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Research Article

Investigating The Anxiolytic Potential Of Helianthus Annuus L. Seeds: A Comprehensive Study

Ved Prakash[1], Ashwani Kumar[2*], Yashodhar Chaudhary[3],Om Prakash Joshi[4],Ravindra Kumar[5]

[1,3]Research Scholar, Department of Pharmaceutical Sciences, Gurukula Kangri Deemed University Haridwar (Uttarakhand)- 249404.
[*2,4,5]Assistant Professor, Department of Pharmaceutical Sciences, Gurukula Kangri Deemed University Haridwar (Uttarakhand)- 249404.

Corresponding author: Ashwani Kumar
*[2]Assistant Professor, Department of Pharmaceutical Sciences, Gurukula Kangri Deemed University Haridwar (Uttarakhand)- 249404.

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ABSTRACT

Anxiety can cause fear, dread, and unease. You can start to perspire, have tightness and agitation, and feel your heart pounding. Emotional anxiety is more common in women than in males during adolescence. The current research was based on the investigating the anxiolytic potential of helianthus annuus. seeds. Helianthus annuus, indigenous to Europe, possess an erect rough-hairy stem, reaching typical heights of 3 metres the common sunflower, is a large annual forb of the genus Helianthus grown as a crop for its edible oil and edible fruits (sunflower seeds). The seeds of Helianthus annuus (sunflower) were obtained from the local agriculture seeds store, at Haridwar, UK. The seeds were washed making dust-free and dried at room temperature or shade and extracted through Soxhlet apparatus using water solvent. After 72 hours of extraction, the extract was filtered-off using cotton plug and kept on rotatory evaporator for evaporation process. Albino rats of either sex weighing 130-150g were obtained from the Animal House, Gurukula Kangri Deemed University Haridwar (Uttarakhand). The animals were maintained in proper conditions, at room temperatures of 25±1°C with 12-hour light/dark cycle. All the rats were divided into 4 groups (n=6) i.e., group 1: Rats given normal saline daily, group 2 given Diazepam (4mg/kg, p. o.), group 3 given aqueous seeds extract of Helianthus annuus (ASHA) (100mg/kg, p. o.), and group 4 given aqueous seeds extract of Helianthus annuus (ASHA) (200mg/kg, p. o.) up to 21 days. The anxiolytic effect was evaluated through EPM, light-dark arena and actophotometer. In results, in all the models, hydroalcoholic seeds extract of Helianthus annuus significantly demonstrated anxiolytic potential in both the doses when compared to control. It significantly increased no. of entries and time spent in open arm/light arena. In conclusion, aqueous seeds extract of Helianthus annuus is significant anxiolytic herbal drug. It can be effectively used in the treatment of depression, mental agitation, and other neurological disorders after successfully evaluating mechanism of action of the seeds.

Keywords: Helianthus annuus, anxiolytic, EPM, Light-dark arena, Actophotometer,

INTRODUCTION

Anxiety can cause fear, dread, and unease. You can start to perspire, have tightness and agitation, and feel your heart pounding. Emotional anxiety is more common in women than in males during adolescence. Anxiety disorders are 1.5–02 times more common in women than in men [1]. While anxiety episodes, separation anxiety disorder, and agoraphobia without even a history of panic attacks were more frequent, they were less common overall in adolescents aged 13 to 17 than in adults aged 18 to 64 [2]. Because of this, anxiety disorders are commonly misdiagnosed and undertreated in primary care [3]. Approximately 700,000 people commit suicide each year. The fourth leading cause of mortality for those between the ages of 15 and 29 is suicide [4].

Plant profile

Helianthus annuus, indigenous to Europe, possess an erect rough-hairy stem, reaching typical heights of 3 metres the common sunflower, is a large annual forb of the genus Helianthus grown as a crop for its edible oil and edible fruits (sunflower seeds) [5]. This sunflower species is also used as bird food, as livestock forage, and in some industrial applications. Wild Helianthus annuus is a widely branched annual plant with many flower heads. The domestic sunflower, however, often possesses only a single large in florescence (flower head) atop an unbranched stem. The name sunflower may derive from the flower's head's shape, which resembles the sun, or from the false impression that the blooming plant appears to slowly turn its flower towards the sun as the latter moves across the sky on a daily basis [6].

Taxonomy [7]

Kingdom: Plantae
Division: Angiospermae
Subdivision: Eudicots
Class: Asterids
Order: Asterales
Family: Asteraceae
Subfamily: Helianthoideae
Genus: *Helianthus*
Species: *annuus*

Description

Sunflower leaves are broad, coarsely toothed, rough and mostly alternate. What is often called the "flower" of the sunflower is actually a "flower head" or pseudanthium of numerous small individual five-petaled flowers ("florets"). The outer flowers, which resemble petals, are called ray flowers [8]. Each "petal" consists of a ligule composed of fused petals of an asymmetrical ray flower. They are sexually sterile and may be yellow, red, orange, or other colors. The flowers in the center of the head are called disk flowers. These mature into fruit (sunflower "seeds"). The disk flowers are arranged spirally [9]. Generally, each floret is oriented toward the next by approximately the golden angle, 137.5°, producing a pattern of interconnecting spirals, where the number of left spirals and the number of right spirals are successive Fibonacci numbers [10]. Typically, there are 34 spirals in one direction and 55 in the other; however, in a very large sunflower head there could be 89 in one direction and 144 in the other. This pattern produces the most efficient packing of seeds mathematically possible within the flower head. Sunflower oil, extracted from the seeds, is used for cooking, as a carrier oil and to produce margarine and biodiesel, as it is cheaper than olive oil [11]. A range of sunflower varieties exist with differing fatty acid compositions; some 'high oleic' types contain a higher level of monounsaturated fats in their oil than even olive oil [12][13].

a. Flower & leaves **b. Seeds**

Fig 1. Different parts of *Helianthus annuus* (sunflower)

Chemical constituents

Numerous chemical constituents including helikauranoside A, (−)-kaur-16-en-19-oic acid, grandifloric acid, and paniculoside IV, e heliangolide niveusin B, Caffeic acid, clorogenic acid, dicaffeoylquinic acid, Four tocopherol (α,β,γ and δ) isomers, helianthinin, flavonol tambulin, the chalcones kukulcanin B and heliannone A and the flavanones heliannones B and C, Nevadensin have been reported and isolated from the Helianthus *annuus* extract [14][15][16].

The current research was based on the investigation of the anxiolytic potential of *Helianthus annuus* L. seeds.

MATERIALS AND METHODS

Experimental requirements

Helianthus annuus seeds, Diazepam, distilled water, Wistar albino rats (either sex), elevated plus maze, light-dark arena, actophotometer, rotatory evaporator and digital weighing machine.

Collection, authentication, and extraction of plant material

The seeds of *Helianthus annuus* (sunflower) were obtained from the local agriculture seeds store, at Haridwar, UK. and authenticated from a botanist with ref. no Bot.-Micro/02/2023 at Department of Botany and Microbiology, Gurukul Kangri (Deemed to be University), Haridwar. The seeds were washed making dust-free and dried at room temperature or shade and extracted through Soxhlet apparatus using water solvent. After 72 hours of extraction, the extract was filtered-off using cotton plug and kept on rotatory evaporator for evaporation process. Thus, a concentrated residue of extract was obtained; further dried to get in dried powder form. The percentage yield was calculated on the basis of practical yield [17].

Phytochemical screening

1. Detection of Alkaloids

Each extract was separately dissolved in diluted HCl before being filtered.

Mayer's Test: Potassium mercuric iodide, or Mayer's reagent, was applied to the filtrates. Alkaloids are present when a precipitate with a yellow hue forms.

Wagner's Test: Wagner's reagent, which is iodine in potassium iodide, was applied to the filtrates. Alkaloids are present when a brown or reddish precipitate forms.

Hager's Test: Hagers Reagent was used to treat the filtrates. The appearance of yellow precipitation suggests the presence of alkaloids.

Detection of Glycosides

Fehling's test: With distilled water dilution, Fehling's solutions A and B were heated for one minute. There were 8 drops of plant extract added to this transparent blue solution. It was then combined with 1 ml of Fehling's solution and heated for 5 minutes in a water bath. Brick red precipitation is an indication of glycoside content.

Detection of Saponins

Foam test: For a stable, long-lasting froth, about 2g of the plant extract was combined with 10ml of distilled water and vigorously shaken. Saponins are indicated by the appearance of foam [17].

2. Detection of Tannins

Ferric chloride test: In a test tube, 0.5 grams of the dried powdered material was cooked in 20 milliliters of water before being filtered. After adding a few drops of 0.1% FeCl3, the coloration was checked for brownish green-black or blue-black.

Lead acetate test 2 ml of distilled water and 2 ml of plant extract were mixed together. After adding 0.01g of lead acetate to the mixture, give it a good shake. Tannins are present when white turbidity and precipitate develop [18].

3. Detection of Flavonoids

NaOH test: After treating a little amount of extract with aqueous NaOH and HCl, the production of a yellow-orange color was noticed.

H_2SO_4 test: Conc.H2SO4 was applied to a portion of the extract, and the production of orange color was monitored.

5. Detection of terpenoids

After mixing 2.0 ml of chloroform with 5 ml of the aqueous plant extract, the mixture was added, allowed to evaporate on the water route, and then heated to a boil using 3 ml of concentrated H2SO4. A grey coloration developed as terpenoids took shape.

6. Detection of Steroids

5 ml of aqueous plant crude extract was combined with 2 ml of chloroform and concentrated H2SO4. The presence of steroids was detected by the appearance of red hue in the lower chloroform layer.

7. Tests for sugars and carbohydrates

Molisch's test

Add a few drops of α-naphthol solution in alcohol to 2-3 ml of extract of each solvent, agitate, and then add concentrate H2SO4 from the test tube's sides. a violet ring where two liquids converge.

Fehling's test
It is utilised to find decreasing sugars. Make a volume of 500 mL by dissolving 34.66 grammes of copper sulphate in distilled water (solution A). 50 grammes of sodium hydroxide and 17.3 grammes of potassium sodium tartrate should be dissolved in distilled water to a volume of up to 50 millilitres (Solution B). Prior to usage, combine two solutions in an equal volume. Fehling's A and B solution in a 1 mL mixture should be boiled for one minute. Equal parts of the test solution should be added. Heat for five to ten minutes in a kettle of boiling water. There came a flash of brick red, followed by yellow.

Preparation of animals
Albino rats of either sex weighing 130-150g were obtained from the Animal House, Gurukula Kangri Deemed University Haridwar (Uttarakhand). The animals were maintained in proper conditions, at room temperatures of 25±1°C with 12-hour light/dark cycle. The relative humidity was maintained at 44-56%, and are fed with standard rodent diet and water *ad libitum*. Animals were kept on fasting but free access to water up to 1 h before involving in the study [18].

Experimental groups
All the rats were divided into 4 groups (n=6) as follows-
Group 1: Rats given normal saline daily for 21 days.
Group 2: Rats given Diazepam (4mg/kg, p. o.) for 21 days.
Group 3: Rats given aqueous seeds extract of *Helianthus annuus* (ASHA) (200mg/kg, p. o.) for 21 days.
Group 4: Rats given aqueous seeds extract of *Helianthus annuus* (ASHA) (400mg/kg, p. o.) up to 21 days.

Evaluation parameters
1. Elevated Plus Maze (EPM) Test
The Elevated Plus Maze (EM) consists a 5cm wide circular pathway; elevated 27 cm from the floor and diameter of maze kept 65 cm. The circular pathway is divided into 4 quadrants in which 2 are open and 2 are closed quadrants- where wall is 27 cm in height. Rats are placed facing towards anyone of the closed quadrants during each trial. Rats are allowed to explore the apparatus for 5 minutes only. No. of entries and time spent in open quadrants are recorded till 5 minutes [19].

2. Light-Dark Arena Model
In light-dark arena model, a 100Watt bulb is being placed 30 cm above to base of box. Rats are kept in centre of light arena (box) and have to expose for 5 minutes. No. of entries and time spent in light arena segment are recorded till 5 minutes. It is cleansed every time before keeping a new rat [19].

3. Locomotion Activity
Actophotometer is tuned on to check and make sure that all the photocells are working properly for accurate readings. Rats are placed once at a time in the activity cage for 10 min. Activity score is recorded for each rat till 10 min. Finally, motor activity is observed and compared with standard drug- Diazepam [20].

RESULTS AND DISCUSSION

Percentage yield
The percentage yield for aqueous seeds extract of *Helianthus annuus* was found to be 67.42% when calculated based on its practical yield.

Phytochemicals screening
The aqueous seeds extract of *Helianthus annuus* showed as a rich source for diverse phytochemicals as below-

Table 1. Phytochemicals of aqueous seeds extract of *Helianthus annuus*

Phytochemicals	Aqueous seeds extract of *Helianthus annuus*
Carbohydrates	++
Alkaloids	++
Glycosides	_
Flavonoids	++
Tannins	_
Saponins	_
Triterpenoids	++
Steroids	+
Gum	_

Absent (-), Present (+), Abundance (++)

Evaluation of anxiolytic effect

1. Elevated Plus Maze (EPM) Test

In elevated plus maze test, normal saline treated rats showed no. of entries, time spent and % of time spent in open arm as 3.85±0.14 sec, 67.32±0.32 sec and 19.75±0.56 %, respectively. Whereas, aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.) treated rats showed no. of entries and % of time spent as 5.42±0.43 sec and 34.28±0.19 %, respectively. In contrast, aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.) administered rats demonstrated the no. of entries and % of time spent as 8.25±0.26 sec and 43.24±0.11 %, respectively. Thus, anxiolytic effect was observed in herbal extract when compared with control group. This model clearly confirms that the *Helianthus annuus* seeds are effective in treatment of anxiety and mental disorders in animal model.

Table 2. No. of entries, time spent & % of time spent of *Helianthus annuus*

Treatment	In open arm (sec) *No. of entries*	*Time spent*	*% of time spent*
Normal saline	3.85±0.14	63.11±0.27	19.75±0.56
Diazepam (4mg/kg, i. p.)	8.94±0.27	147.16±0.22	47.42±0.10
Aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.)	5.42±0.43	92.35±0.29	34.28±0.19
Aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.)	8.25±0.26	123.46±0.12	43.24±0.11

Level of significance= P<0.05, P<0.01, P< 0.001

Values were given in Mean ± S.E.M. and found statistically significant at P<0.05, compared to control (n=6)

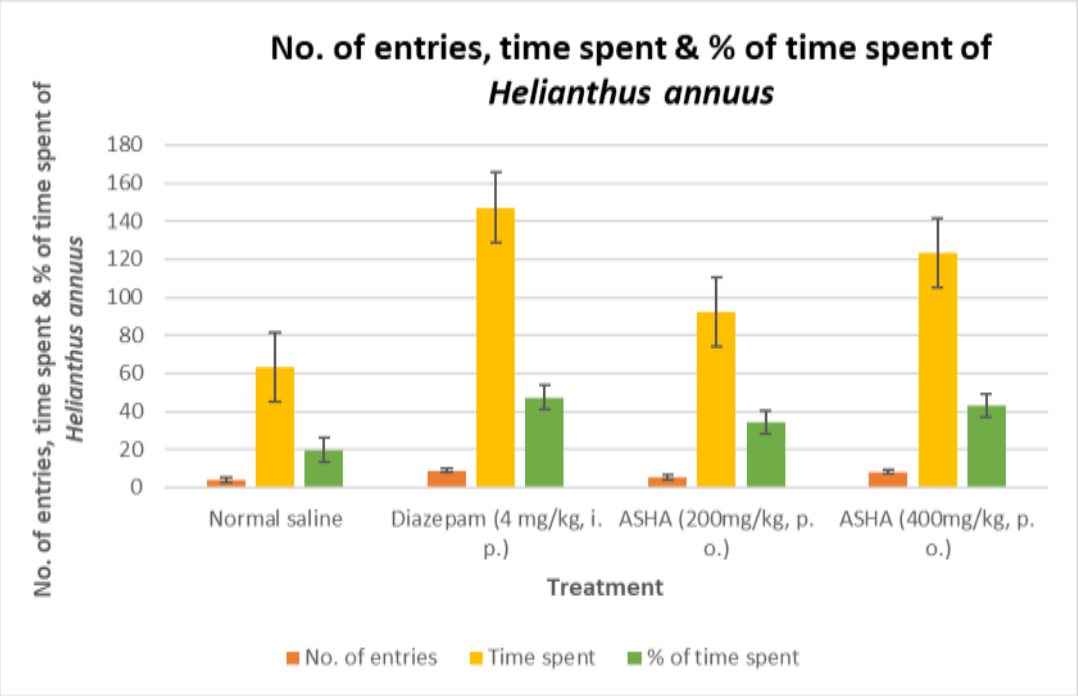

Fig 2. No. of entries, time spent & % of time spent of *Helianthus annuus*

2. Light/dark arena test

In light-dark arena test, the number of entries, time spent and % of time spent in light arena were recorded for 5 min. The normal saline treated rats showed no. of entries, time spent and % of time spent in open arm as 5.10±0.37 sec, 65.35± 0.42 sec and 22.05±0.19 %, respectively. Whereas, aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.) treated rats showed no. of entries and % of time spent as 6.57±0.20 sec and 33.24±0.25 %, respectively. In contrast, aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.) administered rats demonstrated the no. of entries and % of time spent as 7.92±0.47 sec and 41.35±0.32 %, respectively. Diazepam treated rats showed % of time spent as 47.36±0.14 %.

Table 3. Light-dark arena test of control, standard and *Helianthus annuus* treated groups

Treatment	In light arena (sec) *No. of entries*	*Time spent*	*% of time spent*
Normal saline	5.10±0.37	65.35± 0.42	22.05±0.19
Diazepam (4 mg/kg, i. p.)	8.39±0.16	149.26± 0.35	47.36±0.14
Aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.)	6.57±0.20	96.36±0.30	33.24±0.25
Aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.)	7.92±0.47	131.34±0.12	41.35±0.32

Level of significance= P<0.05, P<0.01, P< 0.001

Values were given in Mean ± S.E.M. and found statistically significant at P<0.05, compared to control (n=6)

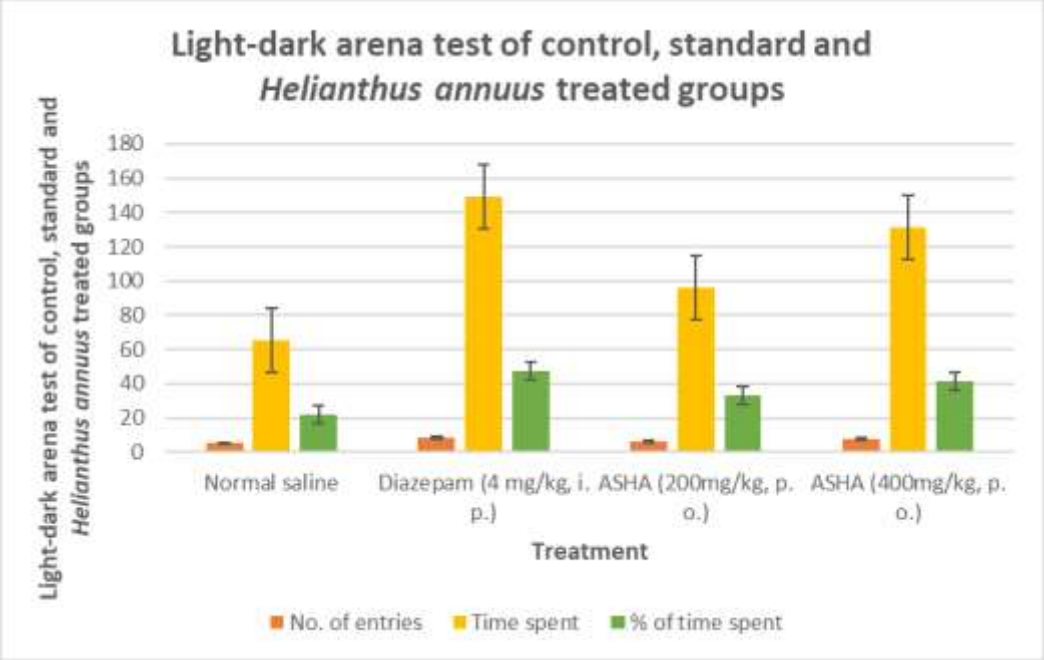

Fig 3. Light-dark arena test of control, standard and *Helianthus annuus* treated groups

3. Locomotor activity

In locomotor activity score test, highest locomotor activity was achieved in control as 149.24±0.11 sec whereas lowest activity score as found in Diazepam treated rats as 98.27±0.24 sec. Aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.) exhibited the locomotor activity score as 134.33±0.29 sec. However, aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.) exhibited the locomotor activity score as 105.19±0.26 sec. It significantly decreased locomotion activity score at both the doses- proving itself a better anti-depressant and anxiolytic moiety.

Table 4. Locomotor test of control, standard and *Helianthus annuus* treated groups

Treatment	Locomotor activity score (Sec ± SEM)
Normal saline	149.24±0.11
Diazepam (4mg/kg, i. p.)	98.27±0.24
Aqueous seeds extract of *Helianthus annuus* (200mg/kg, p. o.)	134.33±0.29
Aqueous seeds extract of *Helianthus annuus* (400mg/kg, p. o.)	105.19±0.26

Level of significance= P<0.05, P<0.01, P< 0.001

Values were given in Mean ± S.E.M. and found statistically significant at P<0.05, compared to control (n=6)

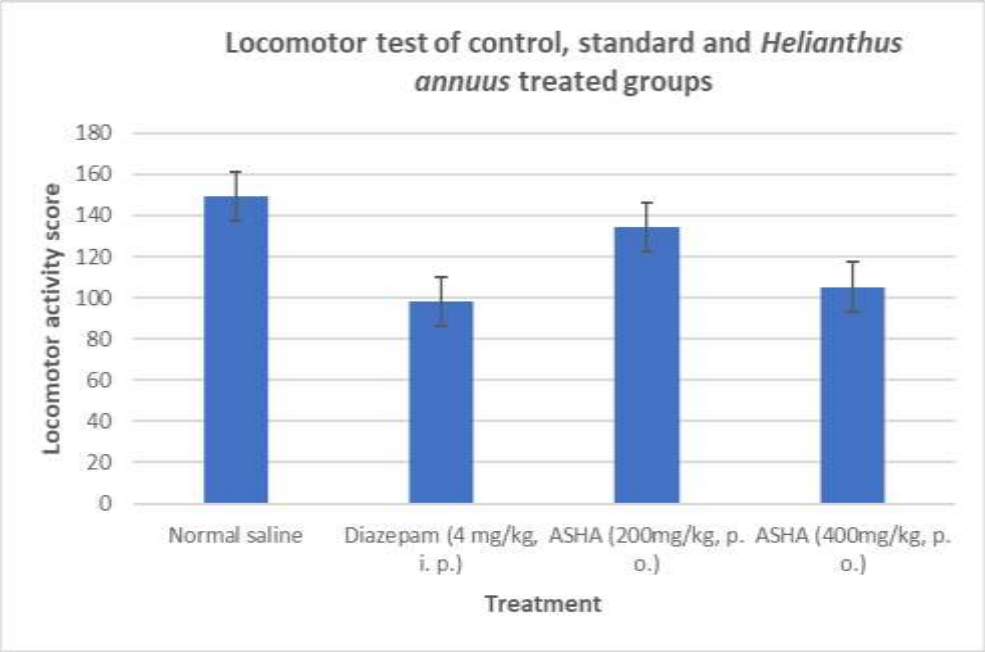

Fig 4. Locomotor test of control, standard and *Helianthus annuus* treated groups.

Coriandrum sativum Linn. is suggested in Iranian folk medicine as a remedy for alleviating anxiety and insomnia. The anxiolytic effect of the aqueous extract was investigated in male albino mice using the elevated plus maze (EPM) as an animal model for anxiety. The extract was administered intraperitoneally at doses of 50, 100, and 200 mg/kg. The impact of the extract on spontaneous activity and neuromuscular coordination was evaluated using an animal activity metre and rotarod, respectively. Within the Elevated Plus Maze (EPM), the administration of an aqueous extract at a dosage of 200 mg/kg resulted in an anxiolytic effect. This was observed by an increase in the duration of time spent on the open arms and the percentage of entries made into the open arms, as compared to the control group. The administration of an aqueous extract at doses of 50, 100, and 200 mg/kg resulted in a substantial decrease in both spontaneous activity and neuromuscular coordination as compared to the control group. The findings indicate that the aqueous extract of CS seed exhibits an anxiolytic effect and may possess sedative and muscle relaxant properties [21][22].

Another study has shown that the leaves of CS have both anxiolytic (anti-anxiety) and central analgesic (pain-relieving) properties. The Elevated Plus Maze (EPM) is presently one of the most extensively employed models for studying animal anxiety. It has been well verified for usage with both male and female mice. Hence, this experiment was selected to examine the anxiolytic properties of the aqueous extract derived from coriander seeds. The indicators of anxiety in this test are the quantity of entries in the open arm and closed arm. The sensitivity to drugs is mediated through the gamma-aminobutyric acid receptor complex, which supports the inclusion of diazepam as a positive control in this investigation. Diazepam enhanced the frequency of admissions into the open arm and the duration of time spent in the open arms, so validating its anxiolytic properties. [23][24].

The water-based extract of coriander seed demonstrated comparable effects on these parameters. The impact of administering 200 mg/kg of coriander in the EPM test was nearly identical to that of administering 0.3 mg/kg of diazepam. The observations provide clear evidence that coriander seed have an anxiolytic effect. The anxiolytic effects of the coriander seed extract were shown in mice at doses of 50, 100, and 200 mg/kg in this study. The aforementioned effects may be attributed to the presence of sterols, tannins, and flavonoids in the extract [25][26].

The antianxiety properties of coriandrum leaf aqueous extract were investigated in our study using doses of 50, 100, and 200 mg/kg. At these specific doses, the extract of coriandrum increases the number of entries in the open arm compared to the control group in a manner that depends on the dose [27]. Additionally, it effectively and significantly decreases the number of entries in the closed arm compared to the control group in a dose-dependent manner. As the dosage of coriandrum grew, the corresponding effect also increased. However, it is worth noting that strong antianxiety effects were observed across all three dosage levels. Therefore, our study found that coriandrum exhibited noteworthy anxiolytic effects at doses of 50, 100, and 200 mg/kg, in comparison to the control group. However, its activity was lower when compared to the conventional drug diazepam. In results, in all the models, hydroalcoholic seeds extract of *Helianthus annuus* significantly demonstrated anxiolytic potential in both the doses when compared to control. It significantly increased no. of entries and time spent in open arm/light arena.

CONCLUSION

In conclusion, aqueous seeds extract of *Helianthus annuus* is significant anxiolytic herbal drug. It can be effectively used in the treatment of depression, mental agitation, and other neurological disorders after successfully evaluating mechanism of action of the seeds.
Its effect was about similar and near to standard drug treated group. It indicates that actions might be similar to Diazepam, Nitrazepam etc. It exhibits antidepressant action probably by facilitating the release of neurotransmitters i.e., serotonin, dopamine. It also increases the release of GABA (Gamma Amino Butyric Acid) and chloride ions influx that leads to hyperpolarization. The effect was determined in dose-dependent manner. When compared to the control, the aqueous seeds extract showed a considerable reduction in immobility period. The plant's successful antidepressant action prompted a futuristic attempt to bypass the blood-brain barrier by blocking P-gp. In contrast, this study confirmed anxiolytic activity in both the doses without targeting the significant and selective constituent produced potential.
As anxiety and depression has become commonest form of mental disability, so it may demonstrate an economic and pharmacological impact in modulating behavioural of humans.

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CONFLICT OF INTEREST

Authors declared for none conflict of interest.

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