NEUROPROTECTIVE EFFECT OF EMBLICA OFFICINALIS LEAVES EXTRACT AGAINST ALZHEIMER'S DISEASE INDUCED IN ANIMAL MODEL

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Abstract

In traditional Indian medicine, all parts of Emblica officinalis Gaertn plant including the fruit, seed, leaves, root, bark and flowers are used in various herbal preparations for the treatment of diabetes mellitus, chronic diarrhoea, anti-inflammatory and antipyretic. Neuroprotective effect of Emblica officinalis leaves extract against Alzheimer's disease induced in animal model. The experiment was designed for 21 days and either sex Wistar rats were divided into 5 groups (n=6). Group 1 served as normal control (treated with normal saline 2ml/kg), Group 2 Served as negative control group (treated with $AlCl_3$ 100mg/kg p.o.), Group 3 Was treated with AlCl3 100mg/kg p.o. + Hydro-methanolic Emblica officinalis leaves extract 100mg/kg p.o., Group 4 treated with AlCl3 100mg/kg p.o. + Hydro-methanolic Emblica officinalis leaves extract 200mg/kg p.o., Group 5 received Rivastigmine 1.5mg/kg p.o. respectively. The neuroprotective effect was measured by behavioral and biochemical parameters, for behavioral parameters, Morris water maze test, elevated plus maze test, Rotarod test, Pole climbing test, Locomotor tests were done. At the end of all experiment rats were sacrificed and brains were dissected and prepared homogenate for determination of behavioral parameters, acetylcholinesterase (AchE) levels and oxidative stress was measured in brain by level of antioxidant markers i.e., superoxide dismutase (SOD), reduced glutathione (GSH), and catalase (CAT) and histopathologic examination. This study indicated that AlCl3 induced AD rats shows reduction in behavior and in biochemical, increase AchE levels, decrease oxidative stress. While rats treated with Rivastigmine and Emblica officinalis in protective and therapeutic groups exhibited significant improvement in behavior, significant increase in brain Ach and decrease AchE levels, increase oxidative stress. The results suggest that the hydro methanolic extract of leaves of Emblica officinalis treated group may effectively normalize the impaired antioxidant status in AlCl3 induced Alzheimer's disease.

Keywords*: Alzheimer's Disease, $AlCl_3$, Emblica officinalis, Acetyl cholinesterase.*

Introduction

In this industrialized world, Alzheimer's disease is the most common neurological disorder and one of the most significant socioeconomic issues. It's a neurological condition that develops with aging and is permanent and progressive. **Rao et al. [16]**, It is also characterised by unusual behaviour, severe memory loss, personality changes, and a progressive, irreversible loss of cognitive function. **Rao et al. [16]**

The primary pathogenic characteristics of AD are the intracellular deposition of neurofibrillary tangles (NFT), which have been related to paired helical filaments (PHF), hyperphosphorylated tau protein, and extracellular amyloid beta (Aβ) peptide build-up in senile plaques. **Selkoe et al. [17], LaFerla et al. [5]** AD attacks nerves and brain cells as well as neurotransmitters, neural cell loss in the cerebral cortex and hippocampus by intraneuronal neurofibrillary tangles (Tau protein) and extracellular beta amyloid (Aβ) plaques deposition. **Boccardi et al. [1].**

There is no treatment exists for AD, currently drugs available to treat only its symptoms and with limited effectiveness. **Rao et al. [16].** four synthetic medications that can inhibit acetylcholinesterase or antagonize the *N*-methyl-D-aspartate receptor (NMDA) are rivastigmine, galantamine, donepezil, and memantine. **Kucwaj et al. [10].**

Rivastigmine is the only cholinesterase inhibitor that is often used and functions as a dual inhibitor of both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). **Bullock & Cameron [2].** Rivastigmine has been demonstrated to be useful in mild to moderate dementia linked with Parkinson's disease as well as AD because it helps patients' cognitive, behavioral, and daily functioning. A potent therapy for mild-to-moderate Alzheimer's disease is rivastigmine, a "pseudo-irreversible" acetyl- and butyrlcholinesterase inhibitor with a phenylcarbamate structure.

Aluminium, is one of the trace elements with a moderate toxic effect, it is naturally present in the Earth's crust and it could be toxic for humans. It's now been hypothesized to play a role in the cause of Alzheimer's disease. In nature, aluminium is the metal that is most abundant, it has also been established that it is not essential to human metabolism at any concentration. The most frequent way for people to be exposed to aluminium is through gastrointestinal absorption. Aluminium has a causative role in humans. Once the metal enters the blood, about 90% of it is bound to transferrin, and the rate of absorption is about 0.22 percent. Al has been linked to the onset and severity of a number of diseases, **Monaco *et al.* [14].** including osteomalacia, dialysis encephalopathy, and microcytic anaemia. Numerous studies have found that patients with Parkinson's disease, amyotrophic lateral sclerosis, and Alzheimer's-type senile dementia had elevated levels of aluminium in their brains. Aluminium is also a well-known neurotoxin that has been shown to increase the oxidative damage to biomolecules. **Kumar *et al.* [11].**

Traditional medicinal herbs have been used to improve cognitive abilities and treat other AD-related pathologies. **Justin Thenmozhi et al. [9]**. *Emblica officinalis* (Amla) is used in a number of disorders by the Ayurvedic, Siddha, and Unani medical systems of India, as well as by Tibetan, Sri Lankan, and Chinese systems of medicine. In Ayurveda, an ancient Indian medical system, *Emblica officinalis* plays a significant role.

A member of the Euphorbiaceae family, it is a deciduous tree. Indian gooseberry, *Phyllanthus Emblica*, and Amla are some of its other names that are used frequently. Native to India, the plant also thrives in subtropical and tropical climates**. Mandal & Reddy [13].** *Emblica officinalis* contains a variety of phytochemicals, including terpenoids, alkaloids, flavonoids, and tannins, as well as flavonoids, tannins, and polyphenolic compounds and the best sources of vitamin C, minerals, and amino acids. **Jain et al. [8].**

The fruit, seed, leaves, root, bark, and flowers of the Emblica officinalis Gaertn plant are all used to make numerous herbal remedies that are anti-inflammatory, antipyretic, and used to treat diabetes mellitus and chronic diarrhoea. The tannin content of the fruits, leaves, and bark is high. **Singh & Agarwal [18].** *EO* known as rasyana, is mentioned as having anti-aging and promoting longevity qualities. It is a component of triphala and several other herbal remedies.

Material and methods-

Animals-

Thirty Wistar albino either sex rats, body weight of animal was selected between 100–150g each for this study. The animals were procured from CSIR-Central Drug Research Institute, Sector 10, Jankipuram Extension, Sitapur Road, Lucknow, Uttar Pradesh 226031.

Six rats were housed in each animal cage, and the rats were kept in standard environmental conditions (25 ± 2 ° C temperature, 60 ± 5% relative humidity) with a half day light and dark cycle. Water was given ad libitum; animals were maintained on standard animal diet.

Chemicals- AlCl3, EDTA, DTNB were procured from HIMEDIA, Mumbai, India. All other chemicals used were of analytical grade. The ***Emblica officinalis*** belonging to the family **Euphorbiaceae** were obtain from herbal garden of Mahatma Gandhi Institute of Pharmacy, in the month of January 2020. And leaves were washed and shadily dried for extraction. Before extraction dried leaves are coarsely powdered with the help of motor pestle.

Preparation of leaves extract-

The coarse powder (250g) extracted in a Soxhlet extractor for 6-7 hours at 64 °C, which shouldn't be greater than the boiling point of the solvents (20:80). The extract filter out through Whatman filter paper No. 1 before being concentrated in a rotary evaporator at 40°C. The collected material stored at -80 °C in a freezer for additional testing. **Nain et al. [15].**

Experimental design:

The animals were handled gently before the experimental procedures began for 10 minutes in a daily schedule for 5 days, afterwards the rats were divided into 5 groups each group contain 6 rats. All the groups will be treated simultaneously for 21 days. The animals will be weighed, and behavioral observations will be recorded before and at the end of the experiment.

Group I- Served as normal control and treated with normal saline 2ml/kg,

Group II- Served as negative control group and treated with AlCl3 100mg/kg p.o.,

Group III- Was treated with AlCl3 100mg/kg p.o. + *Emblica* officinalis leaves extract 100mg/kg p.o.,

Group IV- Treated with AlCl3 100mg/kg p.o. + *Emblica* officinalis leaves extract 200mg/kg p.o.,
Group V- Was treated with Rivastigmine 1.5mg/kg p.o. respectively.
After the last dose's delivery, a sodium pentobarbitone overdose will cause the animal to be sacrificed after 24 hours. The organ (brain) will be taken out, cleaned, and washed with phosphate buffer saline (pH 7.4), and further various studies will be performed. **Lakshmi *et al*. [12].**

Behavioral parameters

Morris water maze

Evaluating learning and memory in experimental animals involved using the Morris water maze. Compared to other learning and memory models, Morris water maze has a number of advantages. **Goverdhan *et al*. [6].** The Morris water maze (MWM) is a circular pool with a depth of 20 cm, filled with water, and maintained at a temperature of 25 °C. It is 60 cm in diameter and 25 cm high. With the use of a non-toxic white dye, the water became opaque. A platform that is positioned inside the pool at a depth of 1 cm and has a top surface measuring 6 cm x 6 cm and is painted white. The platform's position would remain constant during the training. The mouse was gently placed into the water, facing the pool wall, with the location of the drop varying with each attempt, and given 120 seconds to find the platform. If the mouse cannot locate the platform within 120 seconds, it is gently lead onto the platform and given 20 seconds to stay there. **Dhingra & Kumar [4]**

Elevated plus maze

The elevated plus maze is made up of two covered arms (16 cm 5 cm) and two open arms (16 cm 5 cm), both of which extended from a central platform (5 cm 5 cm). The maze is raised 25 centimetres above the ground. On the first day, each rat is placed at the end of an open arm, facing away from the platform. Transfer latency (TL) is the length of time it takes an animal to go from an open arm to a covered arm. On the first day, TL kept a record of each animal. If the animal did not enter one of the two covered arms after 90 seconds, the TL is set at 90 seconds and it is gently guided for entering into one of the two covered arms. After another two minutes of maze exploration, the mouse is allowed to leave and taken back to its own cage. 24 hours following the first day of testing, the retention of this learnt task (memory) has been assessed. **Dhingra & Kumar [4].**

Rotarod Test

Maintain the posture on the rotarod, which has a diameter of 3 cm and rotates at a constant rate of 20 rev/min, all the rats did two initial training sessions lasting 300 seconds, timed approximately 10 minutes apart. A 120-second baseline experiment was undertaken following the initial training trials. Each animal's time spent on the rotarod was noted. The animals received a maximum score of 120 seconds if they did not fall off the rotarod. Using the Rotarod (Techno) test, the impact of drugs and plant extracts on muscular performance was assessed. **Lakshmi *et al*. [12].**

Pole climbing test

Animals attempt to flee from electrical stimulation and move to a nearby secure place. When a stimulus is produced, this equipment is built in such a way that it will climb the pole. Animals were trained before the test. A= 25 × 25 × 40cm chamber that is enclosed in a sound-attenuating, low light box is used for training and testing. The chamber's grid floor receives a scrambled shock. A hole in the upper middle of the chamber was punctured by a smooth pole with a diameter of 2.5 cm. Each time a rat climbs the pole, a reaction is noted. **Goverdhan *et al*. [6].**

Locomotor Activity

Most CNS medications have an impact on locomotor activity in both humans and animals. Using a photo actometer made by Medicraft, it is possible to analyse the locomotor activity of drugs. **Goverdhan *et al*. [6].** The photo actometer consists of an animal-moving square arena (30 x 30 x 25 cm) with a wire mesh floor. A single mouse can only block one of the six beams created by the placement of the six lights and six photocells on the bottom's outside edge. Technically speaking, the theory behind it is that a photocell activates when an animal blocks the light rays that are falling on it. A count is made as the photocell is energized. The photocells are linked to a machine that automatically counts the number of "cut offs" using electronic technology. And calculate the change decrease or increase in locomotor activity. **Dhingra & Kumar [4].**

B. Biochemical parameter's

Brain sample preparation-

Animals were killed with sodium pentobarbitone, and after each rat's brain was taken, it has cleaned with saline to eliminate any blood, and minced into small pieces and prepare tissue homogenate. For preparation of the total of 10 % tissue homogenate involved the use of a homogenizer (REMI) with a Teflon plunger,

added phosphate buffer (0.1 M, pH 7.4), 0.25 M sucrose,1 mM phenyl methyl sulfonyl fluoride (PMSF) and10 mM potassium chloride (KCL). the supernatant produced by centrifuging the sample at 4 °C for 30 minutes at 800 rpm.

After the preparation, supernatant used for the estimation of acetyl cholinesterase (AChE) and antioxidant parameters (MDA, GSH, CAT, and glutathione reductase).

Measurement of acetylcholine esterase (AChE) content-

The tissue homogenate was prepared by using a homogenizer (REMI) with a Teflon plunger, added phosphate buffer (0.1 M, pH 7.4), 0.25 M sucrose,1 mM

phenyl methyl sulfonyl fluoride (PMSF) and10 mM potassium chloride (KCL). the supernatant produced by centrifuging the sample at 4 °C for 30 minutes at 800 rpm. The treated animals' hippocampal tissues were preserved for 30 min in a 0.25 M sucrose buffer suspension. Following a 10,000-rpm centrifugation of the samples, the supernatant was utilized to conduct a spectrophotometric examination to determine the AChE level. Measure absorption at 412 nm. **(Chen *et al*. [3].**

Catalase (CAT) Assay

The tissue homogenate was prepared by using a homogenizer (REMI) with a Teflon plunger, added phosphate buffer (0.1 M, pH 7.4), 0.25 M sucrose,1 mM phenyl methyl sulfonyl fluoride (PMSF) and10 mM potassium chloride (KCL). the supernatant produced by centrifuging the sample at 4 °C for 30 minutes at 800 rpm.0.1 ml of supernatant was added to cuvette containing 2.9 ml of 50 mM phosphate buffer (pH 7.0). 1.0 ml of freshly made, 30 mM H2O2 was added to the reaction to begin it.

When catalase, an enzyme, breaks down hydrogen peroxide, its UV absorbance can be measured at 240 nm, and it loses absorbance. The rate of H2O2 oxidation was measured, and Catalase activity was calculated in units of grams per kilogram of wet tissue. **Singh & Agarwal [18].**

Reduced Glutathione (GSH) Assay

The tissue homogenate was prepared by using a homogenizer (REMI) with a Teflon plunger, added phosphate buffer (0.1 M, pH 7.4), 0.25 M sucrose,1 mM phenyl methyl sulfonyl fluoride (PMSF) and10 mM potassium chloride (KCL). the supernatant produced by centrifuging the sample at 4 °C for 30 minutes at 800 rpm.

1 mL of 10 percent tricyclic antidepressant added in to tissue homogenate (1 mL), precipitates are formed. DTNB and sodium phosphate (4 mL) were mixed with an aliquot of the supernatant (0.5 mL). In the spectrophotometric analysis, absorbance measurements at 412 nm have obtained against a blank when the entire reaction became complete. The amount of GSH activity measured in nmol of GSH per kilogram of moist tissue. **Hira *et al*. [7].**

Superoxide Dismutase (SOD) Assay

The tissue homogenate was prepared by using a homogenizer (REMI) with a Teflon plunger, added phosphate buffer (0.1 M, pH 7.4), 0.25 M sucrose,1 mM phenyl methyl sulfonyl fluoride (PMSF) and10 mM potassium chloride (KCL). the supernatant produced by centrifuging the sample at 4 °C for 30 minutes at 800 rpm.

Homogenate has combined with 0.1 mL of the pyrogallol solution and 2.8 mL of potassium phosphate buffer (0.1 M, pH 7.4). A UV-visible spectrophotometer measured the absorbance at 312 nm. SOD calculated by using a standard line of analysis. **Hira *et al*. [7].**

Statistical Analysis

Data were expressed as MEAN ± S.E.M. for 6 animals in each group. One-way analysis of various (ANOVA) followed by Dunnett's comparison tests. All the grouped data was statistically evaluated, P-values of less than 0.05 were considered to indicate statistical significance.

Result

1.1 Effect of *Emblica officinalis* leaves extract on Morris water maze activity in rats.

All values were expressed as MEAN ± S.E.M. significantly difference between various group (ANOVA) and individual comparison was done by Dunnett's t-test.

**P<0.01 = significant when compared with toxic vs normal group, ##P<0.01 = significant when compared with treatment group vs toxic group, #P<0.05 = significant when compared with treatment1 group vs toxic group, $$ P<0.01 = significant when compared with rivastigmine group vs toxic group.

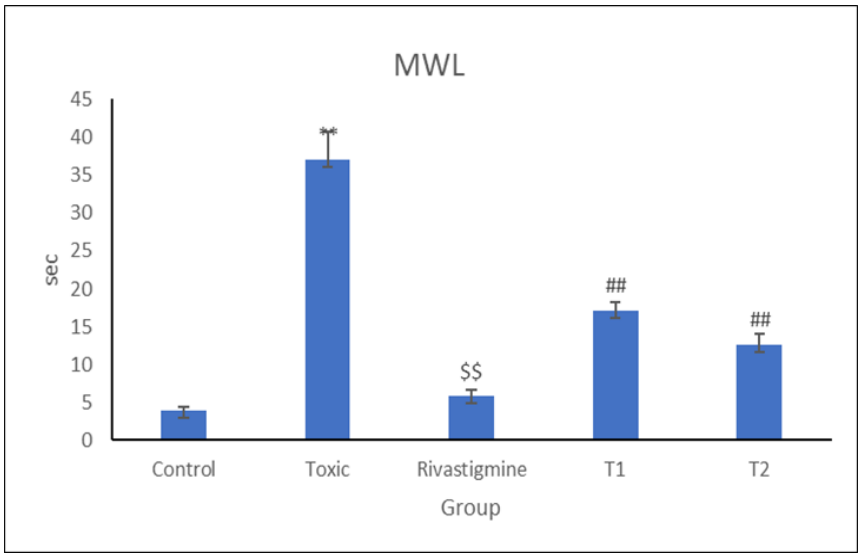


Fig.1 It was found that in Morris water maze test significantly increase in toxic group (AlCl3) (37±3.651) when compared with control group (4±0.365). While in treated group Rivastigmine (5.833±0.792), 100mg/kg (17.166±1.046), 200mg/kg (12.666±1.308) was significantly decrease when compared with toxic group.

1.2 Effect of *Emblica officinalis* leaves extract on pole climbing activity activity in rats.

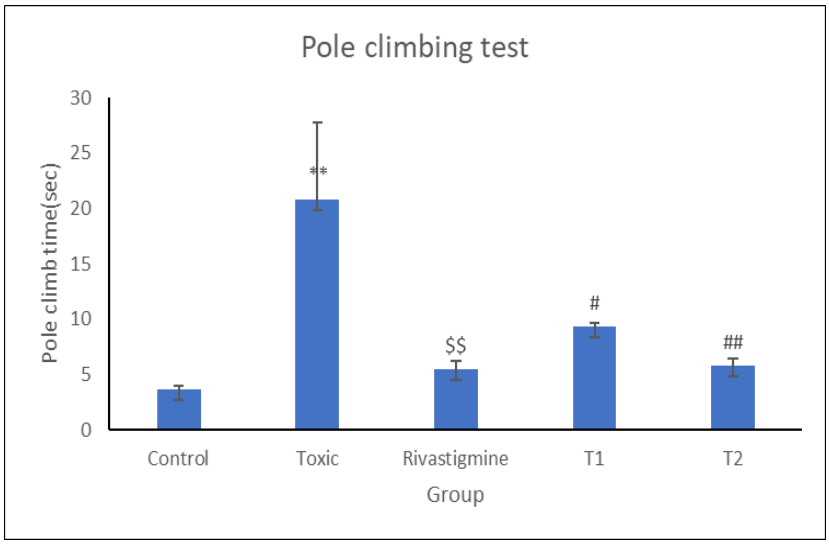


Fig.2 It was found that in Pole climbing test significantly increase in toxic group (AlCl3) (20.83±6.882) when compared with control group (3.66±0.333). While in treated group Rivastigmine (5.5±0.763), 100mg/kg (9.33±0.333), 200mg/kg (5.83±0.6) was significantly decrease when compared with toxic group.

1.3 Effect of *Emblica officinalis* leaves extract on Actophotometer activity in rats.

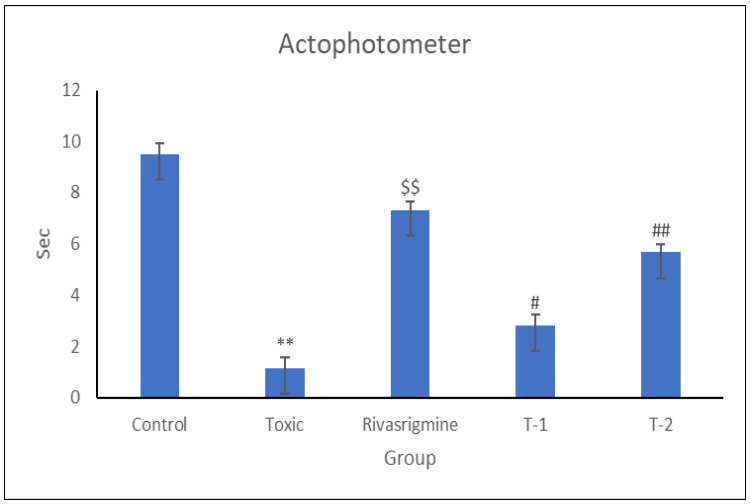


Fig.3 It was found that in Actophotometer test significantly decrease in toxic group (AlCl3) (1.16±0.40) when compared with control group (9.5± 0.428). While in treated group Rivastigmine (7.33±0.33), 100mg/kg (2.83±0.40), 200mg/kg (5.66±0.33) was significantly increase when compared with toxic group.

1.4 Effect of *Emblica officinalis* leaves extract on Rota- rod activity in rats.

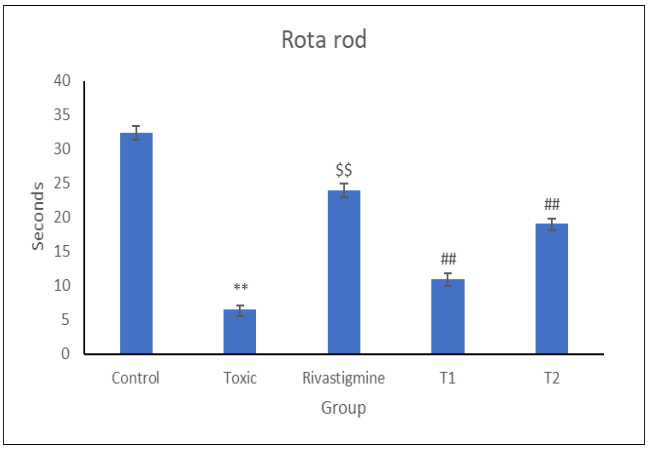


Fig.4 It was found that in Rota rod test significantly decrease in toxic group (AlCl3) (6.501±0.637) when compared with control group (39.5±3.403). While in treated group Rivastigmine (24.015±0.956), 100mg/kg (11.025±0.823), 200mg/kg (19.073±0.704) was significantly increase when compared with toxic group.

1.5 Effect of *Emblica officinalis* leaves extract on Elevated plus maze activity in rats.

All values were expressed as MEAN ± S.E.M. significantly difference between various group (ANOVA) and individual comparison was done by Dunnett's t-test.

**P<0.01 = significant when compared with toxic vs normal group, ##P<0.01 = significant when compared with treatment group vs toxic group, $$ P<0.01 = significant when compared with rivastigmine group vs toxic group.

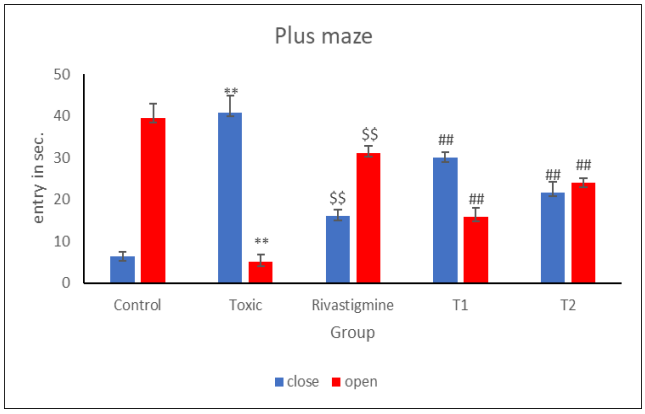


Fig.5 It was found that in plus maze closed arm test significantly increase in toxic group (AlCl3) (40.83±3.962) when compared with control group (6.333±1.002). While in treated group Rivastigmine (16±1.528), 100mg/kg (30±1.291), 200mg/kg (21.66±2.472) was significantly decrease when compared with toxic group. It was found that in plus maze open arm test significantly decrease in toxic group (AlCl3) (5±1.826) when compared with control group (39.5±3.403). While in treated group Rivastigmine (31.166±1.537), 100mg/kg (15.83±2.072), 200mg/kg (24±1.125) was significantly increase when compared with toxic group.

2. Biochemical test report

2.1 Effect of *Emblica officinalis* leaves extract on AChE and antioxidant parameters in AlCl3-induced Alzheimer's disease in rats.

All values were expressed as MEAN ± S.E.M. significant difference between various group (ANOVA) and individual comparison was done by Dunnett's t-test.

**P<0.01 = significant when compared with toxic vs normal group, ## P<0.01 = significant when compared with treatment group vs toxic group, # P<0.05 = significant when compared with treatment1 group vs toxic group, ns P>0.05 = non-significant when compared with rivastigmine group vs toxic group, $$ P<0.01 = significant when compared with rivastigmine group vs toxic group, $ P<0.05 = significant when compared with rivastigmine group vs toxic group.

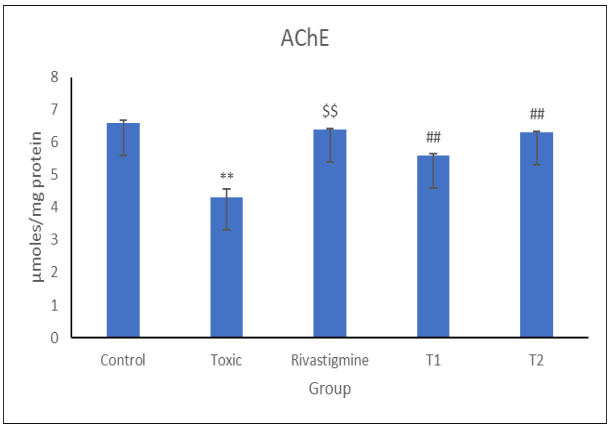


Fig.6 It was found that in the given table where n=6 in each group, from the study in case of AChE significantly decrease in toxic group (AlCl3) (4.3±0.28) when compared with control group (6.6±0.08) which was significant. While in treated group Rivastigmine (6.4±0.03), 100mg/kg (5.6±0.06), 200mg/kg (6.3±0.04) was significantly increase when compared with toxic group.

2.3 Effect of *Emblica officinalis* leaves extract on Catalase activity parameters in AlCl3-induced Alzheimer's disease in rats.

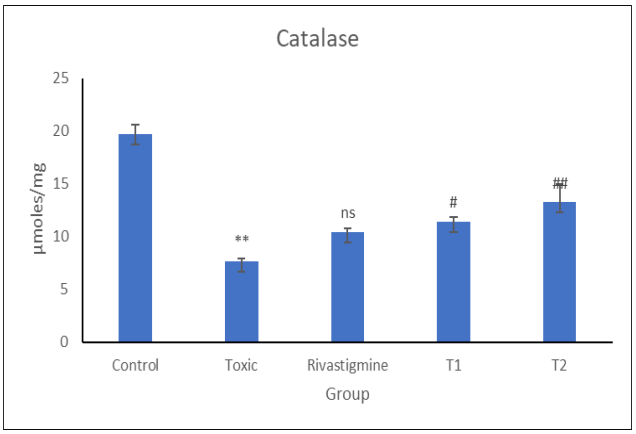


Fig.7 It was found that in the given table where n=6 in each group, from the study in case of Catalase test significantly decrease in toxic group (AlCl3) (7.68±0.26) when compared with control group (19.68±0.9) which was significant. While in treated group Rivastigmine (10.44±0.3), 100mg/kg (11.43±0.42), 200mg/kg (13.25±1.68) was significantly increase when compared with toxic group.

2.4 Effect of *Emblica officinalis* leaves extract on Glutathione activity parameters in AlCl3-induced Alzheimer's disease in rats.

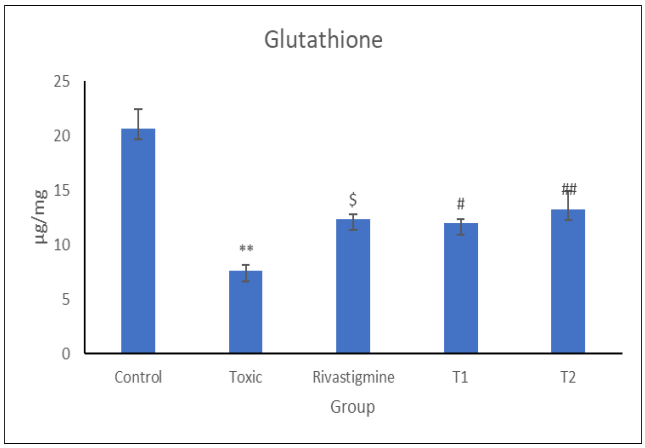


Fig.8 It was found that in the given table where n=6 in each group, from the study in case of Glutathione significantly decrease in toxic group (AlCl3) (7.58±0.602) when compared with control group (20.65±1.788) which was significant. While in treated group Rivastigmine (12.35±0.42), 100mg/kg (11.94±0.41), 200mg/kg (13.26±1.68) was significantly increase when compared with toxic group.

2.5 Effect of *Emblica officinalis* leaves extract on Superoxide dismutase activity parameters in AlCl3-induced Alzheimer's disease in rats.

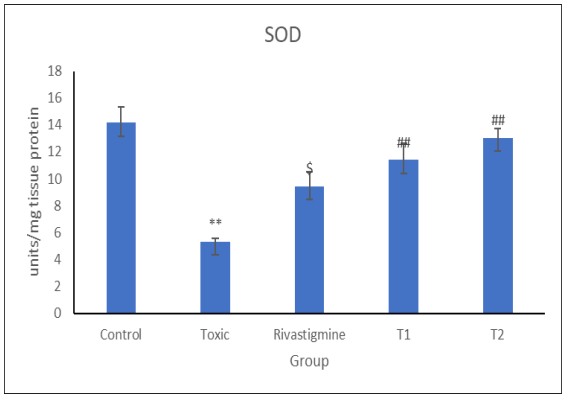
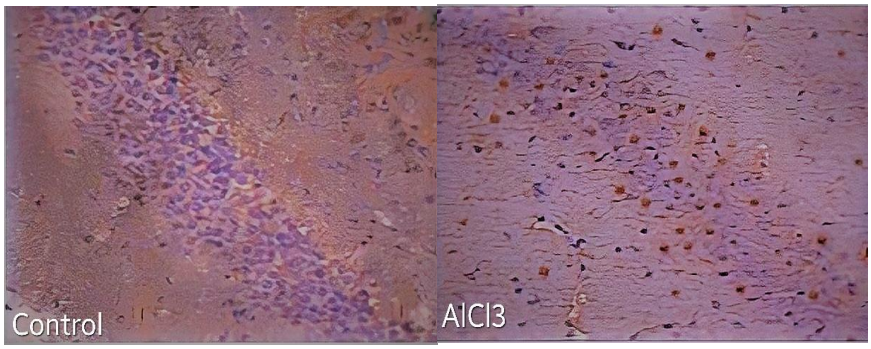
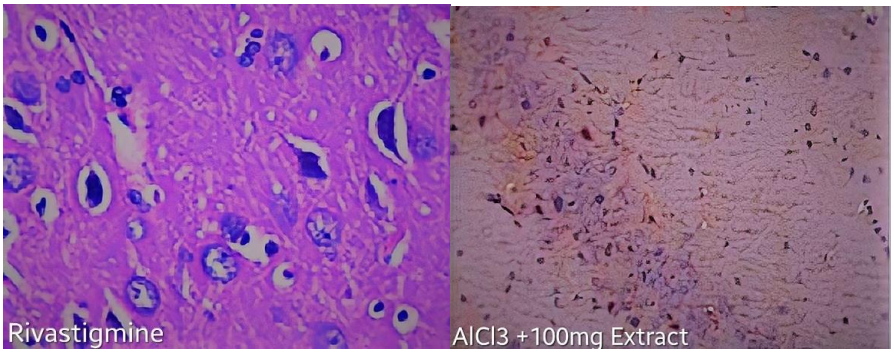


Fig.9 It was found that in the given table where n=6 in each group, from the study in case of SOD we observed that significantly decrease in toxic group (AlCl3) (5.32±0.23) when compared with control group (14.16±1.19) which was significant. While in treated group Rivastigmine (9.45±1.05), 100mg/kg (11.4±1.23), 200mg/kg (13.05±0.7) was significantly increased level of SOD when compared with toxic group.

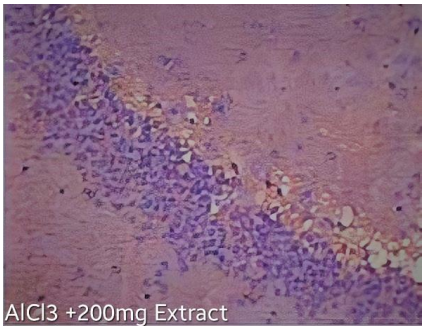
Histopathological study



A. B.



C. D.



E.

A= Control group, B= Toxic group, C= Rivastigmine, D= 100mg/kg, E= 200mg/kg.

Discussion

These days, the most common cause of dementia is Alzheimer's disease (AD). The possibility of developing AD rises with age. Short-term memory impairment is usually the initial clinical symptom. Additional cognitive functions, including as the ability to calculating and the use of everyday objects, are affected as the disease progression. According to Anders and Martin, there are currently 35.6 million people living with dementia globally. By 2030, that number will rise to 65.7 million, and by 2050, it will reach 115.4 million.

Phytochemicals, which play an important role in the treatment of many diseases, are rich in medicinal plants. The treatment of cognitive impairment based on by aging and neurodegenerative disorders stands to benefit from the phytoconstituents of medicinal plants. The purpose of the current investigation was to determine whether an extract of *Emblica officinalis* leaves could protect Wistar rats from developing Alzheimer's disease after exposure to aluminium chloride. According to this study, AlCl3 treatment for 21 days caused a progressive loss of spatial memory.

In the present study we tried to investigate the protective and therapeutic effects of *Emblica officinalis* leaves extract (100mg/kg and 200 mg/kg) aqueous infusions compared to rivastigmine (as a reference drug). By assessing their impact on the behavioural status (MWM, plus maze, Locomotor activity etc.) and brain Ach level and AchE activities of the rats used in animal model simulating AD (by using AlCl3). However, the high dose of *Emblica officinalis* leaves extract (200 mg/kg) exhibited a better effect than the low dose (100 mg/kg).

Aluminium enters into the brain, the cortex and hippocampus are essential for cognitive processes such as spatial learning and memory, and these sites are the most vulnerable regions in both AD and Al toxicity. Oral administration of doses of *Emblica officinalis* leaves extract to AlCl3-intoxicated rats showed significant reduction in the aluminium content.

Al has been reported as neurotoxin and its enhanced brain levels might be resulted in cognitive deficiency and dementia. Administration of Emblica officinalis leaves extract doses significantly improved MWM performance of rats, elevated plus maze task of rats and in other tasks. AlCl3 indicating the neuroprotective potential of *EO* leaves extract in relieving memory deficits. Oral treatment of rodents with *E. officinalis* leaves extract and its phytoconstituents significantly reversed memory deficits in AlCl3 induced AD.

AlCl3 administration to rats resulted in a significant increase in AChE activity in both brain regions. Whereas, co-treatment of *E. officinalis* leaves extract significantly inhibited the activities of AChE. The actophotometer and Pole climbing was used to measure the animal's locomotor and exploring abilities. The Al treatment reduced significantly the mobility and activities in this test. In the current study, coadministration of *E. officinalis* leaves extract reduced the locomotor and exploratory deficits in aluminium-intoxicated rats. *E. officinalis* demonstrated antioxidant properties and provided neuroprotection against oxidative stress (Catalase activity, GSH, SOD) caused by AlCl3 in several parts of the brain.

Conclusion

It is concluded from this study that *Emblica officinalis* leaves extract has a protective and therapeutic effect on AD, its 200mg/kg extract showed marked beneficial effects improving the learning, memory, and antioxidant potential.

In AlCl3-induced Alzheimer's disease, a model of oxidative stress-mediated neurodegeneration, *Emblica officinalis* leaves extract's chemical constituents (flavonoids, tannins and vit. C, B, etc.) was effective in the aluminium-induced neurotoxicity in AD-rats, by reducing brain damage and increase AChE inhibition activity, antioxidative, and anti-inflammatory activities against AlCl3-induced cerebral damages. This study showed that Phenolic compound treatment could represent a beneficial therapeutic approach against behavioral and biochemical changes associated with Alzheimer's disease.

The results suggest that the hydro methanolic extract of leaves of *Emblica officinalis* treated group may effectively normalize the impaired antioxidant status in AlCl3 induced Alzheimer's disease.

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