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ANTIPSYCHOTIC AND NEUROPROTECTIVE ACTIONS OF BERGENIA CILIATA ROOT EXTRACT IN RAT MODELS

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ABSTRACT: Traditional remedies, along with the phytochemicals and antioxidants included in plants, may assist individuals suffering from psychosis, a persistent mental condition. These compounds and antioxidants safeguard organ health while also reducing the chance of schizophrenia. The efficacy of Bergenia ciliata as an antidepressant was evaluated using a methanolic root extract. Subsequently, it was examined in rat models exhibiting psychotic symptoms. Biochemical assays were conducted on cerebral tissue to detect TNF-α, glutathione (GSH), and acetylcholinesterase (AchE) to ascertain inflammation. Alongside histological examinations of the frontal cortex and hippocampus, behavioral assessments were conducted to evaluate the animals' locomotion and conduct. The apomorphine control group demonstrated more stereotypy than the B. ciliata 60 and 90 minute dosing groups and the apomorphine plus conventional therapy group. Moreover, substantial disparities were observed in the levels of GSH, AchE, and TNF-α across the three groups: the control group, the group administered B. ciliata, and the group receiving haloperidol as a traditional treatment. The actophotometer data indicated no more significant alterations, save for a reduction in the positive control group. Following the administration of diazepam, the B. ciliata group exhibited enhanced motility. Histological investigations indicated that the neuronal structures in the treated groups were unaltered, and the overall architecture of the hippocampus and cortex was maintained in B. ciliata. The brains administered diazepam exhibited the minimal extent of damage. The findings indicate that B. ciliata may possess neuroprotective and antipsychotic properties by reducing inflammation and enhancing brain structure and function.

Keywords: *Psychosis; Antipsychotic activity; Bergenia ciliata; Neuroprotection; Methanolic root extract; Rat model; Stereotypy; Locomotor activity; Glutathione (GSH); Acetylcholinesterase (AchE); TNF-α; Inflammation; Histopathology; Haloperidol; Diazepam*

1. INTRODUCTION

An absence of reality awareness can define a mental health condition called psychosis. The global impact is estimated at 450 million, with one million individuals suffering from mental illness risking their lives annually by committing suicide. Schizophrenia symptoms may include delusions of grandeur, feelings of isolation, illogical behavior or speech, concentration difficulties, anxiety, depression, and suicidal thinking. Patients, especially from affluent countries such as Nigeria, continue to seek the services of folk doctors despite the societal repercussions, primarily due to the occasional inadequacies of conventional treatment. Climazapine, haloperidol, and risperidone exemplify atypical antipsychotics that are purportedly more user-friendly, cost-effective, and easier to evaluate than traditional

therapies. Extended use of these drugs exacerbates extrapyramidal symptoms and oxidative degradation. This may lead to diabetic problems, heart failure, and other severe disorders.

The need for herbal medicine remains robust. Herbal drugs represent a commendable alternative for managing chronic central nervous system disorders, such as psychosis, for which effective treatments are currently unavailable, owing to their minimal adverse effect profiles. "Curled bergenia featuring shaggy foliage." This is an alternative designation for it in Hindi. Approximately six species exist within the Bergenia family. They reside in the eastern and central parts of Asia, together with the temperate Himalayan Mountains. This plant is located in subtropical hilly regions from Kashmir to Nepal, at elevations between 2000 and 2700 meters, blooming biennially. This spherical plant can attain a height of 50 cm. It is frequently observed on the mountains encircling Murree.

Many individuals believe that bergenia root and gentiana root are equivalent in terms of their health benefits. They also assert that it possesses anti-irritant and obstruction-eliminating effects. As a mild emmenagogue and diuretic, it assists in relieving rib and chest pain caused by an excess of cold humor. Eliminate toxins, kidney stones, or obstructions from the digestive tract that may hinder the kidneys' waste excretion. According to some, asthma, epilepsy, spasmodic reflexes, and different respiratory conditions may be more effectively managed through diffusion rather than addressing the underlying cause. For chronic vaginal infections, the root serves as an efficacious therapy alternative.

Bergenia ciliata, a member of the Saxifragaceae family, has a longstanding history of therapeutic application. It is commonly referred to as "Pakhanabhed" and "Zakhmehayat." B. ciliata is renowned for its efficacy in addressing various medical conditions, including gallstones, kidney stones, gastrointestinal disorders, pulmonary infections, cardiac ailments, visual impairment, hemorrhoids, among others. Researchers have identified its antibacterial, anti-inflammatory, and anti-cancer characteristics, as well as its efficacy in reducing pain, inflammation, and liver disease.

Phytochemical analysis has identified the presence of compounds such gallic acid, bergenin, catechin, gallicin, arbutin, β-sitosterol, afzelechin, among others, in the plant. Catechin, known as epicatechin or (+)-catechin, is a phenolic molecule that has demonstrated potential in the treatment of mental disorders. Encapsulation using cyclodextrins enhances its flavor and increases its functionality, or so the rationale suggests. The likelihood of a reduction in the local immune system caused by histamine diminishes when employing the catechin histidine decarboxylase inhibitor. Flavonoids that include epicatechin possess antioxidant qualities and can stimulate neuronal networks in the brain.

Memory loss and Alzheimer's disease are among the neurological illnesses that their constituent compounds have aided in alleviating. This research aims to determine if the plant B. ciliata, known for its medicinal use and few side effects, could serve as a safer, long-term treatment for psychosis and other neuropsychiatric illnesses. Conventional medicine is notoriously expensive and laden with adverse consequences. Damage impacts around 450 million individuals worldwide. The principal aim of the research is to examine a prospective plant-based treatment that may be more accessible, economical, and safer, especially in countries with deficient healthcare infrastructure.

Flavonoids, bergenin, and catechins are among the phytochemicals in B. ciliata that possess antioxidant and neuroprotective activities. This study supports the concept that phytomedicines may be effective in treating central nervous system illnesses that are resistant

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to conventional therapies. The likelihood of B. ciliata being incorporated into a wider classification of eco-friendly, cost-effective, and culturally endorsed botanical treatments is significant, especially in areas where traditional medicine is dominant. The integration of ancient knowledge and contemporary research can significantly advance the scientific objectives of ethnopharmacology.

2. MATERIALS AND METHODS

Plant Material and Authentication

The roots of B. ciliata were verified by Drs. V. Rama Rao and S. H. Doddamani of the Central Ayurveda Research Institute in Bangalore, following their collection in June from Gangtok, Sikkim. The verification of Number Authentication/SMPU/CARI/BNG/2024-25/967 is required.

Preparation of Plant Extraction

Following several days of shade drying, the B. ciliata roots were pulverized into a fine powder and further filtered to achieve uniform particle size. A total of one thousand milliliters of methanol was utilized in three extractions to obtain approximately 250 grams of powdered roots. Whatman filter paper number 1 was employed to exclude solid particulates from the solution. By permitting the filter to evaporate completely, we successfully eliminated all solvents and achieved a uniform weight for the methanolic extract. The extract was reserved for additional research to ascertain its potential antipsychotic properties. This technique optimizes the extraction of bioactive constituents from B. ciliata roots while maintaining their integrity.

Experimental Design

Stereotype Assessment Animal Model

The study utilized male Wistar albino rats weighing between 150 and 200 grams. The subjects were maintained in regulated conditions within polypropylene enclosures. All experiments were performed in compliance with the guidelines established by the Institutional Animal Ethics Committee (IAEC), and the rats had a seven-day acclimatization period before the experiment.

Each cage had six rats. To assess the antipsychotic efficacy of B. ciliata, the apomorphine-induced stereotypic behavior model was employed with five groups of six rats each (N = 30). Prior data indicates the acute toxicity of the plant extract. Group I animals (Normal reference) received standard saline as a control. Group II (Disease Control): Rats were administered apomorphine to elicit psychotic-like stereotyped behaviors. Rats in Group III (Control Group) received haloperidol intraperitoneally at a dosage of 1 mg/kg following standard protocols. Group IV animals (First Test Group) received an oral administration of 250 mg/kg of a methanolic extract of B. ciliata. Test Group 2 (Group V) animals received a high dosage of methanolic extract of B. ciliata (500 mg/kg, orally).

Apomorphine (1.5 mg/kg, subcutaneously) was administered to all groups, excluding the standard control, 60 minutes later. Stereotypical behaviors were observed at 10, 30, 60, and 90 minutes post-apomorphine injection. This study aims to compare the efficacy of B. ciliata extract with the conventional antipsychotic haloperidol in mitigating apomorphine-induced stereotyped behaviors through known methodologies.

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Induction of Apomorphine

Apomorphine was delivered subcutaneously at a dosage of 1.5 mg/kg to all groups, excluding the control group, which remained unchanged. Each group was administered apomorphine one hour subsequent to the initial dose of the test medication B. ciliata and the conventional treatment haloperidol.

To assess the normalcy of the rats' behavior, we employed a standardized scoring system that focused on the level of activity and specific behaviors exhibited by the rats. Concerning the scoring system for behavioral analysis, the subsequent definition is provided:

0 — animal asleep or still
1 — active movement
2 — predominantly active with occasional stereotyped actions (sniffing, rearing)
3 — constant stereotyped activity with locomotion
4 — continuous stereotypy restricted to one place
5 — stereotypy with licking/gnawing/biting
6 — continual licking of cage grids
7 — continual biting of cage grids

This scoring approach enables precise quantification of stereotyped behaviors, facilitating equitable comparisons among different experimental groups.

Sacrifice and Analysis

The animals were euthanized with a high dosage of phenobarbital sodium following the administration of apomorphine to induce antipsychotic symptoms, for ethical considerations. The cerebral tissue was excised at a subsequent date. Subsequent to the extraction of the tissue from the circulatory system, it was rinsed with a pre-chilled PBS buffer. We employed Lowry's (1951) methodology to ascertain the total protein content. The materials were subsequently stored at -20 °C for additional analysis.

Locomotor Activity Animal Model

Eighteen animals participated in the trial, with two groups receiving distinct drugs and one group acting as a control. Before the experiment commenced, the positive control group received 5 mg/kg of diazepam hourly. The experimental groups administered B. ciliata extract orally once daily for 23 days at doses of 250 mg/kg and 500 mg/kg, respectively. Diazepam was the efficacious medicine.

Rats were evaluated using an actophotometer ten minutes post-medication delivery on days 1, 8, 15, and 23. The experimental medication was administered orally for a duration of 23 days.

Biochemical Parameters: From Brain Tissue Homogenates

Estimation of Glutathione

Glutathione (GSH) is a crucial antioxidant that helps preserve the brain's oxidative equilibrium. To provide a more in-depth analysis, we conducted a GSH assay utilizing homogenate, DTNB, disodium hydrogen phosphate, and trichloroacetic acid (TCA). We quantified the absorbance at 412 nm.

A combination of 0.3 mL of the homogenate and 0.3 mL of 10% w/v trichloroacetic acid was initially made. The mixture was centrifuged for 10 minutes at 1000 rpm. Subsequently, 0.3 mL of 0.3 M disodium hydrogen phosphate and 0.25 mL of DTNB were combined with 0.5 mL of the supernatant. The GSH concentration was determined in µg/mg following the absorbance measurement at 412 nm.

Acetylcholinesterase Activity Assay (AChE)

A cuvette contained 100 µL of DTNB solution, 2.6 mL of 0.1 M PBS (pH 8), and 0.4 mL of homogenate, all in equal volume. We employed a LKB spectrophotometer to accurately quantify the absorbance at 412 nm while meticulously agitating the liquid by introducing air bubbles. A baseline measurement was obtained following stabilization. Absorbance variations were documented every two minutes for a duration of ten minutes following the addition of 20 µL of acetylthiocholine as the substrate.

We employed the rate of absorbance change per minute as an indicator of enzyme activity.

$$R = 5.74 \times 10^{-4} \times A/CO$$

R = rate in moles of substrate hydrolysed/minute/gram tissue

5.74×10^{-4} = constant (extinction coefficient of thionitro-benzoic acid, 1.36×10^{4}/molar/cm)

A = change in absorbance/min

CO = original concentration of tissue (mg/mL)

The rate of hydrolyzed material per minute per gram of tissue was utilized to assess the activity.

Tumor necrosis factor-α (TNF-α)

Tumor necrosis factor alpha, a cytokine, is synthesized by various cell types, including endothelial cells, macrophages, and T lymphocytes. One approach is the BD OptEIATM Biosciences Solid Phase Sandwich ELISA.

To prepare the samples and diluents, 50 microliters of ELISA diluent must be promptly added to each well of a 96-well plate. Accurately dispense 50 µL of each sample and standard into the specified wells. Allow the sealed plate to remain at ambient temperature for two hours.

Upon the conclusion of the incubation period, evacuate the wells by aspirating or transferring the liquid. Subsequently, dispense 300 µL of the pre-mixed wash buffer into each well. Following the aspiration or decantation of the wash buffer, cleanse the item an additional four times, resulting in a total of five washes. To achieve optimal results, employ absorbent paper to wipe the plate following the last wash to eliminate any remnants of the buffer.

Dispense 100 µL of the detection antibody into each well, cover the plate, and incubate at room temperature for one hour. To prepare the enzyme-working reagent, introduce the requisite volume of enzyme diluent into a clean container subsequent to the addition of the specified quantity of enzyme concentrate. Integrate comprehensively.

After the removal of all unbound detection antibodies by five washing cycles, 100 µL of the enzyme-working reagent must be applied to each well. After sealing the plate, allow it to rest at ambient temperature for thirty minutes. Subsequently, rinse the wells seven times to ensure they are thoroughly clean.

Upon completion of the washings, introduce 100 µL of TMB one-step substrate reagent into each well and allow the plate to incubate at room temperature in the absence of light for 30 minutes. Subsequently, dispense 50 µL of stop solution into each well following the completion of the 30-minute incubation period. Verify accurate measurements by assessing the absorbance of each well at 450 nm within 30 minutes following the addition of the stop solution.

Histopathological examination of the brain

Upon completion of the experiment, the rats' brains were meticulously excised and positioned in a sterile petri dish. The rapid excision of the frontal cortex and hippocampus areas of the brain inhibited premature tissue decomposition. The brain sections were promptly submerged in 10% formalin post-dissection to guarantee tissue preservation for histological analysis.

Statistical Analysis

The data for the six participants is shown as Mean ± SEM. The statistical analysis was conducted with GraphPad. Subsequent to the analysis of variance (ANOVA), the researchers conducted group comparisons utilizing Bonferroni and Tukey's tests. The comparison of the untreated normal control group to all other groups was considered statistically significant when the p-value was below 0.05.

3. RESULTS AND DISCUSSION

Individuals afflicted with psychosis, a persistent mental disorder, experience a disconnection from reality. This significant public health concern affects millions of persons globally. Its features include perceptual abnormalities and challenges in differentiating between illusion and reality, which may last throughout one's lifespan. Bipolar disorder, substance-induced psychosis, and schizophrenia are several classifications of psychotic disorders. Symptoms include hallucinations, delusions, disorganized speech, and cognitive impairments.

Plants possess phytochemicals that support the body in various ways and are essential for both disease prevention and treatment. Research has shown that B. ciliata and other traditional herbs possess medicinal properties and can be utilized to address many human illnesses. Antioxidants have been shown to diminish the risk of schizophrenia. Phytochemical research have identified active chemicals in B. ciliata, including gallic acid, bergenin, catechin, gallicin, paashaanolactone, arbutin, β-sitosterol, and afzelechin, among others. Tannic acid, mucilage, catechin, glucose, albumin, metarbin, mineral salts, and wax exemplify bioactive compounds. The plant's diverse pharmacological properties, which render it a superior choice for addressing diseases such as psychosis, originate from these bioactive constituents. Figure 1 illustrates a study that investigated the impact of B. ciliata at two distinct dosages (250 and 500 mg/kg) on stereotypy counts over time within an apomorphine model. The research additionally investigated the prolonged effects of haloperidol (1 mg/kg) on stereotypy frequencies.

Key Observations

Throughout all time intervals (10, 30, 60, and 90 minutes), the stereotypy score of the apomorphine control group remained unchanged.

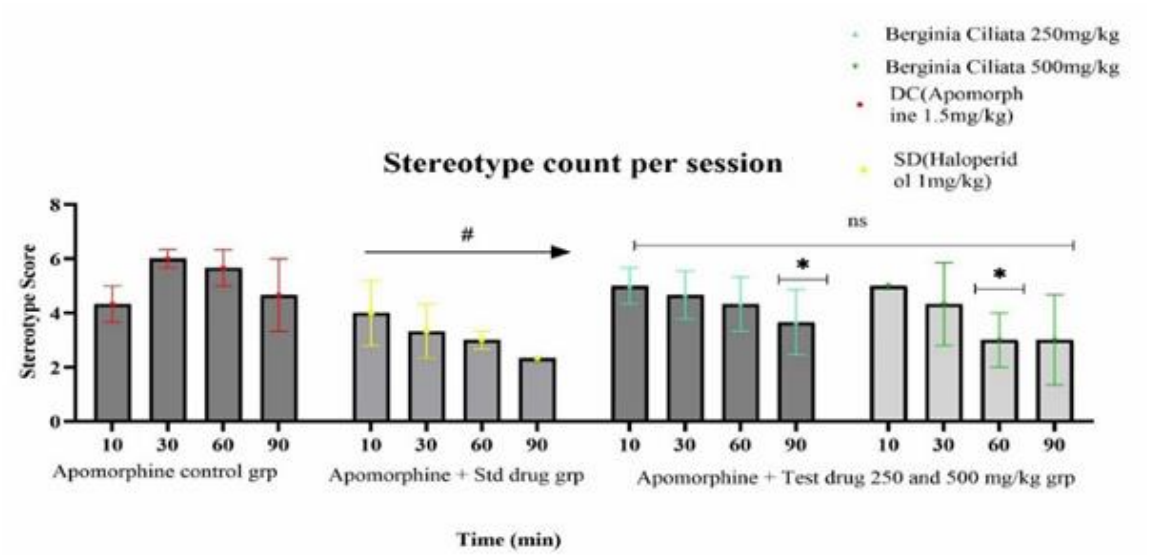


Fig. 1: Graphical representation of apomorphine induced stereotype behavior in rats (Behavioral study)

The values (n = 6 rats per group) are shown as Mean ± SEM.

A statistically significant difference exists between the two groups when the p-value is below 0.05.

In comparison to the control group, ns (not significant) denotes an absence of significant change ($p > 0.05$).

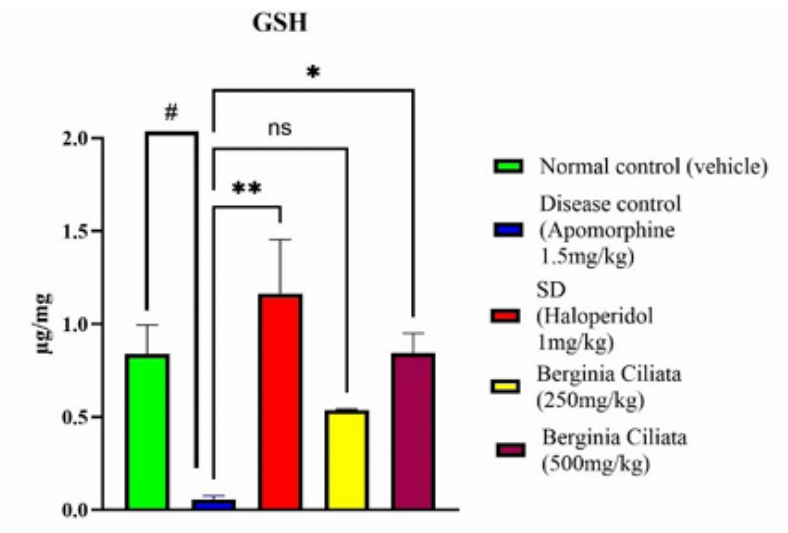
At dosages of 250 mg/kg and 500 mg/kg, $*p < 0.05$ at 60 and 90 minutes indicates a statistically significant effect of the test medicine.

exhibiting heightened stereotypy associated with the medication. The Apomorphine + Standard medication group (Haloperidol 1-mg/kg) demonstrates a significant reduction in stereotypy ratings at both the 60- and 90-minute marks compared to the positive control group (shown by $\#p < 0.05$). Groups administered apomorphine and test substances (B. ciliata 250 and 500 mg/kg): In comparison to the apomorphine control group, both doses of B. ciliata markedly diminished stereotypy ratings at 60 and 90 minutes ($*p < 0.05$). This suggests that B. ciliata may mitigate apomorphine-induced stereotyping. At $p < 0.05$, a statistically significant disparity exists in stereotypy ratings between the conventional medicine group and the control group.

$*p < 0.05$ signifies that, in comparison to the apomorphine control group, the stereotypy scores of the test drug groups were markedly reduced. After 30 minutes, ns denotes that no significant differences were observed between the groups. The study indicates that B. ciliata exhibits a notable anti-stereotypic impact akin to that of haloperidol, especially over extended time intervals. Researchers examined the level of GSH. The normal control (vehicle), apomorphine at 1.5 mg/kg, apomorphine combined with haloperidol at 1 mg/kg (standard treatment), apomorphine with B. ciliata at 500 mg/kg, and haloperidol with B. ciliata at 250 mg/kg exhibited substantial differences (Fig. 2). The remaining group couples exhibited no significant differences from each other.

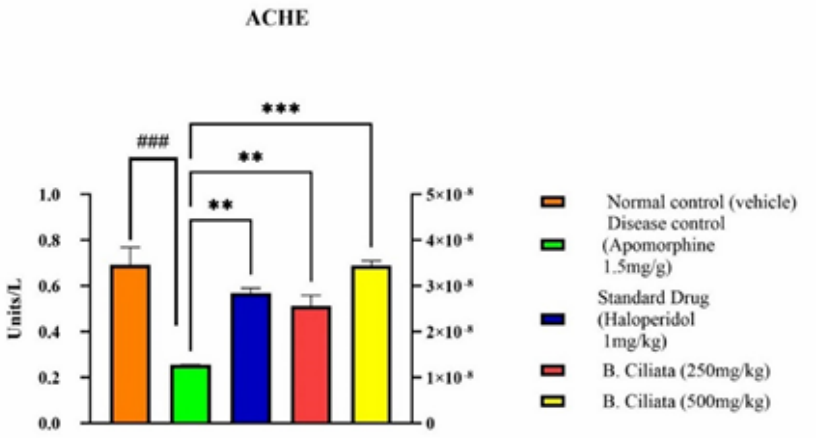
Examination of AChE (Fig. 3): Apomorphine and haloperidol, apomorphine and B. ciliata (500 mg/kg), and apomorphine and B. ciliata (250 mg/kg) exhibited significant differences compared to the usual control (vehicle). The remaining group pairs exhibited minimal variation.

Research on TNF-α (Fig. 4): Apomorphine and B. ciliata exhibited a substantial difference at a dosage of 500 mg/kg. The remaining group pairs had no observable alterations.



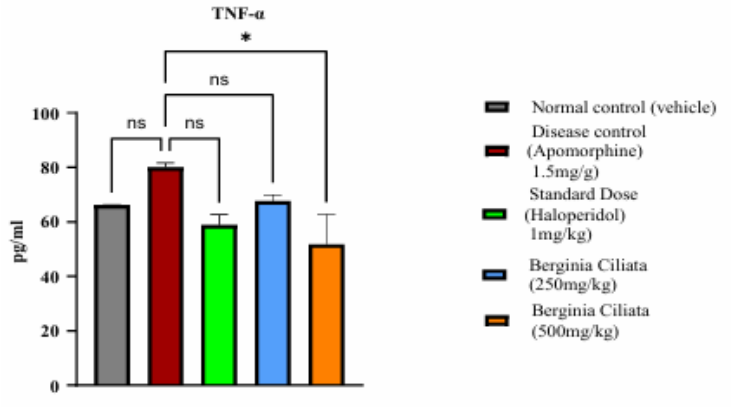
Values are expressed as Mean ± SEM, (n=6 rats in each group). #$p < 0.05$ indicates a statistically significant difference compared to the apomorphine disease control group vs normal control. ns (not significant) $p > 0.05$ indicates no significant difference when compared to the disease control group. *$p < 0.05$ and **$p < 0.01$ compared to the disease control group.

Fig. 2: Effect of B. ciliata in the level of GSH in apomorphine- induced stereotypy in rats



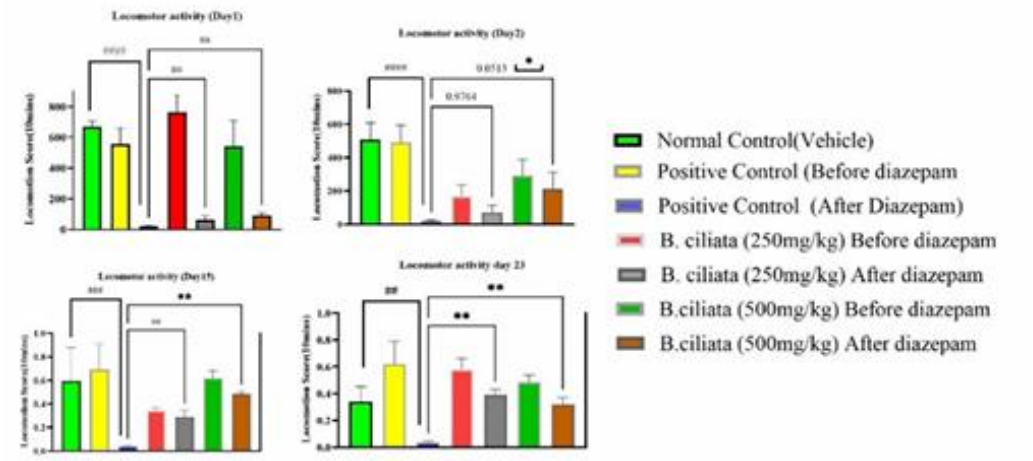
Values are expressed as Mean ± SEM, (n = 6 rats in each group). ###$p < 0.001$ indicates a statistically significant difference compared to the apomorphine disease control group vs normal control. ***$p < 0.001$ and **$p < 0.01$ compared to the disease control group.

Fig. 3: Effect of B. ciliata on AchE in apomorphine - induced stereotypy in rats



Values are expressed as Mean ± SEM, (n=6 rats in each group). *$p < 0.05$ compared to the disease control group. Rest all other groups were showing non-significant

Fig. 4: Effect of B. ciliata on TNF-α in apomorphine - induced stereotypy in rats



Values are expressed as Mean ± SEM, (n = 6 rats in each group). ####$p < 0.0001$, ###$p < 0.001$, and ##$p < 0.01$ compared to normal control, **$p < 0.01$ and *$p < 0.05$ compared to the disease control group. Rest all other groups were showing non-significant

Fig. 5: Diazepam associated locomotor activity of over time

The second study examined locomotor activity associated with diazepam. On the 1st, 8th, 15th, and 23rd days, we conducted recordings with an actophotometer.

Essential Findings (Fig. 5):

Day 1 locomotor activity

Aside from the positive control, which exhibits a notable reduction compared to the normal control, all treatments display comparable locomotor ratings, with no significant differences (ns) seen across the groups.

Day 7 locomotor activity

Comparison of the positive control group (post-diazepam therapy) with the normal control group demonstrated significant differences (####p < 0.0001). Administration of 500 mg/kg of B. ciliata subsequent to diazepam resulted in a considerable enhancement of locomotor activity relative to the positive control (*p < 0.05). Evaluations of locomotor activity on day

15 indicated substantial differences (####p < 0.0001) between the positive control and the other groups, as well as the normal control. In comparison to the positive control, B. ciliata at 500 mg/kg markedly enhanced locomotor activity (**p < 0.01). B. ciliata at doses of 250 mg/kg and 500 mg/kg exhibited the greatest locomotor ratings on day 23, significantly surpassing the positive control and all other groups (**p < 0.01). The positive control demonstrates a marked reduction in locomotor activity relative to prior days following diazepam administration. The study indicates that B. ciliata influences locomotor activity, evidenced by a consistent increase in activity over several days at a dosage of 500 mg/kg, particularly following diazepam administration. The herbal treatment may diminish the efficacy of diazepam, which appears to decrease locomotor activity. GSH (Fig. 6), AChE (Fig. 7), and TNF-α (Fig. 8) were examined about diazepam-induced locomotor activity.

GSH

The positive control (Diazepam) and the standard control (vehicle) exhibited substantial differences. B. ciliata (500 mg/kg) and the positive control (Diazepam) The remaining group couples exhibited no significant differences from each other.

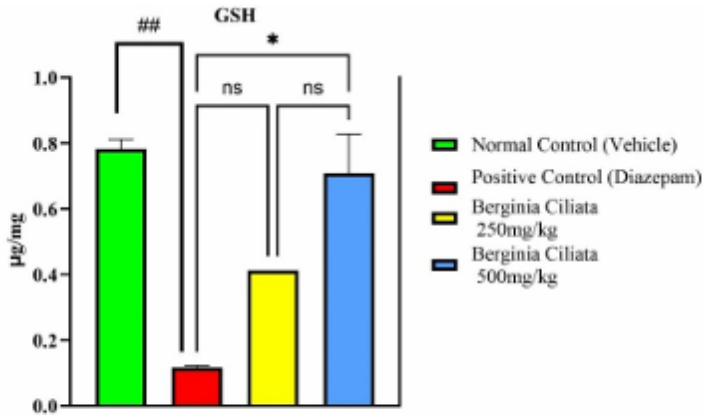
AChE

B. ciliata (500 mg/kg) exhibited a substantial difference compared to the positive control (Diazepam). 250 mg/kg of B. ciliata and 500 mg/kg of B. ciliata The remaining group pairs exhibited no significant differences from each other.

TNF-α

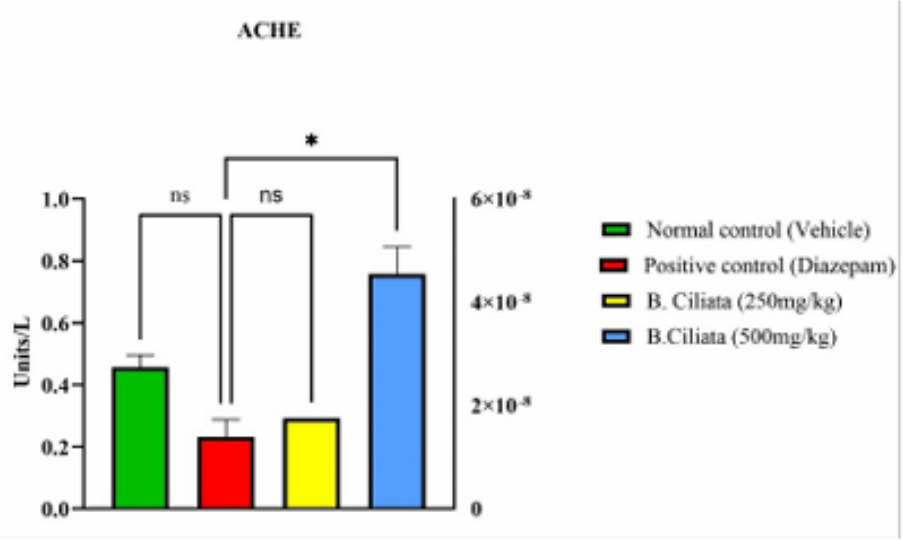
The positive control (Diazepam) and the standard control (vehicle) exhibited substantial differences. Diazepam utilized as a positive control alongside B. ciliata at a dosage of 250 mg/kg Positive controls comprise B. ciliata (500 mg/kg) and diazepam. The different group pairs exhibited no significant differences from each other.

The histological examination of the frontal cortex, hippocampus, and cerebellar cortex of the brain in various contexts. The inherent architecture of the cerebellar cortex, characterized by discrete layers and cellular types, remains evident in Fig. 9. An arrow in the image denotes cortical neurons.



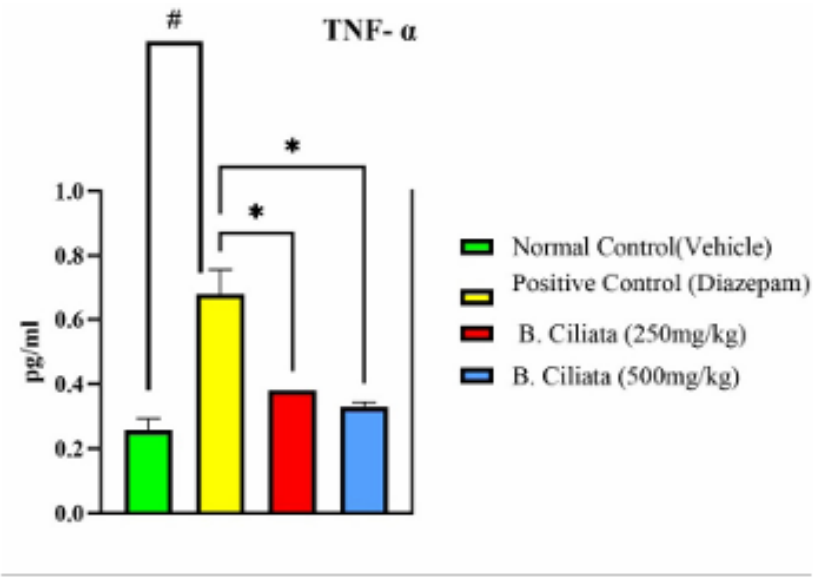
Values are expressed as Mean ± SEM, (n=6 rats in each group). ##p<0.01, compared to normal control, *p<0.01 and nsp>0.05 compared to the disease control group

Fig. 6: Effect of B. ciliata on diazepam associated locomotor activity in GSH



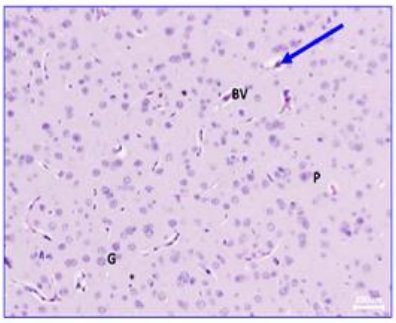
Values are expressed as Mean ± SEM, (n = 6 rats in each group). nsp>0.05 compared to normal control, *$p < 0.05$ compared to the disease control group. Rest all other groups were showing non-significant.

Fig. 7: Effect of B. ciliata on diazepam associated locomotor activity in AchE

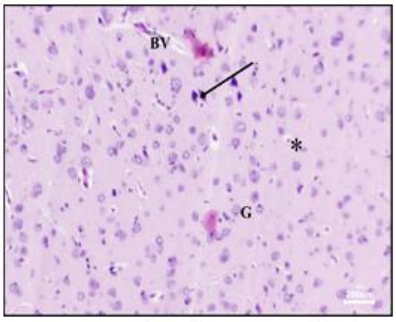


Values are expressed as Mean ± SEM, (n=6 rats in each group). #p<0.05 compared to normal control, *p<0.05 compared to the disease control group.

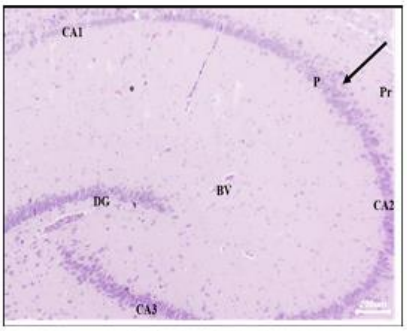
Fig. 8: Effect of B. ciliata on diazepam associated locomotor activity in TNF-α



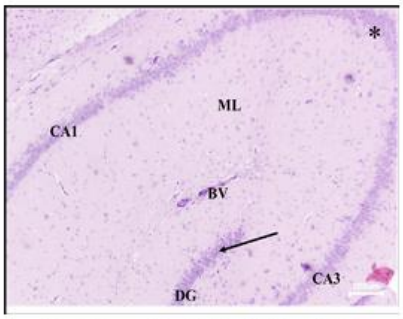
Normal Control: (Untreated)
Fig. 9: Frontal cortex structure
haematoxylin and eosin stain, Scale bar = 200 µm.



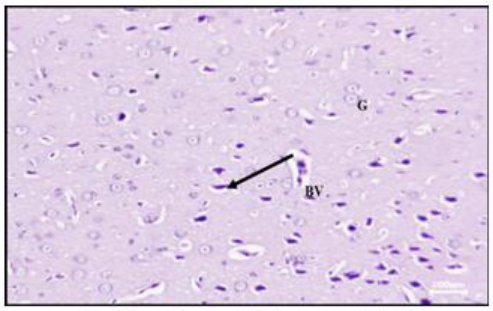
Test Drug (*B. ciliata* 250mg/kg)
Fig. 13: Frontal cortex Structure:
Haematoxylin and Eosin stain, Scale bar = 200µm



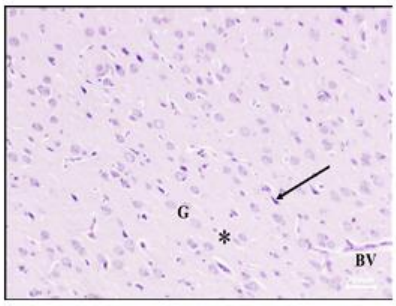
Normal Control (Untreated)
Fig. 10: Hippocampal structure:
haematoxylin and eosin stain, scale bar = 200 µm.



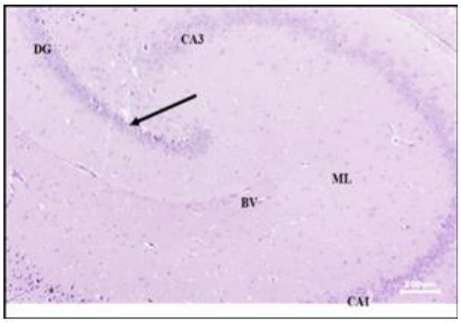
Test Drug (*B. ciliata* 250mg/kg)
Fig. 14: Hippocampal structure:
haematoxylin and eosin stain, scale bar = 200 µm



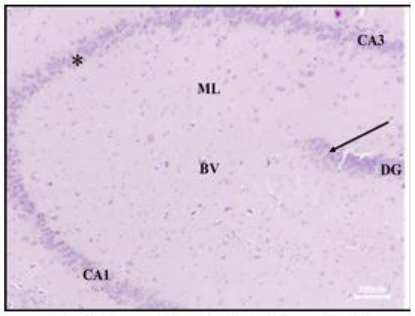
Positive Control (Diazepam Only)
Fig. 11: Frontal cortex structure:
haematoxylin and eosin stain, Scale bar = 200 µm



Test Drug (*B. ciliata* 500mg/kg)
Fig. 15: Frontal cortex structure:
haematoxylin and eosin stain, scale bar = 200 µm



Positive Control (Diazepam Only)
Fig. 12: Hippocampal structure:
haematoxylin and eosin stain, scale bar = 200 µm



Test Drug (*B. ciliata* 500mg/kg)
Fig. 16: Hippocampal structure:
haematoxylin and eosin stain, scale bar = 200 µm

Both pyramidal and cortical cells (P) appear to be in optimal condition, exhibiting no indications of injury or degeneration. The distinctive spherical morphology and black nuclei, denoted by an asterisk, are features of glial cells (G). As anticipated in the cerebellum, the granule cells are densely arranged and display typical nuclear morphology. The existence of a blood vessel (BV) signifies that the tissue is sufficiently vascularized. The hippocampus

comprises three regions: CA1, CA2, and CA3. All of these pertain to the polymorphic layer (Pr) and the cornu ammonis (CA). Illustration 10: A healthy hippocampus is indicated by the typical organization of pyramidal cells in the CA1, CA2, and CA3 regions. The pyramidal cells, characterized by basophilic cytoplasm and big, spherical vesicular nuclei, are in optimal condition. The arrow demonstrates this.

Molecular Layer: Includes blood vessels, glial cells, and neuronal cells; the asterisk denotes the proper positioning of the cells and blood vessels. The dentate gyrus (DG) is well-preserved due to the substantial quantity of ganglion cells in a single layer. A blood artery in the molecular layer (Fig. 11) demonstrates that the vascularization is operating as expected. The arrow indicates that the cortical neurons display moderate degeneration with vacuolations, suggesting that the diazepam therapy caused neuronal stress or injury. A blocked blood artery may signify an alteration in the blood flow or integrity of the cerebellar cortex. The asterisk signifies that diazepam may not substantially affect oligodendrocytes, which exhibit a normal morphology characterized by a rounded shape, dark nuclei, and aggregated chromatin. Pyramidal cells, characteristic of these cell types, possess big, spherical nuclei and abundant cytoplasm. This signifies minimal influence on these cells. Despite diazepam medication, the granular layer remains preserved, with numerous granular cells characterized by prominent nucleoli and vesicular nuclei. Histological examination of the frontal cerebellar cortex from a brain subjected to diazepam treatment reveals evidence of modest neuronal degeneration, characterized by an obstructed blood artery and vacuolations inside cortical neurons. Nevertheless, the granular layer, pyramidal cells, and oligodendrocytes seem to be less affected. Figure 12 illustrates the mortality of neurons in the CA1 and CA3 regions. Pyknosis (shown by an asterisk as black nuclear staining) and vacuolated cytoplasm illustrate this phenomenon. Exhibits substantial, spherical nuclei within pyramidal cells. The cytoplasm was noted to be diminishing in thickness inside this stratum. There exist blood vessels, glial cells, and neuronal cells. The polymorphic layer, which is diminishing in thickness, consists of many ganglion cells. The arrow indicates that certain cells are undergoing disintegration, as evidenced by their pyknosis and vacuolated cytoplasm. The granular layer remained unaltered. There was an absence of inflammatory cell infiltration and intercellular bleeding. Figure 13 illustrates normal architecture, featuring basophilic nuclei located at the periphery (shown by the arrow). The illustration illustrates a blocked blood vessel (BV). The asterisk denotes oligodendrocytes, which are spherical cells characterized by black nuclei containing clumped chromatin and a pericytoplasmic halo.

Pyramidal cells (P): exhibit substantial, spherical, basophilic cytoplasm. exhibits prominent nucleoli and many granular cells (G). The eosinophilic backdrop consists of glial and neuronal processes, with these cells distributed throughout the background.

A low-dose test drug is affecting the natural histological structure of the frontal cortex. The cells in the CA1 and CA3 regions exhibited blue-staining nuclei (asterisk) and pink-staining cytoplasm, as illustrated in Figure 14, and comprised pyramidal cells with basophilic cytoplasm.

Molecular Layer (ML): demonstrates the existence of blood vessels (BV), glial cells, and neuronal cells. The dentate gyrus (DG) comprises layers of granular and ganglion cells (shown by arrow). No indication of intercellular bleeding or infiltration by inflammatory cells was observed. The frontal cortex is mostly intact, as the image (Fig. 15) illustrates the standard organization of cortical neurons.

Basophilic nuclei: The arrow signifies that these are located at the periphery, which is characteristic of the molecular layer. The morphology and vitality of oligodendrocytes are indicated by their spherical cell bodies, prominent nuclei, and aggregated chromatin. Oligodendrocytes are crucial for myelination in the central nervous system. They are readily identifiable by their prominent, spherical vesicular nuclei and basophilic cytoplasm. The brain's capacity for reasoning and motor control is significantly reliant on pyramidal cells. The existence of prominent nucleoli and vesicular nuclei in granular layer cells signifies active protein synthesis and normal cellular activity. The existence of blood vessels signifies an adequate supply of vascular structures inside the molecular layer.

The appropriate arrangement and morphology of neurons, glial cells, and blood vessels indicate that the brain tissue is in a healthy state. Figure 16: The nuclei (asterisk) are stained blue, but the cytoplasm in the CA1 and CA3 areas is stained pink. include tiny pyramidal cells characterized by basophilic cytoplasm and prominent, circular vesicular nuclei, signifying healthy, operational neurons.

The intricate architecture of the hippocampus comprises various cell types located in the polymorphic layer. The ML demonstrates the presence of glial cells, neuronal cells, and blood vessels (BV), which are essential for preserving the structural and functional integrity of hippocampus tissue. a representative segment of the DG that exemplifies its conservation. The arrow denotes the substantial quantity of ganglion cells, essential for message transmission within the hippocampus. The granular cell layer comprises several densely packed neurons that facilitate information processing. With adequate organization and circulation, the neurons and glial cells exhibit vitality.

4. CONCLUSION

The investigation's results suggest that B. ciliata possesses significant promise as an antipsychotic agent. The primary findings include a reduction in TNF-α levels, an elevation in AChE activity, and a decline in GSH levels, suggesting potential psychotropic effects through the modulation of inflammation. The impact on diazepam-related locomotor activity and apomorphine-induced behavior reinforces B. ciliata's potential as a viable alternative for treating psychotic illnesses. Its potential to benefit humans is mostly attributable to its varied phytochemical composition.

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