International Journal of
Pharma Medicine and Biological Sciences

IJPMBS
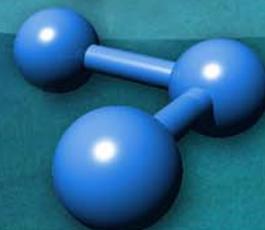
WWW.IJPMBS.COM

Research Paper

ANXIOLYTIC PROFILE OF A POLYHERBAL DRUG MENTAT

Amitabh A Kumar[1]* and Reddy Kiran K P[1]

*Corresponding Author: **Amitabh A Kumar** ✉ aks552914@gmail.com

Background: Mentat, a polyherbal psychotropic preparation, used for its memory enhancing property. Limited studies established its antianxiety property, so we evaluated antianxiety profile of mentat in animal models. Materials and Methods: Antianxiety activity of mentat was assessed in four groups of rats (n=6). The animals were treated orally (p.o.) with 300 and 600 mg/kg of mentat for seven days. On seventh day animals were subjected to Elevated Plus Maze (EPM) test, alprazolam (0.25 mg/kg), was a reference drug. Increase in time spent and number of entries in open arm was considered as an index of antianxiety activity. Results: Mentat exhibits dose dependent antianxiety activity in EPM. Mentat in dose of 300 mg/kg depicted significant antianxiety activity as compared to control group only ($P<0.001$), while at dose of 600 mg/kg showed antianxiety activity, which was significant as compared to control and reference drug ($P<0.001$) in EPM. Conclusion: Results of this study if substantiated by further experimental research suggests that mentat has antianxiety activity. Clinical trials document antianxiety profile of mentat but these trials had limitations like small sample size and single institutional setting. More research is required to develop novel plant products which are safe and have minimal adverse drug effect.

Keywords: Antianxiety, EPM, GABA, Mentat

INTRODUCTION

Anxiety has been described as recurring and alarming malady affecting the mankind, unrelated to ethnicity, and is deemed as a paramount token of many psychiatric disorders (Tijani *et al.*, 2012). Anxiety affects one-eighth of the world population and has emerged as an imperative area of research. Anxiety, a condition of extreme panic, is distinguished by sympathetic hyperactivity, motor tension, uneasiness and alertness syndromes. One of the major compounds used in the treatment of anxiety is benzodiazepines, however, these drugs produce many undesirable effects such as muscle relaxation, sedation, amnesia, ataxia and tolerance (Lader and Morton, 1991). Research in the domain of psycho-pharmacology has bestowed greatly to the

[1] Department of Pharmacology, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh, 524002, India.

diagnosis and treatment of anxiety disorders such as stress, phobias, panic, generalized anxiety, and post traumatic stress disorders. Sizeable number of patients affected by anxiety disorders have to endure the sequel of the adverse effects of the current therapeutic regimens and present comorbid hazard in memory and cognitive chore (Eyseck and Calvo, 1992).

Importance of alternative medicines sourced from plants that influence the mind is evolving. It is estimated that about 45% of patients suffering from anxiety use some form of complementary therapy. The most popular include herbal medicines (Yadav *et al.*, 2008). Medicinal plants have found ample of acceptability and efficacy in the treatment of various neuropsychiatric disorders like depression, cognition impairment and anxiety. One such polyherbal psychotropic preparation, Mentat, an Ayurvedic medicine is found to be useful in the management of nervous disorders. Mentat (BR-16A) is a herbal amalgam of various ingredients, the chief herbs in the mentat are Brahmi (*Bacopa monnieri*), Ashwagandha (*Withania somnifera*), Mandookaparni (*Centella asiatica*), Jatamansi (*Nardostachys jatamansi*), Tagar (*Valeriana wallichi*), Shankhapuspi (*Evolvulus alsinoides*), Vach (*Acorus calamus*), Malkangni (*Celastrus paniculatus*), Guduchi (*Tinospora cordifolia*), Kuth (*Saussurea lappa*), *Terminalia chebula*, Amla (*Embelica officinalis*) and *Terminalia belerica*. Among these *B. monnieri*, *W. somnifera*, *C. asiatica*, *N. jatamansi*, *V. wallichi*, *E. alsinoides*, *A. calamus*, *C. paniculatus* and *T. cordifolia* have been categorized in Ayurveda as *Medharasayanas* and asserts to enhance intellect and memory (Kumar, 2006; Babu *et al.*, 2010).

Pharmacological investigations have revealed it to be a safe preparation with central action. Mentat improves memory quotient, memory span, concentration and stress threshold. Clinical trials have reported it to be efficacious in behavioral disorder following post natal organic lesions of CNS and in case of minimal brain dysfunction (Kumar, 2006; Babu *et al.*, 2010). Very few experimental studies document antianxiety effect of mentat as it is mainly used for its memory enhancing property. Therefore, we conducted this study to evaluate antianxiety effect of mentat in rats using the Elevated Plus Maze (EPM), a standard behavioral model in which aversive behavior of rats in response to open elevated areas is considered as an index of anxiety.

MATERIALS AND METHODS

Animals

Adult Wistar albino rats weighing between 200-250 g were used for this study. Rats were procured from central animal house of Narayana Medical College, Nellore. The animals were housed in cages in temperature-regulated rooms with air cooling and 12 h light and dark cycle, and had an access to food and water ad libitum. They were allowed to acclimatize to the laboratory conditions for a period of one week. The study was approved by the Institutional Animal Ethics Committee (proposal number 7/2010/NMC), Narayana Medical College and all the experiments were performed as per the Committee for the purpose of control and supervision on experiments on animals (CPCSEA) guidelines.

Drugs

Mentat (The Himalaya Drug Co.), different concentrations of mentat were prepared by serial dilution from a stock solution of 100 mg/ml in sterile

water. Alprazolam (Micro labs) was used as reference drug, it was diluted with saline to the required strength before use. All the solutions were prepared fresh on the test day and administered orally (p.o.).

Assessment of Antianxiety Activity

Grouping

The animals were randomly divided into four groups, each containing 6 animals (Table 1). Group I was control group treated with normal saline (10 ml/kg p.o.), Group II treated with standard drug alprazolam (0.25 mg/ kg, p.o.), Group III and Group IV were given mentat 300 mg/kg (p.o) and mentat 600 mg/kg (p.o.) respectively. Both Group III and Group IV were given the mentioned doses of mentat twice a day for seven days. On the seventh day animals were subjected to EPM test.

Elevated Plus Maze (EPM) Test

As demonstrated by Lister (1987), the method of EMP was performed to evaluate antianxiety effect of mentat on the rats. This method is based on the principle of natural propensity of rats to develop anxiety towards a novel and potentially unsafe settings signified by open and high spaces. The EPM is a plus (+) shaped apparatus consists of two opposite open arms (50 cm X 5 cm X 10 cm) crossed with two enclosed arms of same dimensions with 30 cm high walls and these arms extended from a common central square (10 cm X 10 cm). The entire maze was elevated to a height of 50 cm above the floor level.

Procedure

Rats in each group were subjected to a standard 5 min test. Rats were placed on the maze after administration of the normal saline (NS), test and standard drugs. After one hour of oral administration of NS, test drug (mentat 300 mg/kg and 600 mg/kg) and the standard drug (alprazolam 0.25 mg/kg), the animals were placed at the centre of the maze, facing one of the open arms and were allowed to explore the maze freely for 5 min. The time spent and number of entries in both enclosed and open arms were recorded. Increase in the number of entries and the time spent in open arm of EPM was considered as an index of antianxiety activity. Thorough cleaning of the maze was performed with the help of tissue paper moistened with 70% alcohol after each test.

STATISTICAL ANALYSIS

The data was collected in case record forms. Then they were entered into excel spreadsheet 2007. Microsoft Excel-2007 and Sigma Graph pad prism version-5 USA was used to perform

S. No.	Group & Dose (mg/kg)	No. of entries mean(SD)		Time spent in sec mean(SD)	
		Open arm	Closed arm	Open arm	Closed arm
1.	Group I Control	1.33(0.51)	2.5(0.54)	34.5(6.28)	265.5(6.25)
2.	Group II Alprazolam 0.25 mg/kg(p.o)	4.8(0.75)**[a]	1.83(0.75)	143.16(10.49)**[a]	156.83(10.5)
3.	Group III Mentat 300 mg/kg (p.o)	1.66(0.51)[ns]	2.16(0.74)	54.83(7.11)**[a]	245.1(7.1)
4.	Group IV Mentat 600 mg/kg (p.o)	2.83(0.75)*[a]	2.33(0.51)	83.16(9.55)**[ab]	216.8(9.5)

Table 1: Effect of Mentat on Elevated Plus Maze Apparatus in Rats (n=6)

**Note:** * $p < 0.01$, ** $p < 0.001$; [a] when compared with control; [b] compared with standard.

statistical analysis. Data was described as Mean (Standard deviation, SD) (Curran-Everette and Benos, 2004). One way ANOVA followed by Dunnets test to compare control with all other columns and Newman-Keuls Multiple Comparison Test was used for analysis of data between the inter individual groups. For all inferential statistical tests a two tailed $P < 0.05$ was considered significant. All the results of test drug (mentat 300 mg/kg and 600 mg/kg) were compared with control as well as standard groups.

RESULTS

Effect of Mentat on Time Spent in Open Arm of EPM (Table 1, Figure 1A).

Mentat 300 mg/kg significantly increased the time spent in open arm of EPM as compared to control ($P<0.001$), whereas mentat 600 mg/kg significantly increased the time spent in open arm of EPM as compared to control ($P<0.001$) and test (alprazolam) group ($P<0.001$).

Figure 1A: Effect of Mentat on Elevated Maze Apparatus in Rats (as per Table 1)
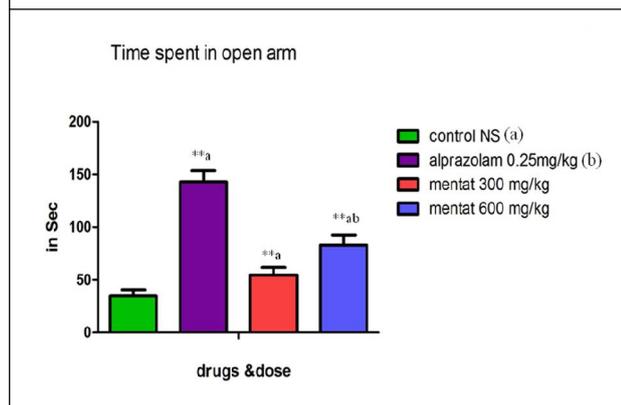
Effect of Mentat on Entry in Open Arm of EPM (Table 1, Figure 1B).

Mentat 300 mg/kg showed no significant results with respect to entry into open arm as compared to control and test group ($P>0.05$), whereas mentat 600 mg/kg significantly increased the number of entries in open arm as compared to control only ($P<0.01$).

Figure 1B: Effect of mentat on Elevated Maze Apparatus in Rats (as per Table 1)
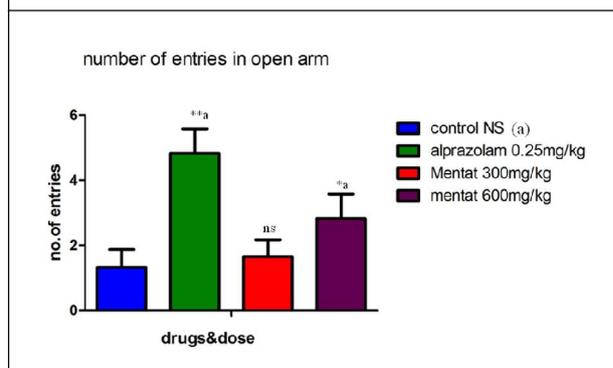
DISCUSSION

Since last four decades benzodiazepines are considerably used for the treatment of numerous forms of anxiety; owing to their undesirable effects such as memory impairment and amnesia, hunt for alternative therapies with beneficial effects such as antianxiety efficacy and memory enhancing profile together with reasonable costs are of great attraction. Polyherbal formulations used in Ayurvedic medicines, bestow synergistic therapeutic effect. Research has been conducted to investigate anxiolytic profile of mentat. Results of our study show that mentat, a polyherbal drug has dose dependent antianxiety effect in EPM model of anxiety. The EPM test is one of the most popular and extensively used animal model for screening of antianxiety drugs (Lister, 1987). Anxiolytics augment the number of entries and time spent in the open arm of the EPM, whereas anxiogenic compounds produce the opposite effect (Lister, 1987).

In our study, mentat 600 mg/kg significantly increased the time spent (Figure 1A) and number

of entries (Figure 1B) in open arm of EPM as compared to control (P<0.001) and test (alprazolam) group (P<0.001) (Table 1). The results of our study are in accordance with the study carried out by Kumar *et al.* (2007). They showed that mentat demonstrated a significant anxiolytic effect in rats tested on various models of anxiety such as open field exploratory behavior, elevated zero maze behaviour and novelty induced suppressed feeding latency tests. They concluded that mentat may modulate $GABA_A$ receptor complex for its antianxiety profile.

The three major components of mentat are *Bacopa monnieri* (Brahmi), *Centella asiatica* (Mandookaparni) and *Withania somnifera* (Ashwagandha). Brahmi contains five chief saponins bacoside A3, bacopasaponin C isomer, bacopaside II, bacopasaponin C and bacopaside I (Phrompittayarat *et al.*, 2007). Bacosides present in Brahmi reduces heat shock protein (Hsp) expression in hippocampus and modulates activity of Hsp70 as well as it increases superoxide dismutase activity (SOD) in stressed rats (Kar Chowdhury *et al.*, 2002). In a recent randomized, double blind, placebo controlled clinical trial, Brahmi treated participants showed significant improvement in the scores of anxiety, recall memory and depression as compared to placebo treated group (Calabrese *et al.*, 2008).

Another component of mentat, Mandookaparni, enhances EPM performance, decrease locomotor activity and attenuate acoustic startle response (Chen *et al.,* 2006). Clinical trial carried out in 33 volunteers for two months by Jana *et al.* (2010), documented antianxiety effect of Mandookaparni.

Bhattacharya *et al.* (2000) showed that *Withania somnifera* (WS) induced an anxiolytic effect in the EPM, social interaction and feeding latency tests. WS has $GABA_A$ agonistic property so it may be beneficial in anxiety related disorders. A double blind placebo control studies in patients with anxiety disorder were treated with WS for the period of 6 weeks and the results showed that WS possesses anxiolytic activity as compared to placebo (Andrade *et al.*, 2000).

Polyherbal preparations used in Ayurveda (Medharasayanas) are based on the concept that ingredients may work in synergism, thereby enhancing GABA neurotransmission which may be the possible explanation for the antianxiety effects of mentat in our study, so a drug like mentat can serve as a good therapeutic option as compared to benzodiazepine like drugs which induce loss of memory, impair cognition and tolerance in their routine use in patients suffering with anxiety.

CONCLUSION

In our study mentat depicts dose dependent antianxiety profile. Traditional medicines have been used to alleviate the suffering of human beings since the dawn of human civilization. Despite their wide spread usage traditional medicines have not been evaluated scientifically with regard to their safety, efficacy and has many limitations. However, our findings if substantiated by further experimental and clinical studies on the antianxiety profile of mentat will be fruitful in development of newer compounds (plant products) which are safe and have minimal adverse drug effect.

ACKNOWLEDGMENT

REFERENCES

1. Andrade C, Aswath A, Chaturvedi S K, Srinivasa M and Raguram R (2000), "A double-blind placebo-controlled evaluation of anxiolytic efficacy of an ethanolic extract of Withania somnifera", *Indian Journal of Psychiatry,* Vol. 42, pp. 295–30.

2. Babu B H, Lakshmi M S and Kumar S A (2010), "A review on traditional system of medicine for treats epilepsy", *Int J Biol & Pharm Res*, Vol. 1, pp. 1-6.

3. Bhattacharya S K, Bhattacharya A, Sairam K and Ghosal S (2000), "Anxiolytic-antidepressant activity of *Withania somnifera* glyco with anolides: an experimental study", *Phytomedicine,* Vol. 7(6), pp. 463-469.

4. Calabrese C, Gregory W L, Leo M, Kraemer D, Bone K and Oken B (2008), "Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial", The *Journal of Alternative & Complementary Medicine*, Vol. 14, pp. 707-713.

5. Chen S W, Wang W J, Li W J, Wang R, Li Y L, Huang Y N and Liang X (2006), "Anxiolytic-like effect of asiaticoside in mice", *Pharmacology Biochemistry & Behavior*, Vol. 85, pp. 339-344.

6. Curran-Everette D, Benos D J (2004), "Guidelines for reporting statistics in journals published by the American Physiological Society", *Am J Physiol Regular Integr Comp Physiol*, Vol. 287, pp. 247-249.

7. Eysenck M W and Calvo M G (1992), "Anxiety and performance: the processing efficiency theory", *Cognition and Emotion*, Vol. 6, pp. 409-434.

8. Jana U, Sur T K, Maity L N, Debnath P K and Bhattacharyya D, (2010), "A clinical study on the management of generalized anxiety disorder with *Centella asiatica*", *Nepal Medical College Journal*, Vol. 12, pp. 8-11.

9. Kar Chowdhury P, Parmar D, Kakkar P, Shukla R, Seth P K, Srimal R C (2002), "Anti-stress effect of bacosides of *Bacopa monniera*: Modulation of Hsp 70 expression, superoxide dismutase and cytochrome P450 activities in rat brain", *Phytotherapy Research,* Vol. 16, pp. 639-645.

10. Kumar V (2006), "Potential medicinal plants for CNS disorders: an overview", *Phytother Res*, Vol. 20, pp. 1023-1035.

11. Kumar V, Husain G M and Mridula S (2007), "Comparative anxiolytic activity of Mentat and Shankhapushpi", *Pharmainfo.net*, Vol. 5(3).

12. Lader M and Morton S (1991), "Benzodiazepine problems", *Br J Addict*, Vol. 83, pp. 823-828.

13. Lister R G (1987), "The use of plus-maze to measure anxiety in the mouse", *Psychopharmacology* (Berlin), Vol. 92, pp. 180-185.

14. Phrompittayarat W, Putalun W, Tanaka H, Jetiyanon K, Wittaya-Areekul S and Ingkaninan K (2007), "Determination of pseudojujubogenin glycosides from Brahmi based on immunoassay using a monoclonal antibody against bacopaside I", *Phytochemical analysis*, Vol. 18, pp. 411-418.

15. Tijani A Y, Salawu O A, Anuka J A and Isah M H (2012), "Sedative and Anxiolytic effects of *Crinum zeylanicum* methanolic bulb extract in mice", *Med. Chem. & Drug Dis,* Vol. 3, pp. 20-29.

16. Yadav A V, Kawale L A and Nade V S (2008), "Effect of *Morus alba* L (mulberry leaves) on anxiety in mice", *Ind J of Pharmacol,* Vol. 40, pp. 32-36.