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Original Research Article

Effect of aqueous Extract of Terminalia bellirica fruit pulp on Alcohol affected learning in swiss albino mice

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ABSTRACT

Aim: To evaluate the effect of Aqueous extract of Terminalia bellirica fruit pulp (AETB) on learning by Hebb William maze model in mice with acute alcohol consumption.**Materials and Methods:** Swiss albino mice (n=48) of either sex weighing 20-30g will be divided into eight groups of six mice each. Drugs were given orally after 12 hours of fasting. Group I mice received 10ml/kg of Normal Saline, Group II mice received Piracetam 200mg/kg, Group III received AETB 36mg/kg, Group IV received ethanol 1.5g/kg orally, Group V received ethanol(1.5g/kg)+ piracetam (200mg/kg), Group VI mice received ethanol(1.5g/kg)+AETB(9mg/kg), Group VII mice received ethanol(1.5g/kg)+AETB (18mg/kg), Group VIII mice received ethanol(1.5g/kg)+AETB(36mg/kg). Time taken by the animal to reach the reward chamber from the start chamber (TRC) in Hebb-William maze was used as a parameter to evaluate the learning.**Results:** Acute alcohol administration showed increase in TRC. Whereas, acute administration of Aqueous extracts of Terminalia bellirica fruit pulp showed a decrease in TRC when compared to the control group. The TRC values for the groups that were administered AETB along with acute alcohol administration showed decrease in TRC values compared to the negative control.**Conclusion:** Current study showed acute alcohol administration caused impairment of the learning ability in mice. Whereas, acute administration of Aqueous extracts of Terminalia bellirica fruit pulp (AETB) caused enhancement of learning. Pre-treatment with AETB before acute alcohol administration indicated protective action of AETB on alcohol affected learning in mice.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Learning is a process by which brain acquires new information about the events occurring in the given surroundings whereas, memory is a facility by which sensations, impressions, and ideas are stored and recalled.¹

Acute alcohol intoxication results from excess intake of alcohol in a single episode of drinking. The accumulation of ethanol in the body results in various clinical manifestations with hepatic, cardiac, gastrointestinal, pulmonary, metabolic, behavioural and neurological effects.² The

hippocampus which is closely related to learning and memory function, can especially be affected by ethanol.^{3,4}

Terminalia bellirica belongs to family Combretaceae. Fruit is globose, silky-brownish-velvety.⁵ Fruit contains terpenoids (belleric acid and chebulagic acid), saponin (bellericoside and bellericanin)⁶ and tannins (23.60%-37.36%), which are composed of chebulinic acid, chebulagic acid, 1, 3, 6-trigalloylglucose and 1,2,3,4, 6-pentagalloylglucose, corilagin, and glucogallin etc.⁷

Fruits are useful in treatment of hepatitis, bronchitis, asthma, dyspepsia, piles, diarrhoea, coughs, hoarseness of voice, eye diseases, scorpion-sting and also used as a hair tonic.⁸ Decoction of the green fruit is used for cough. Pulp

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of the fruit is useful in dysenteric-diarrhoea, dropsy, piles and leprosy. Half ripe fruit is used as purgative. Kernel of the fruit is narcotic. Seed oil is used in rheumatism. The triterpenoid present in the fruits possess significant antimicrobial activity. Kernel oil has purgative action and its prolonged use is well tolerated in mice.⁹

Studies have established various properties of Terminalia bellirica but its effect on alcohol induced learning and memory impairment is not yet studied. Studies show that even acute administration of Terminalia Chebula, enhances learning in mice.¹⁰ It belongs to the same genus and is one of the three components of triphala along with Terminalia bellirica. This explains the need for study.

2. Materials and Methods

2.1. Animals

Institutional Animal Ethics Committee permission was obtained before starting the study. (Ref. No. IAEC/02/03/2019/CPSEA). 48 Swiss albino mice of either sex weighing 20-30 grams bred and maintained under standard conditions in the central animal house in AJIMS and RC were used. They were kept at the animal house of the institute, in clean, clear polypropylene cages in groups of six and maintained at standard laboratory temperature and humidity (40-60%) with light/dark cycle of 12:12 hours. Animals were provided with standard diet and water ad libitum. They were allowed to acclimatize to the laboratory conditions for one week.

The experiment was performed as per the Committee for Purpose of Control and Supervision on Experiments on Animals (CPCSEA) guidelines.

2.2. Drugs

The standard drug Piracetam was obtained from micro labs. The dried fruit of Terminalia bellirica was obtained by Sri Lakshmi Ayurvedic Dispensary, Mangalore. Ethanol was obtained from Changshu Yanguan Chemical, China.

2.3. Extract preparation

About 1000 g of air-dried crude powder of Terminalia bellirica fruit pulp was extracted with water in Soxhlet extractor for 36 hours. It was dried and reduced under controlled pressure and temperature (40-50°C) using a rotator evaporator. The aqueous extract had a yield of brownish mass weighing 145g. The yield obtained was 14.5% w/w with respect to dried powder.¹¹

2.4. Drug Administration

Piracetam 200mg/kg Body weight, administered orally.

Alcohol (15%) 1.5g/kg, administered per oral¹²

Aqueous Extract of Terminalia bellirica fruit pulp [AETB] -Investigational product.

AETB (dose1) – 9mg/kg orally.

AETB (dose2) – 18mg/kg orally.

AETB (dose 3) - 36mg/kg orally¹¹

2.5. Methodology

Swiss albino mice (n=48) of either sex weighing 20-30g were divided into eight groups of six mice each. Drugs were given orally after 12 hours of fasting. Group I mice received 10ml/kg of Normal Saline, Group II mice received Piracetam 200mg/kg, Group III received AETB 36mg/kg, Group IV received ethanol 1.5g/kg orally, Group V received ethanol (1.5g/kg) + piracetam (200mg/kg), Group VI mice received ethanol (1.5g/kg)+AETB(9mg/kg), Group VII mice received ethanol (1.5g/kg) + AETB (18mg/kg), Group VIII mice received ethanol (1.5g/kg) + AETB(36mg/kg). Time taken by the animal to reach the reward chamber from the start chamber (TRC) in Hebb-William maze was used as a parameter to evaluate the learning.¹²

2.6. Apparatus

2.6.1. Hebb- William Maze¹³

It is a tool for incentive based exteroceptive behavioural model. The total time taken by the mice to reach the reward chamber from the start box indicates learning. The animals are acclimated to the maze environment through timed exposure periods. During the testing phase, the mice is placed in the start box and the door is opened to facilitate the entry of the mice into next chamber. The door of the start box is closed immediately after the animal moves into the next chamber to prevent back entry. The time taken by the animal to reach the reward chamber from the start box is recorded. (TRC)

2.6.2. Statistics

Results were analysed by ANNOVA followed by post hoc Dunnet's multiple comparison test. The observations were mean \pm SD $p < 0.05$ was considered statistically significant. (Figure 1)

3. Results & Discussion

Ethanol can cause direct alteration of various ion channels, receptors and enzymes. These actions contribute to changes in synaptic function and plasticity. Ethanol augments the actions of certain GABA receptors and inhibits the effects of glutamate. Ethanol also promotes neurosteroid synthesis locally in the brain. This increases steroid levels in the hippocampus within few minutes of exposure. These are likely to cause changes in cognition.¹⁰

In the present study, Piracetam (200mg/kg) and AETB (36mg/kg) significantly reduced the time taken to reach the reward chamber ($p < 0.001$), while Ethanol (1.5g/kg) significantly increased the latency when compared to vehicle treated groups ($p < 0.001$). Animals pre-treated with

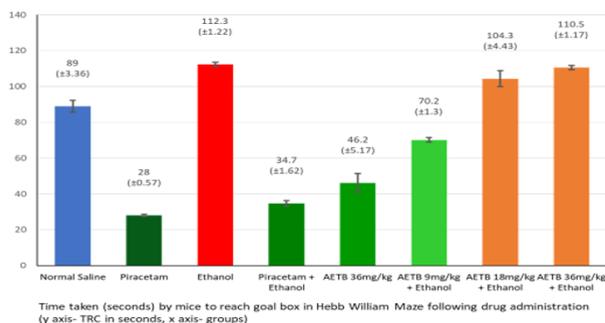


Fig. 1: Effect of Aqueous extract of *Terminalia bellirica* fruit pulp (AETB) on learning by Hebb William maze model in mice with acute alcohol consumption. (mean \pm SD) $p < 0.001$ - Highly significant.

Piracetam (200mg/kg) and AETB (9mg/kg) significantly reduced the enhanced latency induced by Ethanol when compared to Ethanol alone treated group ($p < 0.001$). However, the test drug AETB at higher doses (18mg/kg and 36mg/kg) failed to reduce the enhanced latency induced by Ethanol. Decrease and increase in latency period in Hebb-Williams Maze is indicative of improvement and impairment of learning process respectively. In the present study, the test drug alone at the highest dose tested, produced the effect similar to that of Piracetam and opposite to that of Ethanol. This suggests that the test drug enhances learning process.

The terpenoids (belleric acid and chebulagic acid), saponins (bellericoside and bellericanin) and tannins in general are known to have neuroprotective activity.¹⁴ This was a single day study, and the protective action of *Terminalia Bellirica* was evaluated for acute alcohol induced impairment in learning process. Further chronic studies would be useful in evaluating the long term effects of *Terminalia Bellirica* and its effects on chronic alcohol induced memory impairment.

4. Conclusion

Our study indicates that the test drug enhances the learning process and is comparable to the standard drug Piracetam at higher doses (36mg/kg). Also, it can oppose the alcohol induced learning impairment at lower doses (9mg/kg).

5. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

6. Source of Funding

None.

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