1	Vehicle control	8	23	18	35	-
2	Standard	15	20	30	48	166.6
3	NJEE (150mg/kg)	11.25	13	20.5	146.7	113.6
4	NJEE (300mg/kg)	14.5	12.25	28.5	140	158.3

Discussion

N. Jatamansi is an vital herb with multiple remedies. It is essential plant of Ayurvedic material medica. Present study state that the N. Jatamansi has numerous pharmacological activity, thereby enlarging the use of it. The study conducted was to evaluate the anti-depressant and anxiolytic activity of N. Jatamansi in rats to provide scientific evidence for its usage in the treatment of depression and anxiety. From the above results obtained the administration of ethanolic extract of N. Jatamansi in rats produced reduction of depression and anxiety in dose dependent manner. To determine whether there was statistical difference in depression and anxiety achieved by the two doses (150 and 300 mg/kg). Orally administered, the data were compared with the standard (Diazepam and imipramine) group. The ethanolic extract of N. Jatamansi produced a significant reduction in depression and anxiety.

From the study observed that the ethanolic extract of the N. Jatamansi reduced depression and anxiety generated by forced swim test, tail suspension method, actophotometer and EPM.

Summary

Depression is considered as an effective disorder characterized by change in mood, lack of interest in the surrounding retardation and melancholia which is hilled by anti-depressant, anxiety and fear can be define as the response of a subject to real or potential threats that may impair his/her homeostasis that can significantly mar the function and quality of life. *N. Jatamansi* study on the two group having different concentration of the drug *N. Jatamansi* (150 and 300 mg/kg). Animal were grouped as control standard and treated with *N. Jatamansi* (150 and 300 mg/kg). The instrument used for thise is forced swim test, tail suspension method, actophotometer and EPM and the ethanolic extract of *N. Jatamansi* shows the anti-depressant and anxiolytic activity in the rat.

Conclusion

The finding of the present study suggested that the ethanolic extract of N. Jatamansi roots had anti-depressant and anxiolytic activity. It can be over that ethanolic extract of N. Jatamansi has dose dependent anti-depressant activity and can also be used in patient suffering from depression due to sleep disturbances which also improve the locomotor activity in sleep deprived rat. So, *N. Jatamansi* will be an important plant to carry research for anti-depressant activity. The result from the study observed the anxiolytic properties of the herb in rat and suggest that the herb could serve as a approach in the treatment of anxiety.

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