Available online on 15.06.2024 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Research Article

Examining the Bioactive Elements of *Urtica urens* Hydroalcoholic Extract and Its Possible Antidepressant Effects in Mice

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Article Info:

Article History:

Received 09 March 2024
Reviewed 21 April 2024
Accepted 23 May 2024
Published 15 June 2024

Cite this article as:

Bhagat A, Shrivastava S, Examining the Bioactive Elements of *Urtica urens* Hydroalcoholic Extract and Its Possible Antidepressant Effects in Mice, Journal of Drug Delivery and Therapeutics. 2024; 14(6):70-73

DOI: http://dx.doi.org/10.22270/jddt.v14i6.6567

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Abstract

The majority of antidepressant medications reduce depression symptoms, but they also have a number of undesirable side effects. The hunt is on for medications that are both more effective and well-tolerated. In light of this, the current investigation set out to assess the hydroalcoholic extract of Urtica Urens L.'s aerial parts' (HAUU) antidepressant potential in mice. The Tail Suspension Test (TST) and the Forced Swimming Test (FST) on mice were used to assess it. For 14 days, the HAUU (250 and 500 mg/kg, po) was given orally to distinct groups of 20–25-weight Swiss albino mice in order to conduct TST and FST testing. The presence of alkaloids, glycosides, phenols, flavonoids, and tannins was discovered through phytochemical examination. The HAUU demonstrated a dose-dependent decrease in the amount of time that mice were immobile. Mice's immobility duration was considerably shortened in both the FST and TST when 500 mg/kg of HAUU was administered. The extract's effectiveness was discovered to be on par with fluoxetine (20 mg mg/kg, po). It was discovered that when given orally at a dose of 2000 mg/kg, it was toxicologically safe and did not cause any mouse deaths. The results of the current investigation indicate that the HAUU is toxicologically safe and has strong antidepressant activity, as demonstrated by the TST and FST tests.

Keywords: Urtica Urens L, Depression, Tail suspension test, Forced swimming test, Fluoxetine

INTRODUCTION

In 2000, depression ranked fourth in the world in terms of disease burden and was the primary cause of disability. Depression is currently the second leading cause for both sexes combined in the 15-44 age group. For men, the lifetime risk of depression is from 5% to 12%, whereas for women it is 10% to 25%. One of the main outcomes of the majority of depressive disorders is suicide. Depression and associated diseases account for about 60% of deaths[1]. Emotional and physical symptoms, including feelings of worthlessness, powerlessness, hopelessness, guilt or indecision, appetite changes, sleep patterns, agitation, mental and motor slowing, loss of interest, pleasure, and social withdrawal, are some of its hallmarks[2]. Centella asiatica, Rauwolfia serpentine, Hypericum perforatum, and Withania somnifera are considered to be potential new antidepressant herbs without side effects. Antidepressant drugs, such as tricyclic antidepressants and selective serotonin reuptake inhibitors, are used to treat depression, but they have a variety of side effects. Our knowledge of the neurobiology of depression has significantly increased throughout decades of scientific and clinical neuroscience study. With a strong foundation underpinning it, basic and clinical neuroscience research is advancing quickly and has great promise for the future. Crucially, new targets for treatment are emerging as our understanding of the pathophysiology of depression deepens. There is no scientific evidence supporting this plant's antidepressant properties[3]. Thus, the main objective of our research was to assess Urtica Urens Linn's potential as an antidepressant in lab animals[4]. Common names for the leaves of Urtica urens L. (Urticaceae) include annual nettle, dwarf nettle, little nettle, dog nettle, and flaming nettle. These leaves have a comparatively high (66%), higher-quality protein content than other green vegetables[5]. Nettle leaves are an excellent source of several important minerals and vitamins[6, 7]. Flavonoids, fatty acids, terpenes, protein, vitamins, and minerals are all present in nettles. The leaves of stinging nettles are high in calcium, iron, magnesium, phosphorus, potassium, sodium, and B group and vitamin K vitamins[8]. Nine carotenoids are found in nettle leaves: the three primary carotenoids are lutein, lutein isomers, and b-carotene[9]. Therefore, the goal of this study was to assess the hydroalcoholic extract of Urtica Urens L's aerial parts' antidepressant effect in mice by employing the Tail Suspension Test (TST) and Forced Swimming Test (FST).

MATERIALS AND METHODS

Plant material

Aerial parts of *Urtica urens* were collected from local area of Bhopal (M.P.) in the month of December, 2018.

Chemical reagents

All the chemicals used in this study were obtained from Hi Media Laboratories Pvt. Ltd. (Mumbai, India), Sigma Aldrich Chemical Co. (Milwaukee, WI, USA), SD Fine Chem. Ltd. (Mumbai, India) and SRL Pvt. Ltd. (Mumbai, India).All the chemicals used in this study were of analytical grade.

Extraction of plant material

Urtica urens aerial components were gathered, thoroughly cleaned, and rinsed. They were mechanically powdered after being dried in the shade. For the purpose of extracting phytochemicals, approximately 100 grams of the plant powder were macerated with 80% methanol and kept for 48 hours. Whatmann No. 1 filter paper was used to filter the extract after it had been left for 48 hours in order to get rid of any material that could not be extracted, such as cell debris and other substances that were insoluble in the extraction solvent. Using a rotary flash evaporator operating at lower pressure, the extract was fully concentrated to dryness and then preserved in a contaminant-free, airtight container until needed. Ultimately, the dried extracts' % yields were computed.

Qualitative phytochemical analysis of plant extract

The *Urtica urens* extract obtained was subjected to the preliminary phytochemical analysis following standard methods by Khandelwal and Kokate[10,11]. The extract was screened to identify the presence or absence of various active principles like phenolic compounds, carbohydrates, flavonoids, glycosides, saponins, alkaloids, fats or fixed oils, protein and amino acid and tannins.

Animals

In the present investigation the Swiss albino mice (20-25 gm of either sex) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C, 55–65%). Mice received standard rodent chow and water *ad libitum*. Mices were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of mices was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Acute oral toxicity

Acute toxicity studies were performed according to OECD (Organization for Economic Co-operation and Development) 425 guideline. Animals were acclimatized to laboratory condition five days prior to the experiment. Body weight of animals was recorded and individual identification was done, fixed dose method: Test procedure with a starting dose of 2000 mg/Kg body weight of hydroalcoholic extract aerial parts of *Urtica urens* L. Starting dose of extract was administered orally to 5 animals and animals were observed for behavioral changes and death. No animals were found dead after 14 days. The study was repeated with same dose and again no death was observed[12].

Evaluation of antidepressant activity

Forced swimming test (FST)

The FST is the most widely used pharmacological *in vivo* model for assessing antidepressant activity. Mice were individually placed in cylinder (45×20 cm) containing 15 cm water (25±2°C), so that it could not touch the bottom of the cylinder with its hind limb or tail, or climb over the edge of the chamber. Mice were divided into groups of 4 and received the hydroalcoholic extract aerial parts of *Urtica urens* L at different doses *viz*. 250 and 500 mg/kg and fluoxetine (20mg/kg) was used as standard drug. One hour post administration each mice were placed individually in a tank. Period of immobility (i.e. the total time the animal remained floating in water without struggling and making only those movements necessary to keep its head above water) during the 6 min test period was measured[13].

Tail suspension method

Each mouse in the group was suspended individually by the end of tail (50 cm above the floor) with adhesive tape placed approximately 1cm from the tip of the tail. Mice were divided into groups of 4 and received hydroalcoholic extract aerial parts of *Urtica urens* L at different doses *viz*. 250 and 500 mg/kg control and fluoxetine (20mg/kg) was used as standard drug on the test day after 60 min of the administration of last dose. The Duration of immobility was observed for a period of 8 minutes. After the early escape oriented actions, the rat rapidly turns out to be immobile and immobility (when it did not show any movement of body and hanged passively) was recorded during last 5 min of observation period[14].

Statistical Analysis

The data were expressed as mean ±standard error mean (SEM). The significance of differences among the groups was assessed using one way analysis of variance (ANOVA). The test was followed by Dunnett's'-test, p values less than 0.05 were considered as significance.

RESULTS

The crude extracts so obtained after maceration extraction process was concentrated on water bath by evaporation the solvents completely to obtain the actual yield of extract. The yield of extracts obtained from the aerial part of the plants using hydroalcoholic (Water: Methanol 20:80) as solvents are depicted in the Table 1. The results of preliminary phytochemical screening tests revealed the presence of saponins, diterpines, carbohydrates and amino acids in the crude extract (HAUU) Table 2. The extract HAUU was studied for acute toxicity at doses of 2000 mg/kg b.wt., po. The extract was found devoid of mortality of all animals. So, the doses selected for the antidepressant activity were 250 and 500 mg/kg, po. In forced swim test, the immobility time of control, test (250and500mg/kg) and standard was 132±1.80, 102±1.64 *, 78±2.42** and 65±0.65** respectively. The immobility time of test and standard was significant (**p < 0.01) and more significant (***p< 0.001) respectively. The immobility time decreases with increase in dose of the extract. The immobility time of test was gradually decreases when compared to control. Mice pretreated with hydroalcoholic extract of aerial parts of *Urtica urens* L show significant improvement in the swimming time as compared to standard control. The antidepressant effect of the *Urtica urens* L was prominent at 500mg/kg. In the forced swimming test all the doses administered were able to reduce immobility time and simultaneously enhance swimming Table 3. In the tail suspension test, the mice shown immediate sign of struggles or escape like behaviors when they were suspended in the air followed by temporary increasing periods of immobility. The tail suspension method revealed in the present study that anti stress activity increases with decrease in immobility time compared to control mice of *Urtica urens* L. In tail suspension test, the immobility time of control, test (250 and500 mg/kg) and standard was 218±2.64, 198±3.74*, 174±2.68** and 162±2.48** respectively. The immobility time of test and standard was significant (**p < 0.01) and more significant (***p < 0.001) respectively. The immobility time decreases

with increase in dose of the extract. The immobility time of test was gradually decreases when compared to control Table 4.

Table 1: % Yield of hydroalcoholic extract

S. No.	Plant	% Yield (w/w)
1.	**Aerial parts of *Urtica urens***	3.8%

Table 2: Result of phytochemical screening of hydroalcoholic extract

S. no.	Constituents	Hydroalcoholic extracts
1.	**Alkaloids**	
	Dragendroff's test	-ve
	Wagner's test	-ve
	Mayer's test	-ve
	Hager's test	+ve
2.	**Glycosides**	
	General glycosides test	-ve
3.	**Flavonoids**	
	Lead acetate test	+ve
	Alkaline test	-ve
5.	**Phenolics**	
	$Fecl_3$ test	-ve
6.	**Amino acids**	
	Ninhydrin test	+ve
7.	**Cabohydrates**	
	Molichs test	+ve
8.	**Diterpines**	
	Copper acetate test	+ve
9.	**Saponins**	+ve

Table 3: Effect of extract of *Urtica urens* L on animal in forced swim test

Group	Treatment	Immobility time (in Sec.)
Group 1	Control-Water	132±1.80
Group 2	HAUU (250 mg/kg, p.o.)	102±1.64 **
Group 3	HAUU (500 mg/kg, p.o.)	78±2.42**
Group 4	Fluoxetine (20 mg/kg. p.o.)	65±0.65***

Each values represents the mean±SEM; (n=6), *p<0.05, **p<0.01, ***p< 0.001 respectively when compared with control group (one-way ANOVA followed by Dunnett's test).

Table 4: Effect of extract of *Urtica urens* L on animal in tail suspension test

Group	Treatment	Immobility time (in Sec.)
Group 1	Control-Water	218±2.64
Group 2	HAUU (250 mg/kg, p.o.)	198±3.74 **
Group 3	HAUU (500 mg/kg, p.o.)	174±2.68**
Group 4	Fluoxetine-(20 mg/kg. p.o.)	162±2.48**

Each values represents the mean±SEM; (n=6), *p<0.05, **p<0.01, ***p< 0.001 respectively when compared with control group (one-way ANOVA followed by Dunnett's test).

DISCUSSION

Today's antidepressant medications in the health center come with a high price tag, a variety of adverse effects, and a heterogeneous therapeutic response. Moreover, 70% of patients treated for depression experience a complete improvement with conversional antidepressant medication[15]. As a result, research into the potential antidepressant properties of herbs is receiving more and more attention[16]. Herbal-based medical therapies have garnered substantial attention in the past ten years due to the increasing body of studies on their potential benefits in treating depression[17,18]. Aerial sections of Urtica Urens L have been investigated in this regard. In TST and FST[1] tests, it was found that HAUU, at dosages of 250 and 500 mg/kg b.wt, significantly reduced immobility duration in a dose-dependent manner in comparison to the control group. As anticipated, the animals given Fluoxetine (20 mg/kg b.wt) also had a notable reduction in the amount of time they were immobile. When the animals are given medication that raises serotonin, norepinephrine, and dopamine levels in the nerve terminals, they exhibit greater swimming and climbing activities in the FST[19]. An increase in all three neurotransmitters may result from a reduction in the brain's monoamine oxidase (MAO) activity. An increasing amount of research suggests that depression may also arise from a number of different pathophysiological pathways in addition to the depletion of serotonin and catechoamine neurotransmitters. According to research, depression may prevent hippocampal neurogenesis[20,21]. The observation that antidepressants can stimulate neurogenesis lends credence to this theory[22]. When given orally at a dose of 2000 mg/kg, the hydroalcoholic extract of the aerial portions of Urtica Urens L. has no toxicological effect and appears to have potential antidepressant effects in mice, as demonstrated by the TST and FST tests. The HAUU demonstrated a dose-dependent decrease in the amount of time that mice were immobile. The extract's effectiveness was discovered to be on par with fluoxetine (20 mg/kg, po).

CONCLUSION

From the present study, it can be concluded that The hydroalcoholic extract of the aerial parts of *Urtica Urens* L possess potent antidepressant activity as shown by the TST and FST tests and is toxicologically safe.

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