RESEARCH ARTICLE

Pharmacological Activity of *Manilkara hexandra* and *Stereospermum colais* Buch Leaves Extract for CNS Disorders in Mice

Amit Kumar Agrahari*, Vivek Chourasia

Faculty of Pharmacy, Mansarovar Global University, Sehore Madhya Pradesh, India

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ABSTRACT

Depression is a major mental illness worldwide. It is also difficult to identify patients with multiple stressors. For thousands of years, traditional medicine has used many medicinal plants to treat stress due to their effectiveness, efficacy, and safety. This aimed to screening the anxiolytic effect of ethanolic extracts of *Manilkara hexandra* and *Stereospermum colais* Buch leaves in rats such as mice. Anxiolytic activity was evaluated in Swiss albino rats. Leaves of *Manilkara hexandra* and *Stereospermum colais* Buch plants are dried and crushed to coarse powder. This method was used for this stress study by using Soxhlet extraction. A phytochemical qualitative analysis of ethanolic extracts of *Manilkara hexandra* and *Stereospermum colais* Buch was carried out. Lots of models were used for screening the anxiolytic effect of *Manilkara hexandra* and *Stereospermum colais* Buch plant leaves: enhancement plus maze model, social model, light-dark model, and whole plate process. For this purpose hydroalcoholic extract is administered orally400 and 300 mg/kgwere selected respectively, as the anxiolytic standard drug diazepam (2 mg/kg) was used. According to the research results, ethanolic extracts of *Manilkara hexandra* and *Stereospermum colais* Buch leaves show anxiolytic activity in reducing aversive fear. Studies have shown that hydroalcoholic extracts of *Manilkara hexandra* and *Stereospermum colais* Buch leaves have anxiolytic effects. Data show that hydroalcoholic extracts of *Manilkara hexandra* and *Stereospermum colais* Buch leaves have anxiolytic properties compared to control.

Keywords: *Manilkara hexandra* and *Stereospermum colais* Buch, CNS Disorders Activity, Diazepam, Ethanolic Extracts.

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INTRODUCTION

Axiety is the most common CNS disorder in the world is called an spsychological disorder which is most commonly encountered problems in the whole world[1]. It is an unpleasant, emotional state which is associated with discomfort and fear[2].

Depression is a mental illness that is generally thought to be symptomatic, psychological and biological in nature. People suffering from depression worldwide is total 322 million. Between 2005 to 2015, the number of people suffering from depression by approximately 18.4% [3].

Anxiety and depression are the most common types of mental illness, and a combination of the two conditions also occurs. Many people with anxiety disorders also suffer from depression, etc [4].

Stress means that the body does not respond to all demands directed at it, affects the body and threatens homeostasis [5]. Stress affects the immune system and the hormonal system, causing health deterioration. Most studies using stress models have shown that physical and mental stress stimuli activate the brain and leading to the hypothalamic-pituitary-adrenal (HPA) axis, secretion of glucocorticoids and catechol amines by rat brain adrenocortical cells [6]. Excessive glucocorticoids use can cause adverse effects such as hypertension, abdominal pain, immunosuppression and reproductive failure [7]. In addition, stress causes an increase in blood sugar, blood pressure or blood lipids, which can lead to lifestyle effects such as diabetes [8].

Among the many types of dementia, Alzheimer's disease stands out as a leading cause of memory loss and other cognitive declines [9]. Alzheimer's disease is characterized by a cluster of symptoms, including neuro oxidative stress, amyloid plaque deposition, neurofibrillary tangles, inflammation, and functional impairment [10].

Alzheimer's disease is an incurable brain disease that causes dementia and abnormalities in the phosphorylation of intracellular tau protein, particularly affecting the cortical and subcortical pyramids, resulting in poor microtubule assembly and cytoskeletal collapse [11].

Dementia is frequent among the elderly, and the most common kind is Alzheimer's disease (AD), which is marked by memory loss, cognitive decline, and cognitive deterioration. Neurological examination of the AD brain reveals accumulation of beta-amyloid fibrillary deposits (Aβ plaques) atrophy, and neurofibrillary tangles. Aging brings a decline in the brain. However, rejection rates vary widely between specific regions. Reduced cerebral blood flow, gray and white matter, and synapse density are some of the age-related brain alterations [12].

Alzheimer's disease damages and kills brain cells. Alzheimer's disease is a complex disease that can be caused by many factors, including diseases or reduced blood flow

**Author for Correspondence: amitagrahari1997@gmail.com*

Table 1: Drug treatment in different groups of animals

S. No.	Group	Drug received
1.	Group 1 (Positive control group)	Received distilled water (1 mL/100 g)
2.	Group 2 (Negative control group)	Received distilled water (1 mL/100 g)
3.	Group 3 (Standard group)	Received Diazepam (2 mg/kg)
4.	Group 4 (SCBA 400)	Received *Stereospermum colais* Buch leaves aqueous extract (400 mg/kg)
5.	Group 5 (SCBE 400)	Received *Stereospermum colais* Buch leaves ethanolic extract (400 mg/kg)
6.	Group 6 (MHA 300)	Received *Manilkara hexandra* leaves aqueous extract (300 mg/kg)
7.	Group 7 (MHE 300)	Received *Manilkara hexandra* leaves ethanolic extract (300 mg/kg)

and genetic predisposition. While not all the major outcomes are known, scientists already know some commonalities. These include age, genetics, genetics, lifestyle, gender, head injury, head size, vascular risk, and diet [13].

Nootropics are drugs that enhance cognition, while amnestics are drugs that impair learning and memory [14]. These days, cholinesterase inhibitors like donepezil and nootropics like piracetam and aniracetam are used to enhance behavior, mood, and memory (Joshi and Parle 2006). Both in humans and animals, cholinergic neural pathways are crucial for learning and memory. In rats and humans, scopolactone, a well-known central cholinergic probe and nonselective muscarinic cholinergic antagonist, mostly impairs short-term memory and learning. Therefore, scopolamine has been used as an amnestic drug. It is known that learning with acetylcholinesterase inhibitors such as physostigmine, tacrine and donepezil means the acquisition of information and knowledge, and the information stored later is called memory. One of the most challenging tasks faced by neuroscientists is to elucidate the biochemical and molecular mechanisms underlying learning and memory. Mazes are often used in experiments to test animal learning and memory [15].

MATERIALS AND METHODS

Plant Material

Authentication and Collection of Plant Materials

Plant material like *Stereospermum colais* Buch and *Manilkara hexandra* leaves was collected from the local area of Bhopal.Herbarium specimen number provided for future reference; leaves validated by botanist, Head and Professor Botany Department, Janta PG College, APS University, Rewa, M.P.

Preparation of Extracts

Dry powder of different plants i.e. leaves of selected plants (*Stereospermum colais* Buch and *Manilkara hexandra*) were extracted three times in succession by cold maceration process with occasional shaking. The dry powder of plant material (100 g) was saturated with 500 ml of water and ethanol to obtain aqueous and alcoholic extracts respectively. The respective solutions were kept on the mechanical shaker for 3-5 hrs and incubated overnight. The next day, the extracted solutions were filtered through vacuum pump filtration and the residues were again extracted with the 500 ml of respective solvents as mentioned above. The above procedure was repeated two times again and finally mixed the whole filtrate. The filtrate was then vacuumed using a rotary vacuum to obtain a solid residue [16].

Table 2: The effects of SCB, MH, C_1, C_2 and diazepam in EPMT

S. No.	Groups	Dose (mg/kg,p.o)	Time spent in open Arms in 5 min (in sec) after 7 days
1	Control (vehicle)	5 ml	27.50±5.40
2	Anxiety control (AC)	5 ml	$15.00±3.8^{a}$
3	SCB	400	$22.00±3.48^{ns}$
4	SCB	400	$39.85±8.39^{*}$
5	MH	300	$32.00±7.45^{*}$
6	MH	300	$65.75±5.35^{**}$
7	Diazepam	2 mg,i.p.	$86.90±2.84^{***}$

All values are expressed as mean ± SEM, (n=6), $p<0.05$, *$p<0.05$, **$p<0.01$, and ***$p<0.001$ in relation to the control group. (Stress control using Dunnett test after analysis of variance).

Preliminary Phytochemical Screening

Standardized analysis was performed for various botanical properties of the extract. Crude extracts were analyzed for the presence of flavonoids and other metabolites using standard methods.

Preliminary hydro alcoholic extract of phyto chemical screening of *Stereospermum colais* Buch and *Manilkara hexandra leaves* has shown the mark of saponins, steroids, alkaloids, tannins and flavanoids.

Determination of Total Phenolic Contents (TPC)

The total phenolic content of the peel extract of Musa balbisiana was determined using the Folin-Ciocalteu method with all three solvents. To summarize, 2.5 mL of 10% (w/v) Folin-Ciocalteu reagent was mixed with 1 mL of 100-500 µg/mL solution sequentially. Following five minutes, 2.0 mL of 75 percent Na2CO3 was added to the mixture, and it was incubated at 50 °C for ten minutes with stirring every so often. After swapping out the extract-free sample for the original, we let it cool and then used a UV Spectrophotometer (Shimazu, UV-1800) to detect absorbance at 765 nm. Source: Lee et al. (2015). The dry extract's gallic acid equivalents in milligrams per gram (mg GAE/g) have been reported.

Determination of Flavonoid Contents

The flavonoid content of the three Musa balbisiana peel extracts that were extracted using solvents was tested independently. In a mixture that included 5.6 mL of distilled water, 0.2 mL of a 10% (w/v) AlCl3 solution in methanol, and 0.2 mL of potassium acetate (1 M), a 1 mL portion of the extract solution (25-220 µg/mL) was added. A blank was used to compare the measured absorbance at 415 nm after 30 minutes of incubation at room temperature. Results

Table 3: The effects of SCB, MH, C_1, C_2 and diazepam in stair case test

S. No.	Groups	Dose (mg/kg,p.o)	Number of Climbed step in 3 min	Number of Rearing step in 3 min
1	Control(vehicle)	5ml	14.63±1.78	13.33±0.50
2	Anxiety control(AC)	5ml	23.66±0.80[a]	29.18±5.48[a]
3	SCB	400	16.66±0.50[*]	21.00±0.34[ns]
4	SCB	400	10.23±0.30[**]	10.16±0.22[**]
5	MH	300	15.66±0.50[*]	16.34±7.74[*]
6	MH	300	12.23±0.30[**]	14±4.02[**]
7	Diazepam	2mg, i.p.	13.67±5.80[**]	14.12±4.28[**]

All values are expressed as mean ± SEM, (n=6), p<0.05, *p<0.05, **p<0.01, and ***p<0.001 in relation to the control group. (Stress control using Dunnett test after analysis of variance).

were presented as milligrams of quercetin equivalents per gram of dried extract (mg QE/g) according to Aryal et al. (2019).

Experimental Animals

Wistar albino rats of both sexes, weighing 150–200 g, were utilized in recent investigations. They were maintained at 232 °C or at 50–55 percent humidity with 12 hours of light and darkness. Maximum of three animals per polypropylene cage. The experimental animals were given a water and standard diet through out the experimental procedure. Animal experimentation during the study was performed under the approval of IAEC of Mansarovar University, Bhopal (RegNo:837/ac/05/CPCSEA. The study was approved by the IAEC, Department of Pharmacy, Mansarovar University, Bhopal. The animals were placed 10 days for acclimatization before the experiments.

Drug Treatment

For 15 consecutive days, the lyophilized hydroalcoholic leaf extracts of 400 mg/kg of *Stereospermum colais* Buch and 300 mg/kg of *Manilkara hexandra*, as well as 2 mg/kg B.W. of Diazepam, were given orally once daily at two distinct dose levels. Water was given to the animals in the control group. On the fifteenth day, one hour following the last medication administration, experiments were carried out. Following drug and dosing schedule is given on table-1

Ethical Approval

For the investigation, both sexes of 120–200 g wistar albino rats were employed. The animals were kept in hygienic cages with enough ventilation, natural light and dark cycles lasting 12 hours, and unlimited access to water and food. The humidity was maintained at 50±5% and the temperature was maintained at 22°C ± 1°C. The experimental protocols for this investigation were approved by the Institutional Animal Ethics Committee (IAEC) of the Department of Pharmacy at Mansarovar University in Bhopal. The Committee to Control and Supervise the Use of Animals in Experiments (CPCSEA) standard standards were followed in the performance of the in-vivo acute toxicity and anti-stress activities. The animals were placed 10 days for acclimatization before the experiments.

Drugs and Chemicals

All other drugs and materials were classified, with diazepam being the standard anxiolytic agent.

Anti-anxiety Activity

Elevated Plus Maze Test (EPMT)

Five arms make up the supplementary signatures on the

Table 4: The effects of SCB, MH, C_1, C_2 and diazepam in dark and light test

S. No.	Groups	Dose (mg/kg,p.o)	The time spent in light box during 5min (in sec) on7thday
1	Control (vehicle)	5ml	65.70±3.78
2	Anxiety control	5ml	35.80±9.40[a]
3	SCB	400	42.54±13.28[ns]
4	SCB	400	59.85±8.39[*]
5	MH	300	48.70±13.42[ns]
6	MH	300	74.45±5.09[**]
7	Diazepam	2mg, i.p.	107.07±4.22[***]

All values are expressed as mean ± SEM, (n=6), p<0.05, *p<0.05, **p<0.01, and ***p<0.001 in relation to the control group. (Stress control using Dunnett test after analysis of variance).

EPM: two closed (5×10×l5 cm) and two open (5×10 cm). Its 50 centimeters above the ground. With its head turned toward the right arm, position the animal in the middle of the EPM. For five minutes, note how long it takes you to open your hand. When an animal placed all four paws on an arm, that arm was considered reached. This operation took place in an anechoic room [18]. Each of the seven categories contains six different kinds of animals. The second group, known as the AC group, was given black beans (SCBE) as a stress reliever, whereas the first group, known as the control group, got 5 milliliters per kilogram of body weight of vehicle Tween 80 in 2% distilled water orally.

Stair Case Test (SCT)

Five steps make up the installation (2.5 cm high, 10 cm broad, and 7.5 cm deep). For the whole length of the ladder, the wall's interior height remains unchanged. The animal should be placed on the device's first step. For three minutes, count the steps you take both up and down. The animal is considered to have moved forward only when it has placed all four feet on the step. For ease of analysis, the number of downstream steps is not included. Every animal's gear is cleaned to get rid of anything unfamiliar that can affect how the next animal behaves [19]. Treatment and animal groups were similar to the EPMT.

Light and Dark Test (LDT)

Put the animal in the middle of the device. After five minutes, note how much time was spent in the bright and dark box [20].

Statistical Analysis

After a one-way analysis of variance (ANOVA) was used to compare the differences, Dunnett's test was executed. The mean ± S.E.M. is used to represent the results.

RESULTS AND DISCUSSION

In this additional test, treatment (mg./kg) MH with *Stereospermum colais* Buch (SCB) (400 mg/kg), *Manilkara hexandra* (MH) (300 mg/kg) and initial combination (C1=100) on day 7 of treatment animals. (300 mg/kg) increased the arm opening time ($p<0.01$), while the diazepam (2 mg/kg) standard drug increased ($p<0.05$) and caused a negative effect. The length of the open arm was longer ($p<0.01$). The primary impact, as seen by Table 2 ($p<0.001$) and birth time, was a reduction in climbing and care times with a larger SCB (400 mg/kg) ($p<0.01$). When the stress control group(AC), compared to the C1 combination did not exhibit a significant reaction, but the C2 and Kg combinations did ($p < 0.001$). Table 3 presents the findings. The animals administered with a combination of C1, MH (400 mg/kg), and SCB did not exhibit any significant effects; however, the administration of MH (300 mg/kg) and SCB (400 mg/kg) had a stronger effect ($p < 0.05$) had a result. In contrast to the stress control group, the diazepam (2 mg/kg) and C2 combination lengthened the duration spent in the light chamber as shown in Table 4.

CONCLUSIONS

It may be concluded that the standardization and preliminary phytochemical investigations of *Stereospermum colais* Buch, *and Manilkara hexandra* revealed a standard and can be used to determine the identity of the plant materials as well as their quality and purity. These studies can also helpful for the raw material selection for future studies. The study concluded that leaves of *Stereospermum colais* Buch, *and Manilkara hexandra* are rich source of antioxidant. However, the antioxidant potential of these plants was found to be correlated with their phenolic constituents. The results showed that the lyophilized hydroalcoholic leaves extract reversed the behavioral and biochemical changes occur due to stress in dose dependent manner. Finally, our findings imply that oral administration of lyophilized hydroalcoholic leaves extracts of *Stereospermum colais* Buch*, and Manilkara hexandra* are capable of promoting the capacity to endure experimental animals, non-specific stress in evidenced by the wide number of parameters investigated under various types of stress. Since selected plants extracts showed a significant antioxidant activity and anti-stress activity, hence this study may offer new prospective for oxidative stress induced diseases. It is recommended that further investigation be performed to isolate, purify, and quantify the active constituents involved for the anti-stress and antioxidant properties of these plants. The current study would be the leading information pathway.

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