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Antidepressant-like effects of methanolic extract of *Xanthium strumarium* (*Asteraceae*) in mice

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Abstract

Plants and other natural substances have been used as the rich source of medicine. *Xanthium strumarium* plant is reported in ethno-pharmacological study as medicinal plant. Several phytochemical and pharmacological experiments already done of *X. strumarium*. However, there are no scientific reports about the antidepressant-like activity of *X. strumarium*. The aim of study is evaluation the antidepressant-like activity of methanolic extract of *Xanthium strumarium* (MEXS).The antidepressant-like activity evaluated by Tail Suspension Test (TST). Administration of MEXS extract of 50, 100, and 200mg/kg significantly ($p< 0.001$) decreased the immobility periods of mice when compared to the control group (0.9% normal saline water), indicating significant antidepressant-like activity. The positive control imipramine hydrochloride (30mg/kg) also showed similar effect as MEXS.The experimental data clearly demonstrate that the methanolic extract of *X. strumarium* possesses antidepressant-like activity in the animal model.

Keywords: *Xanthium strumarium*;Ethno-pharmacological; Tail Suspension Test; Antidepressant; Imipramine hydrochloride

Introduction

Plants produce a diverse range of bioactive compounds as a rich source of different types of medicines. Higher plants as sources of medicinal compounds have continued to play a dominant role in the maintenance of human health care since ancient period (1). *Xanthium strumarium* L. is a cocklebur or burweed commonly found as a weed in roadsides, rice fields, hedges throughout the tropical parts of Bangladesh and India subcontinent (2). The genus *Xanthium* (Family: *Asteraceae*) is imparted by 25 species, amongst them three species and one variety found in Bangladesh (3). The word "Xanthium" derived from an ancient Greek word "Xanthos" meaning yellow and "strumarium" means "cushionlike swelling," which turn from green to yellow as they ripen (later they become deep yellow to brown) (4). Alternate triangular-ovate or suborbicular leaves, light and bright green in color in an alternate pattern with irregular lobes as well as relatively inconspicuous teeth such as 5–15 cm long, often three-lobed, prominent veins, long petiole, scabrous on both sides.

X.strumarium, used as renowned herbal medicines in China, Europe, Indo-China, Malaysia and America(5).Chinese people used *X. strumarium* fruits for the treatment of different kind inflammatory diseases including bronchitis, chronic rhinitis, allergic rhinitis, lumbago, tympanitis, urticaria and arthritis,ozena and other ailments(6). It has also reported that *X. strumarium* used as a medicine for curing nasal sinusitis, vomiting, and headache (7).Various Native American tribes used *X. strumarium* to relieve constipation and diarrhea (8). In southern part of Bangladesh, people used *X. strumarium* for the treatment of several ailments including asthma, diabetes mellitus, jaundices, gastritis (upper abdominal discomfort), urinary disorders and as blood purifier(9).

X. strumarium leaves have reported to contains alkaloids, flavonoids (flavonol), (10) anthraquinone, cardenolide, leucoanthocyanin, simple phenolics (Catechol) and triterpenoids(11). Several studies have reported *X. strumarium* include phenolic compounds as thiazolidinediones, chlorogenic acids, ferulic acids (12), 1,3,5-tri-*O*-caffeoyl quinic acid, 1,5-di-*O*caffeoyl quinic acid, caffeic acid (13), as well as isoprenoids such as stigmasterol, â-sitosterol(14), monoterpene and sesquiterpene hydrocarbons (15), triterpenoid saponins(16).

Earlier study reported that *X. strumarium* has significant anti-inflammatory and analgesic properties in mice [17]. The whole plant used to treat cytotoxicity and antitumor activity [18]. Furthermore, several investigation has reported that *X. strumarium* possesses anti-ulcerogenic [19], anthelmintic [20], diuretic [21], antimicrobial, antioxidant [22], and antilipidemic activity [23]. *X. strumarium* traditionally used central nervous system (CNS) stimulant agent which may have potential antidepressant activity. Our current study designed to confirm the anti-depressant effects of *X. strumarium*in mice model.

Methods

Plant material and extraction : The fresh plant collected from the area of Narail district during the month of April, 2016. The *X. strumarium* was taxonomically identified by Chief Scientist and Taxonomist of Bangladesh. The leaves parts of the plant *Xanthium strumarium* washed with water to remove adhering dirt and then cut into small pieces, dried for 4 days and finally dried at 45ºC for 36h in an electric oven. After complete drying, the entire portions were pulverized into a coarse powder with help of a grinding machine and stored in an airtight container for further use. About 400g of powdered material soaked in methanol in a beaker at 25±2°C and mixture need to be stirred using a sterile glass rod. The solution filtered through a cloth; the marc strained through a special press. The crude extract used for the investigation of the antidepressant-like effect of the methanolic extract of *X. strumarium* in mice model.

Animals : Swiss albino mice selected for the recent experiment at the age of 3-4 weeks, weighing between 20-25g collected from Jahangirnagar University. Animals maintained under standard environmental conditions (temperature: (23±2ºC), relative humidity: 55-65% and 12h light/12h dark cycle). The animals acclimatized to laboratory condition for one week before the experiment. All protocols for the animal experiment approved by the institutional animal ethics committee, Jessore University of Science And Technology. Animals (1995) formulated by The Swiss Academy of Medical Sciences and the Swiss Academy of Sciences. All experimental rules approved by the Institutional Animal Ethical Committee of Jessore University of Science & Technology.

Drugs and treatments : The investigation of pharmacological activity of X. strumarium we used chemicals and drugs such as methanol (Merck, Germany), Imipramine hydrochloride (Square Pharmaceutical Ltd, Bangladesh) and 0.9% sterile normal saline solution (Beximco Infusion Ltd). The standard drug Imipramine hydrochloride (30mg/kg) used in antidepressant activity test. The MEXS (50, 100, and 200mg/kg) dissolved in Dimethyl sulfoxide (DMSO) whereas, the standard drug Imipramine hydrochloride (30mg/kg) prepared by 0.9% normal saline water.The test and standard groups received MEXS and drugs orally 30 min before the experiments. On the other hand, the control group received 0.1mL/mouse 0.9% normal saline water. All the groups received drugs and samples via gavage. All the chemicals and the drugs were analytical graded and highly purified.

Anti-depressant activity test

Tail suspension test : The tail suspension test (TST) conducted as initially described by *Steru et al.* (1985) with modifications (17). One hour after oral administration and 30min after intraperitoneal injection of test compounds, mice individually suspended by the tail from a horizontal ring-stand bar raised 30 cm above the floor using adhesive tape placed 1 cm from the tip of tail and positioned such that the base of their tail was aligned with the horizontal plane. Test sessions

lasted for 6min. Behaviors for the last 4 of the 6min period were then analyzed. Immobility was measured, a mouse judged to be immobile when it hung by its tail without engaging in any active behavior.

Statistical analysis : The results are presented as mean±SEM. The statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test as appropriate using SPSS 20 software. Differences between groups considered significant at a level of $p< 0.001$.

Result and discussion

The tail suspension test investigated anti-depressant activity of methanolic extract of *Xanthium strumarium* at the doses of 50,100 and 200 mg/kg body weight. TST induced immobility is reduced by a large number of clinically active and atypical antidepressant effect. The antidepressant activity of tail suspension test significantly ($p< 0.001$) increased at the dose of 50 mg/kg and 100mg/kg body weight mostly decreases the immobility time on test animals.MEXS at 200 mg/kg dose also observed decreases the immobility time of the test animals. The mean values of MEXS (50, 100, and 200mg/kg) compare to the negative control group. Dunnett's post hoc analysis demonstrated that the test treatments significantly decreased the duration immobility in comparison to the control group ($p< 0.001$). Likewise, the extract reduced the duration of immobility time in the tail suspension test (Table 1 and Figure. 1). Post hoc analysis confirmed that the extract significantly decreased the immobility time in comparison to the control group ($p< 0.001$).

The aims of this study assessed the antidepressant-like effect of MEXS using animal behavioral models.Our present study indicates that the antidepressant-like effect of MEXS found to comparable with the standard drug Imipramine hydrochloride (30mg/kg).Imipramine hydrochloride acts by inhibiting norepinephrine reuptake and has used as a standard drug in majority studies(18). The beneficial effects of Imipramine hydrochloride in TST model seems to be due to increased availability of these neurotransmitters (NE) and serotonin (5HT) at the postsynaptic site following reuptake inhibition(19). Some studies already have shown the adaptogenic effects of the plant extract via normalization of the various stress parameters and monoaminergic levels which may provide a hint that the extract is bringing their possible antidepressant-like effect through the restoration of normal monoaminergic NE(20). The action of the triterpenoid and saponins resulted in the enhancements of the nerve impulse transmission (21). Neurochemical assays suggested that treatment by triterpenoid and saponins improved brain antioxidant activity to varying degrees after the behavioral despair test(22).The pattern of CNS effects observed through this experiment suggests us the involvement of norepinephrine NE system on its antidepressant-like effect.

Conclusion

In conclusion, the effects of MEXS may possess antidepressant-like effect in the classical

Table1: Anti-depressant activity of MEXS on tail suspension test in mice.

Treatment	Dose	Duration of Immobility (seconds)
Control (saline water)	0.1ml/mouse	84±2.70
Imipramine	30 mg/kg	574±1.67*
MEXS	50mg/kg	560±1.58*
MEXS	100mg/kg	484±1.04*
MEXS	200mg/kg	404±1.76*

Each value represented as the mean±SEM (n=5), MEXS = Methanolic extract of *X. strumarium* leaves. *$p< 0.001$ compared with the control group (Dunnett's Test).

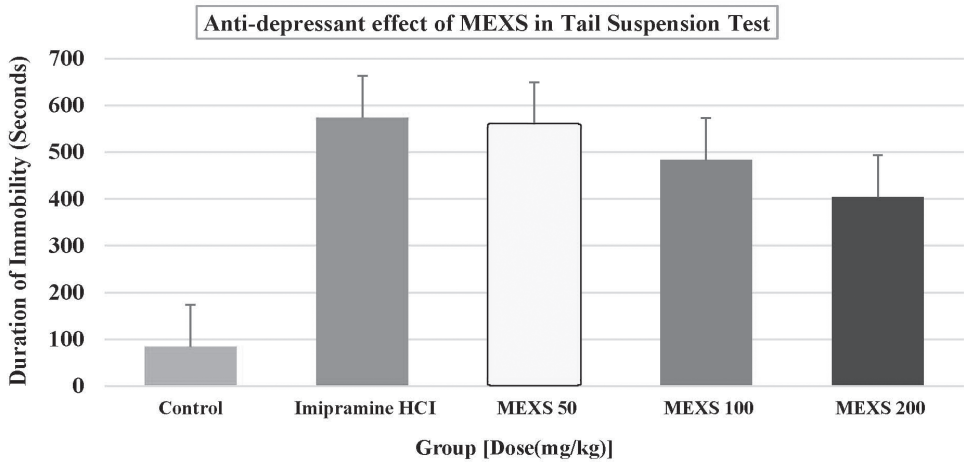

Fig. 1: Anti-depressant activity of MEXS on tail suspension test (duration of Immobility in second) in mice.

model like TST comparable to the standard drug Imipramine hydrochloride.However, further study must need to elucidate the mechanism of action of MEXS in the CNS, the pattern of effects observed in this experiment suggest the involvement of the norepinephrine neurotransmitters system on its antidepressant-like effect.Further investigation needs to identify and isolate the active compounds in *X. strumarium.*

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