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NEUROPROTECTIVE AND ANTIANXIETY POTENTIALS OF *MIMUSOPS ELENGI* IN MICE

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ABSTRACT

Introduction: Anxiety is one of the most disabling features of many disorders, impairing the normal daily activities of the patients and profoundly affecting their families. The current study was undertaken to ascertain the effects of *MIMUSOPS ELENGI*as ananxiolytic agent. **Materials and Methods:** Elevated plus maze, Light and Dark box Test and Open field test were employed to evaluate acquisition and retention parameters. *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) was administered to both young and aged mice. **Result:** *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) significantly improved acquisition and retention in young mice and also reversed the anxiety induced by diazepam (1 mg/kg, i.p.), and scopolamine (0.4 mg/kg, i.p.). *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) was found to possess potential anti-anxiety effects. **Conclusion:** *MIMUSOPS ELENGI*can be a useful as a potential Neuroprotective and Anxiolytic agent.

KEYWORDS: *MIMUSOPS ELENGI*, Acquisition, Retention, Anxiety.

INTRODUCTION

Anxiety is a state characterized by an unpleasant state of mind set often accompanied by nervousness by pacing back and forth complaints. It is an unpleasant feeling of over anticipated events and committing suicide.[1]

Anxiety disorders affect more than one-eighth of the total population world-wide and has become an important area of research interest in psychopharmacology during this decade. Approximately 18% of the US adult population will suffer from any anxiety disorder during their life, making it the most common mental disorder. Fewer than half of these people receive appropriate treatment due to reasons such as lack of appropriate screening lack of access to medication, being non-responders to medication, and exhibiting subclinical symptoms. However, of those 18% diagnosed with an anxiety disorder, 22.8% are classified as severe, 33.7% as moderate, and 43.5% as mild (N=9282).[2] It is a feeling of fear, uneasiness and worry to a situation that seen as menacing.[3]

Anxiety is a response to a real or perceived immediate threat.[4]

MIMUSOPS ELENGI is a phytochemical based formulation comprising of Gangetin and pharmaceutical adjuvants. This suspension was prepared in our research laboratory using Gangetin. Other ingredients of the preparations were ascorbic acid, cardamom oil, methyl paraben, propyl paraben, propylene glycol, sodium carboxy methyl cellulose and purifiedwater.

MATERIALS AND METHODS

Preparation of *MimusopsElengi*: *MIMUSOPS ELENGI*suspension was prepared using ethanol and methanolic extract of dried leaves of *Mimusopselengi*, methyl paraben, propyl paraben, propylene glycol, sodiumcarboxy methyl cellulose and purifiedwater.

Drugs and Reagents: Diazepam (Calmpose, Ranbaxy, India) were diluted in normal saline and administered intra peritoneal. Volume of administration was 1 ml/ 100 g. All the drugs were administered in the morning session i.e. 9.30 AM- 10.30 AM on each day.

Acute Toxicity Studies: Acute toxicity studies were performed according to OECD/OCDE 421 guidelines. Male Swiss mice selected by random sampling technique were employed in this study. The animals were fasted for 4 h with free access to water only. The experimental protocol was approved by the IAEC, Sarada Vilas College of Pharmacy, Mysuru.

Laboratory models for testing anxiolytic effects

Elevated plus Maze Model: The plus-maze apparatus, consisting of two open arms (16 x 5 cm) and two closed arms (16 x 5 x 12 cm) having an open roof. The *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) and vehicle were administered for 8 days once daily p.o. and

the last dose was given on the 9th day, 60 min prior to experiment. The standard drug Diazepam was given at a dose of 2 mg/kg i.p. 60 min before starting the experiment. After proper treatment each mouse was placed at the center of the maze with its head facing the open arm. During the 5 min experiment, the behavior of the mouse was recorded as: the number of entries into the open or closed arms and time spent by the mouse in each of the arms. An arm entry was defined as the entry of all four paws into the arm. After each trial, the elevated plus- maze apparatus was wiped clean with ethanol (10%) solution.[5,6]

Light and Dark Box Test: Light-Dark Box Test Crawley and Goodwin procedure (1980) was done to assess the anxiolytic activity of the compounds (light-dark box test).[7] The apparatus consisted of a light compartment and a dark compartment. Light dark box is a rectangular box of 46 x 27 x 30 cm (l x b x h), which is divided into 2 compartments. A central opening (7 x 7 cm) on the floor level is placed for the joining of the two compartment. For this experiment, albino mice were divided into four groups, each group comprising of four animals. Vehicle (distilled water 10 ml/kg), standard (diazepam 1 mg/kg), and *MIMUSOPS ELENGI* (250 & 500 mg/kg, p.o.) were administered p.o.one hour after administration, each mouse was placed individually in the illuminated part of the light/dark box. During the test session of 5 min., latency (the time it takes for the animal to move into the dark compartment for the first time), number of entries into the light and dark compartments, total time spent in the light compartment were recorded.

Open Field Test: The mouse were treated with *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) or diazepam 1 mg/kg, i.p). After the treatment-Sixty minutes for aqueous extract and 30 min for Diazepam-the animals were placed individually in the center of the arena and were subjected to a 5-min period to the open field test. The open field apparatus was an opaque plexiglass cage (72 x 72-cm) with walls 35-cm in height where the floor was divided with white lines by 16 squares (18 x 18-cm) of identical dimension. A digital video camera was installed above the cage to record the activity of the mice. The entire room, except the OF was kept dark during the experiment. Total number of crossings and central area rearing were measured.[8]

Statistical Analysis: All the results were expressed as mean ± standard error (SEM). The data was analyzedusing one-way ANOVA followed by Tukey's test. P values <0.05 were considered as statistically significant.

Elevated Plus Maze Test: Mimusops Elengi (250, 500 mg/kg) showed dose-dependent reduction in TL of 8th day and 9th day, indicating remarkable improvement in neuroprotective activity. As compared to respective control groups Diazepam (1 mg/kg, i.p.). **(Table1)**

Light and Dark Box Test: Diazepam (0.5 mg/kg) significantly increased the time spent in light compartment (P<0.001) compared to normal group (Table 2). Significant increase in the time spent in the light compartment P<0.05 was seen with administration of *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) as compared to normal.

Open Field Test: *MIMUSOPS ELENGI*(500 mg/kg, p.o.) showed good anxiolytic activity as compared with normal mice. There was marked decrease in locomotion activity in animals treated with *MIMUSOPS ELENGI*(250 & 500 mg/kg, p.o.) as the number of squares crossed in the perimeter was decreased between the *MIMUSOPS ELENGI*treated groups and differed significantly from the control groups. The frequency of rearing also decreased significantly **(Table 3)**. Treated groups and differed significantly from the control groups. **(Table 3)**

Table 1: Antianxiety activity of Effect of *MIMUSOPS ELENGI.*

Treatment	Dose	No. of Entries in open arm	Time spent in open arm
Control	---	5.67±0.211	3.50±0.224
Diazepam	0.5mg/kg	8.50±0.224	7.50±0.224
MIMUSOPS ELENGI	250mg/kg	5.67±0.211	5.17±0.401
MIMUSOPS ELENGI	500mg/kg	7.33±0.333	7.00±0.258

Each values represents mean+S.E.M. **P<0.001compared to normal control. One-way ANOVA followed by Tukey's test.

Table 2: Effect of on *MIMUSOPS ELENGI*on number of squares crossed in open field apparatus.

Treatment	Dose (p.o.) mg/kg	Number of squares crossed	Rearing
Normal	1 ml /kg	139 ±1.57	22.5±0.87
Diazepam	0.5	73.5 ±1.08a	8.12±0.56a
MIMUSOPS ELENGI	250	112.11±5.8	17.45±0.8
MIMUSOPS ELENGI	500	56.40±12.80	9.75±0.12a

P values a <0.001, b<0.01 as compared to normal treated group. Statistical test employed was ANOVA followed by Tukey-Kramer multiple comparison tests.

Table 3: Effect of on *MIMUSOPS ELENGI*time spent by mice behavior in social interaction test.

Treatment	Dose (p.o.) mg/kg	Time spent (sec) in social interaction
Normal	1 ml /kg	36.14 ±2.7
Diazepam	0.5	71.45± 2.14a
MIMUSOPS ELENGI	250	47.16 ±5.2a
MIMUSOPS ELENGI	500	56.13±1.78b

P values a <0.001, b<0.01 as compared to normal treated group. Statistical test employed was ANOVA followed by Tukey-Kramer multiple comparison tests.

DISCUSSION

Anxiety is the most disabling feature of many disorders, impairing the normal daily activities of the patients and profoundly affecting their families. The ancient Ayurvedic physicians had understood the delicate cellular mechanisms of the body and the deterioration of the functional efficiency of the body tissues.[9,10] This revitalization and rejuvenation is known as the '*rasayanachikitsa*' (rejuvenation therapy). *Rasayana*drugs act inside the human body by modulating the nuero-endocrino-immune systems and have been found to be a rich source of antioxidants. *MIMUSOPS ELENGI*successfully reversed induced anxiety, when administered for successive 8 days. Thus, it is possible that enhanced neuroprotection resulting from in decrease the anxiety level in mice explain the anxiolytic effect exhibited by *MIMUSOPS ELENGI*.

CONCLUSION

*MIMUSOPS ELENGI*can be of enormous use in the preliminary management of early symptoms of CNS disorders like anxiety. Further investigations using human volunteers are warranted for further confirmation of nootropicpotential. The possible involvement of other neurotransmitters like glutamate, GABA, catecholamines, serotonin etc. in the pathogenesis of CNSdisorders.

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