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ACUTE ANXIOLYTIC EFFECT OF AQUEOUS EXTRACT OF FRUITS OF *TERMINALIA CHEBULA* (AETC) IN MICE

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ABSTRACT

Anxiety is a psychological and physiological state characterized by cognitive, somatic, emotional, and behavioural components. Benzodiazepines (BZDs) are the major class of compounds used in anxiety and they remain the most commonly prescribed treatment for anxiety. In the present study, we have attempted to evaluate the acute anxiolytic activity of aqueous extract of fruits of *Terminalia chebula* (AETC) by Light and Dark Arena in Swiss albino mice. Mice weighing 25-30gm were divided into 5 groups containing 6 animals for each dose and were housed for 10 days prior to testing. The control (1% Gum acacia), test drug AETC (1.3, 2.6 and 5.2 mg/ kg) and standard drug Diazepam (1.0 mg/kg) were administered orally. One hour after oral administration of the drugs / vehicle, the experiment was conducted by Light and Dark Arena in Swiss albino mice. The results suggest that, behavioural disinhibitory effects of AETC exhibited anxiolytic activity at the dose of 1.3 and 2.6 mg/kg comparable to diazepam.

***KEYWORDS:** Anxiety, Anxiolytic, Light and Dark Arena, Terminalia chebula, Tannic acid*

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INTRODUCTION

Anxiety, is a state of excessive fear which is characterized by motor tension, sympathetic hyperactivity, apprehension and vigilance syndromes.[1] It also includes debilitating physical manifestations as headaches, uncontrolled trembling, sweating, muscle tension and aches.[2] Among world population, about one-eighth is suffering from anxiety and it has become a very important area of research interest in psychopharmacology. Benzodiazepines have remained the most commonly prescribed treatment for anxiety and anxiety related disorders, inspite of the unwanted side effects such as sedation, muscle relaxation, ataxia, amnesia and tolerance.[3] Herbal medicines have been used to treat central nervous system (CNS) disorders from many centuries. Importance of plant-derived medications that affect the "mind" is growing globally. Different herbal medicines have been used as anxiolytic drugs in different parts of the world.[4]

Terminalia chebula belongs to family Combretaceae and is a medium to large-sized tree distributed throughout tropical and sub tropical Asia, including China and Tibet.[5] This tree wildly grows in the forests of Northern India, Uttar Pradesh and Bengal; and is common in Tamil Nadu, Karnataka and in Southern Maharashtra. The fruit is used medicinally in the Indian system of medicine. In Ayurveda, this drug is considered to be a *rasayana* for *Vata*, balances all three *doshas (tridosham),* enhances digestion *(dipanapachana),* sharpens the senses *(medhyam),* and displays alterative, astringent, expectorant, anti-inflammatory, anodyne, cardiotonic, laxative, antiseptic, and antiemetic properties.[6, 7, 8] *Terminalia chebula* exhibits a variety of biological activities, such as anti-diabetic,[9] anti-cancer,[10] anti-mutagenic[11] and anti-viral activity.[12] AETC appeared to have good antioxidant activities as it is known to contain phenolic compounds and tannin.[13] It is believed that tannins have neuroprotective functions capable of reversing 6-hydroxydopamine-induced toxicity. The tannic acid has shown promise as a potential therapeutic agent, which may be beneficial in patients with neurological disease[14].

MATERIALS & METHODS

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Yenepoya Medical College, Yenepoya University, Mangalore, India.

Animals

Adult male Swiss Albino mice weighing 25-30 gm from our breeding stock were used in this study. The animals were housed at 24±2^{o}C with 12:12 h light and dark cycle. They had free access to food and water *ad libitum*. The animals were acclimatized for a period of 10 days before the study. The study was conducted according to CPCSEA guidelines.

Sample Size, Grouping and Dose of the Drugs

Animals were divided in to 5 groups (Control, Standard & Test drug) containing 6 animals making a total number of 30 animals (**Table 1**)

Table 1
Drugs / Dose of the Drugs, Groups and Number of Mice in Each Group

Drugs / Dose	Groups	Number of Mice (n=6)
Control (1% Gum acacia) (10 ml/kg)	I	6
Diazepam (1.0 mg/kg)	II	6
AETC (1.3 mg/kg)	III	6
AETC (2.6 mg/kg)	IV	6
AETC (5.2mg/kg)	V	6

Drugs and chemicals
The standard anxiolytic drug Diazepam was obtained from our institutional pharmacy. The test drug *Terminalia chebula* was provided by Al Thary Enterprises, Mangalore.

APPARATUS

Light and dark arena
The apparatus consisted of an open top wooden box. Two distinct chambers, a black chamber (20 X 30 X 35cm) painted black and illuminated with dimmed red light and a bright chamber (30 X 30 X 35 cm) painted white and brightly illuminated with a 100W white light source, were located 17 cm above the box. The two chambers were connected through a small open doorway (7.5 X5 cm) situated on the floor level at the centre of the partition.

Behavioural assessment
On the day of the experiment, the animals were divided randomly into control and experimental groups (n=6). Group 1 received the vehicle, 1% gum acacia(10ml/kg) and served as the control group, groups 2, 3 and 4 received AETC in doses of 1.3, 2.6 & 5.2 mg/kg, and group 5 received the standard drug Diazepam (1.0mg/kg) per orally. Behavioural evaluation was carried out 60 minutes post drug/vehicle administration. Anxiolytic activity of AETC was evaluated using the experimental model of Light and Dark arena (Table 2). Behavioural assessment was carried out by observing the time spent in Light arena, number of entries in to Light arena and number of rears in Light arena.

STATISTICAL ANALYSIS
The data were analyzed by one-way ANOVA and Post-hoc comparisons were performed by applying Dunnet's multiple comparison test. $P < 0.05$ was considered statistically significant.

Table 2
Effect of Acute Administration of AETC on Mice Behaviour in Light and Dark Arena

Drugs/ Groups	Time spent in Light arena (sec)	Number of entries in to Light arena	Number of rears in Light arena
1% Gum acacia 10.0ml/kg)	60.79±0.93	1.5±0.34	1.33±0.21
Diazepam(1.0 mg/kg)	132.57±2.05	3.5±0.34	5.33±0.33
AETC 1.3 mg/kg	178.64±4.96***	3±0.25**	2.83±0.30***
AETC 2.6 mg/kg	114.47±5.10***	3.33±0.42***	4±0.36***
AETC 5.2 mg/kg	70.2±2.36*	1.33±0.21*	1.83±0.30*

n=6. The observation are mean ± SEM *p>0.05, **p<0.05, ***p< 0.01, as compared control (ANOVA followed by Dunnett's multiple comparison test)
AETC- Aqueous Extract of Terminalia chebula.

RESULTS AND DISCUSSION

Anxiety is a normal reaction to stress, but when it becomes excessive it may fall under the classification of an anxiety disorder. Though safe for short term treatment, benzodiazepines on long term produce many unwanted effects. Hence the search for safe and effective alternate anxiolytic agents. Fruits of *Terminalia chebula* have many medicinal uses and AETC contains phenolic compounds and tannin. Tannins have neuroprotective function and antioxidant property.

In the present study, we have attempted to evaluate the acute anxiolytic activity of AETC by Light and Dark Arena in Swiss albino mice. Behavioural assessment was carried out by observing the time spent in Light arena, number of entries in to Light arena and number of rears in Light arena.

Our results (Table 2) suggest that, behavioural disinhibitory effects of AETC exhibited anxiolytic activity at the dose of 1.3 and 2.6 mg/kg comparable to diazepam by increase in time spent in Light arena ($p<0.01$). In the dose of 1.3 mg /kg ($p<0.05$) and 2.6 mg /kg ($p<0.01$) shows the increase in number of entries in to the Light arena. Number of rears were also increased in the dose of 1.3 and 2.6 mg/kg ($p<0.01$) in the Light arena.

However, further studies are needed to evaluate its mechanism of action and therapeutic benefit as an adjuvant in the treatment of anxiety disorders.

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