



**International Journal of Biology, Pharmacy
and Allied Sciences (IJBPAS)**

'A Bridge Between Laboratory and Reader'

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ANTICATALEPTIC EFFECT OF *XANTHIUM STRUMARIUM* HYDROALCOHOLIC EXTRACT IN LABORATORY ANIMALS

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Received 16th Sept. 2022; Revised 25th Oct. 2022; Accepted 15th Nov. 2022; Available online 1st Aug. 2023

<https://doi.org/10.31032/IJBPAS/2023/12.8.7343>

ABSTRACT

Xanthium strumarium (*Asteraceae*) fruits have been traditionally used in the management of asthma and the current study was undertaken to scientifically validate the benefits of plant as an antihistaminic agent using the suitable animal model. The agents with antihistaminic properties are known to be good antiasthmatic agents; hence, in the current research work, the antihistaminic activity of anhydroalcoholic extract of *Xanthium strumarium* fruits (at a dose of 100 mg/kg, i.p) was evaluated using haloperidol-induced catalepsy and clonidine-induced catalepsy in laboratory rats. The results showed that, the hydroalcoholic extract inhibits the catalepsy induced by the clonidine but no remarkable effect was observed on the catalepsy induced by haloperidol. This strongly suggests that, the inhibition is mediated through an antihistaminic action and there is no role of dopamine. Hence, in the present study, it is concluded that, the hydroalcoholic extract has significant antihistaminic activity. The polar constituents in the hydroalcoholic extract of fruits of *Xanthium strumarium* may be responsible for the antihistaminic effects and therefore, the hydroalcoholic fruits extract can be a better remedy as an antihistaminic agent.

Keywords: *Xanthium strumarium*, Catalepsy, Asthma, Antihistaminic effects

INTRODUCTION:

Diverse range of bioactive compounds are produced by plants which are rich source of different types of medicine, therefore plants of medical sources have continued to play major role in human health maintenance since ancient periods. The genus *Xanthium* belongs to the family *Asteraceae*. *Xanthium strumarium* evolved from Greek word “Xanthos” means yellow and “strumarium” means “cushion like swelling” [1]. The goal of this work is to evaluate the effect of hydroalcoholic extract of *Xanthium strumarium* by acute administration to study cataleptic behavior [1] in laboratory animals. Isolation of phytoconstituents was done from dried fruits of *Xanthium strumarium*. The presence of alkaloids, flavonoids (flavanol), anthraquinone, triterpenoids, cardenolides, simple phenolics (catechol), leucoanthocyanin has been reported [2]. The plant was used in folk therapy for long period of time. From decoction and tinctures more than twenty properties of fruits and roots were found, for example antirheumatic, antisyphilitic, appetizer, diaphoretic, diuretic, emollient, laxative and sedative activities. On the basis of experimental pharmacology other actions such as anti-inflammatory, analgesic [3, 4], antibacterial, anticancer [5, 6], antifungal [7], antihypoglycemic [8],

antimitotic [9, 10], antitrypanosomal, antimalarial [11] were confirmed.

It is a cocklebur or burweed mostly seen as a weed on road sides, rice fields and tropical parts of Indian subcontinents, Bangladesh [12]. The plant has sub orbicular fruits, light green in color, in alternate fashion with lobes that are irregular. It also has inconspicuous teeth 5-15 cm long that are often three lobes, long petiole, prominent veins, scabrous on both sides [13]. *Xanthium strumarium* is popularly used medicine in China, Europe, Indo-China, Malaysia and America [14]. The fruits of this plant were used by Chinese people to treat various inflammatory diseases including bronchitis, chronic rhinitis, allergic rhinitis, lumbago, urticaria, tympanitis, arthritis, ozena and other ailments [15]. It is also used to cure nasal sinusitis, vomiting and headache [16]. Native American tribes also used *Xanthium strumarium* to relief constipation and diarrhea [17]. In southern Bangladesh it was used for the treatment of asthma, jaundice, diabetes mellitus, gastric discomfort, urinary disorders and as a blood purifier [18].

X. strumarium is an annual plant producing conspicuous prickly cocklebur and having height of about 0.5 to 6.5 ft. Its large and linear to oblong cotyledons is the

distinguishing feature of this weed in early stages of development. Its fruit is elliptical to egg shaped with double chambered bur about 0.5 to 1.5-inch-long covered with prickles. The fruit contain two seeds of which one grows during the first year and the other a year later. *Xanthium strumarium* grows in wide range of soils from sands to clays at available moisture. When grows in rich soil and abundance of water and having a little competition it is tall and large. Whereas when grows in poor soil it only is a few centimeters high, drought persistent and with set seeds. It's ability to grow in various soil environment helps it in continuous seed supply [19].

Catalepsy is a condition in which there is lack of response to external stimuli and rigidity in muscles, the limbs endure the same position in which they were placed. Catalepsy can also be induced in body with neuroleptic drugs. Catalepsy is caused by the drugs that increase the histamine release or inhibit the dopaminergic transmission in brain. Dose dependent catalepsy is induced by clonidine, a α_2 -adrenoceptor agonist and it is inhibited by histamine H_1 -Receptor antagonist but not by H_2 -receptor antagonist.

MATERIALS AND METHODS

PLANT MATERIALS

The fruit specimen of *Xanthium strumarium* were collected from Pune district (Maharashtra) in January 2022. The botanical survey of India, Pune authenticated the plant and the accession number of plant was DVPXST1.

ANIMALS

Three groups of male Wistar albino rats weighing 180-200gms were housed under standard laboratory condition with free access to food and water. Each group contain 6 animals for each model. The protocol was approved by IAEC (Institutional Animal Ethical Committee) of Progressive Education Society's Modern college of pharmacy, Yamunanagar, Nigdi, Pune -44.

DRUGS AND CHEMICALS:

The drugs used were: Clonidine (J.B.Chemicals and Pharmaceuticals LTD, Ankleshwar India), Haloperidol (ELIKEM Pharmaceuticals Pvt. Ltd. Gandhinagar, Gujarat, India.), and Pheniramine Maleate (ASPAR Impex, Surat, Gujarat, India); all the drugs and chemicals were procured from available commercial sources. Chemicals used were: Ethanol analytical grade (New Neeta Chemicals, India) and Tween-80 analytical grade (New Neeta Chemicals, India).

PREPARATION OF EXTRACT

For the process of extraction 300gms of dried fruits were powdered and macerated in 450 ml of ethanol:water (80:20) for period of three days at room temperature with occasional stirring, for dissolving the soluble portion completely. The final extract was then filtered and the marc was pressed. The yield of extract was found to be 13.25%.

PHYTOCHEMICAL ANALYSIS [20, 21]

Phytochemical analysis was done as per the reported procedure.

QUANTITATIVE ESTIMATION OF TOTAL PHENOLIC AND FLAVONOID CONTENT [22, 23]

The extract was quantified as per reported procedure.

ANTICATALEPTIC ACTIVITY

EFFECT ON CLONIDINE-INDUCED CATALEPSY:

The catalepsy bar test apparatus was used to analyze the effect of extract on clonidine-induced catalepsy. The groups I, II, III (n=6) were administered with saline, extract (100mg/kg i.p.) and standard medication pheniramine maleate (10mg/kg i.p.) respectively. 30-minutes prior treatment with the inducer clonidine (1mg/kg, s.c.) was administered. Considering the results of previous acute toxicity study the extract dose was selected. The forepaws of the rat were placed on the catalepsy bar (1cm in diameter

and 12 cm above table) and the catalepsy duration was measured at 0, 15, 30, 60, 90, 120, 150 and 180 minutes. The time taken by each rat to withdraw its paws from the bar was recorded.

EFFECT ON HALOPERIDOL-INDUCED CATALEPSY

The catalepsy bar test apparatus was used to analyze the effect of extract on haloperidol-induced catalepsy. The groups I, II, III (n=6) were administered with saline, extract (100mg/kg, i.p.) and standard Levodopa (30mg/kg, i.p.) respectively. 30-minutes prior treatment with the inducer haloperidol (1mg/kg, i.p.) was administered. Considering the results of previous acute toxicity study the extract dose was selected. The forepaws of the rat were placed on the catalepsy bar (1cm in diameter and 12-cm above table) and the catalepsy duration was measured at 0, 15, 30, 60, 90, 120, 150 and 180 minutes and the time taken by each rat to withdraw its paws from the bar was recorded.

STATISTICAL ANALYSIS

The information is presented in the form of a Mean \pm Standard error of the mean (SEM). The data was analyzed using a two-way ANOVA. Prism Graph Pad 8.4.3 was used for statistical analysis. *P<0.001 was used as the significance level.

RESULTS:**A) PHYTOCHEMICAL ANALYSIS**

Using conventional methodologies qualitative phytochemical testing of extracts was carried out to detect the presence or absence of various phytochemical constituents (Table 1).

B) QUANTITATIVE ESTIMATION OF TOTAL PHENOLIC AND FLAVONOID CONTENT (Table 2, 3)**C) ANTI-CATALEPTIC ACTIVITY:**

Effect on Clonidine Induced Catalepsy: (Figure 1)

Effect on Haloperidol induced catalepsy: (Figure 2)

Table 1

| PHYTOCHEMICAL CONSTITUENTS | YES (+)/NO (-) |
|----------------------------|----------------|
| Carbohydrates | + |
| Flavonoids | + |
| Alkaloids | + |
| Tannins | + |
| Vitamins | + |
| Steroids | + |
| Saponins | + |
| Glycosides | + |
| Fats and oils | + |

Table 2

| Total phenolic content of extracts of <i>Xanthium strumarium</i> fruits | |
|---|---|
| Extract | Total phenolic content (mg GAE/g extract) |
| Hydroalcoholic | 65.37±1.39 |

The quantity/concentration of phenols is calculated using the equation $y=0.014x+0.103$, where y is the sample absorbance and $R^2=0.9990$. The results are presented as a mean \pm standard deviation (n=3). SD stands for standard deviation. GAE: Gallic acid equivalents, *X Strumarium*: *Xanthium strumarium*.

Table 3

| Total flavonoid content of extracts of <i>Xanthium strumarium</i> fruits | |
|--|---|
| Extract | Total Flavonoid content (mg QE/g extract) |
| Hydroalcoholic | 3.648±0.7578 |

$Y = 0.008x + 0.179$, where y=absorbance of samples and $R^2=0.9950$, denotes the quantity/concentration of flavonoids obtained from the equation: $y=0.008x \pm 0.179$. The results are presented as a mean standard deviation (n=3). SD stands for standard deviation. *Xanthium strumarium* (*Xanthium strumarium*)

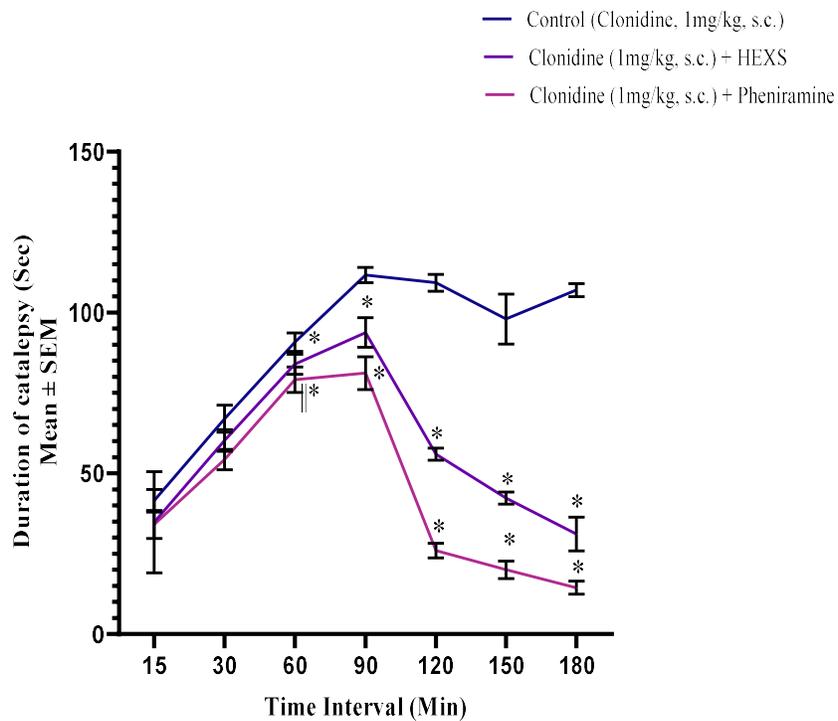


Figure 1

The data was analyzed by Two-way ANOVA followed by Bonferroni's post-test. * ($P < 0.001$) as compared to control group. The catalepsy induced by clonidine was significantly reduced by administration of extract (100 mg/kg, i.p.) at 60, 90, 120, 150 and 180 minutes respectively

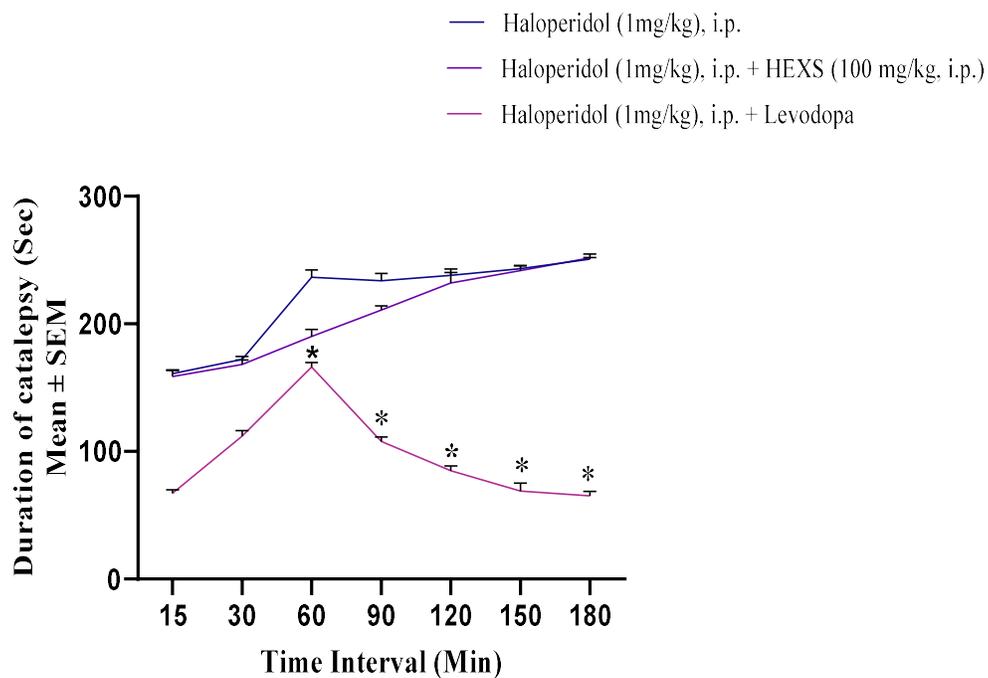


Figure 2

Treatment with extract (100 mg/kg, i.p) had no effect on the duration of catalepsy produced by haloperidol. The conventional medicine Levodopa, on the other hand, dramatically shortened the duration of catalepsy.

DISCUSSION:

The fruits of *Xanthium strumarium* L., Asteraceae, have been used for various diseases in Chinese folk medicine, including allergic rhinitis, tympanitis, arthritis, ozena etc [24].

Various drugs, those particularly acting on CNS have the cataleptic side effects [25].

The relative role of acetyl choline and histamine was investigated by some of the researchers. They have studied the perphenazine induced catalepsy model and concluded that the antidepressants may show the anticholinergic actions. That might be attributed to the elevated levels of the neurotransmitter dopamine in the brain. Also, antidepressants can suppress the release of acetylcholine [26].

Some researchers also concluded that, the concentration of brain histamine is directly correlated to the particular stage of catalepsy [27]. Mast cell degranulation releases the chemical histamine and this postulate was proved after the administration of a compound 48/80 [28].

The clonidine is also reported to work similarly as a degranulating agent, compound 48/80 i.e. after administration, the clonidine also releases the mediator histamine [29].

The researchers discovered that pretreatment with L-histidine, a precursor of histamine, potentiated clonidine-induced catalepsy in a dose-dependent manner. According to Muley et al., intra-cerebroventricular injection of histamine elicited catalepsy in conscious rats, which was inhibited by H₁-receptor antagonist but not by H₂-receptor antagonist [30]. Clonidine is known to cause mast cells to produce histamine. (29) Schwatz discovered histamine-producing mast cells in the brain [31]. Prazosin, a 2-adrenoceptor blocker, prevents mast cell histamine release generated by clonidine [32].

Catalepsy is also caused by neuroleptics, but by a different mechanism: they block dopamine D₂-receptors in the substantia nigra [33, 34]. The hydroalcoholic extract of *Xanthium strumarium* can prevent clonidine-induced catalepsy but not haloperidol-induced catalepsy, according to this study. According to this study, the cataleptic effect of clonidine in rats is mediated through histamine release from mast cells. The effectiveness of this extract to prevent clonidine-induced catalepsy is due to its mast cell-stabilizing effects. The plant has

no effect on dopaminergic transmission. As a result, the polar components could be used to treat asthma and as an antihistaminic.

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