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Pharmacological Evaluation Of Neuroprotective Effects Of Rubus Ellipticus Against Aluminum Chloride-Induced Memory Impairment In Rats

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Abstract
Alzheimer's disease is the most prevalent kind of dementia and is distinguished by a mild, unrecognized memory loss (also known as "moderate cognitive impairment"). Dementia is a pattern of memory loss and cognitive decline that impacts two or more cognitive domains in an individual The current study investigates the therapeutic efficacy of Rubus ellipticus methanolic extract in a aluminium chloride-induced memory impairment in rat model. Aluminium chloride was administered orally for 21 days to induce alzheimer, followed by treatment with Rubus ellipticus extract at doses of 200 mg/kg and 400 mg/kg. Donepezil served as the standard comparator.
Parameters including elevated plus maze, morris water maze and actophotometer were monitored. Histopathological assessment of brain tissue was also performed. The extract at 400 mg/kg significantly reversed alzheimer -associated alterations, as evidenced by decrease AChE activity and restoration of acetylcholine levels is believed to contribute to the improvement of cognitive functions.
Phytoconstituents in Rubus ellipticus, such as flavonoids, polyphenols, anthocyanins, tannins and terpenoids, likely mediated its anti- depressant anti- microbial and antioxidant effects. The methanolic extract's efficacy was dose-dependent and comparable to Donepezil.
Overall, this study highlights the multifactorial efficacy of Rubus ellipticus in managing alzheimer and supports its potential as a phytotherapeutic alternative to conventional treatments.

Keywords: *Alzheimer disease, Rubus ellipticus, Anti-depressant, Aluminium chloride, Donepezil*

1. INTRODUCTION

1.1 ALZHEIMER'S DISEASE:

Brain degeneration neurons is a symptom of Alzheimer's disease [1]. It is the most prevalent kind of dementia and is distinguished by a mild, unrecognized memory loss (also known as "moderate cognitive impairment") [2]. Dementia is a pattern of memory loss and cognitive decline that impacts two or more cognitive domains in an individual [3]. The most typical dementia subtype affects older women frequently compared to older men [4]. This condition, which primarily affects adults over the age of 65, has an impact on language, memory, thinking, understanding, attention, judgment, and reasoning [5]. Therefore, even if growing older is a major increased risk for Alzheimer's, the disease's early stages are more likely to affect younger people [6]. A period of 20 years, it is anticipated that the mortality burden from AD and other dementias will more than quadruple [9]. Among the primary features of AD development is cholinergic neurons' loss [10], an increase in the activities of butyrylcholinesterase (BChE) and acetylcholinesterase (AChE) [11], a build up of -amyloid protein deposits both inside and outside of cells [12].

1.1.1 TYPES OF MEMORY

These are categorised into:

1. **Short-term memory**: memories that last only a short time, if at all.
2. **Memories that are intermediate in length**: those that persist for several days to weeks before fading away.
3. **Memory for a long time**: knowledge that has been saved and may be accessed years, if not a lifetime, from now.

4. **Memory for work**: primarily short-term memory, which is needed for intellectual thinking but diminishes as the problem is solved at each stage [20].

According to the types of information stored memory categorise into:

Declarative memories: It contains memory of facts and events and based on the honesty of the hippocampal and related regions.

Non-declarative memory: It is a term used to describe a unique learning and memory capacity that prevents access to the events that caused a component to change [21].

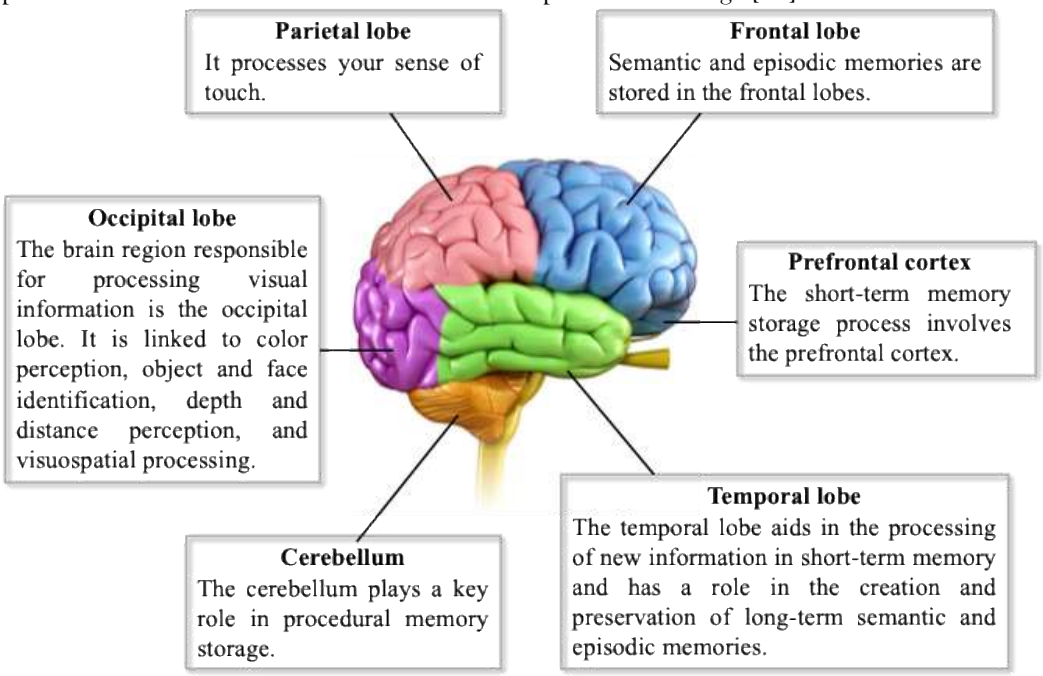


Fig 1: Brain parts involved in memory.

1.1.2 HISTORY

When Alois Alzheimer first discovered Alzheimer's disease (AD) in the late 19th century, he observed the brain anatomy of many patients and noted many of their symptoms (deteriorations). On November 4, 1906, a 55-year-old woman with a mental illness named Auguste D. was diagnosed with AD [22]. Dr. Alois Alzheimer, a German physician, spoke in 1906 about a woman who had endured years of severe memory loss, disorientation, and difficulty answering questions before she passed away. After she passed away, he conducted neuritic plaques, which are thick deposits outside and around nerve cells, were found during an autopsy on her brain. He found neurofibrillary tangles—twisted bands of fibers— within the nerve cells. Prior to the identification of AD in 1907, senility was thought to be a typical aspect of growing older and dementia to be a "natural component of ageing" [23, 24].

1.2 Symptoms of Alzheimer's disease [27, 28]

Psychological symptoms: Memory loss, anxiousness, despair, apathy, hallucinations, and delusions.

Behavioural symptoms: Catastrophic reactions, inappropriate sexual behaviour, aggression, and refusal to care.

1.3 PATHOPHYSIOLOGY OF AD

The hippocampus is primarily affected by AD. There are neurofibrillary tangles and neurotic plaques that can be seen as an indication of AD. Neocortical regions are covered in neuropathic plaques.

1. Hallmarks of AD

Amyloid β hypothesis: The precursor protein for amyloid is broken down by proteases to form Aβ, and its aggregates are thought to be responsible for a number of cellular functions like mitochondrial dysfunction, synaptic degeneration and elevated tau phosphorylation.

Neurofibrillary tau Tangles hypothesis: Normal tau keeps the network of microtubules (MTs) that facilitates intraneuronal trafficking in place [32]. Neurofibrillary tangles are made of tau proteine that has abnormally polymerized. Hyperphosphorylation of tau impairs its typical cellular function and is thought to hasten the development of tangled neurofibrilla [33]. Hippocampal tau phosphorylation is common in individuals with cognitively normal aging, and studies have found no evidence of neuronal loss in these regions [34].

Cholinergic Hypothesis: According to research, ACh appears play a part of memory and learning in both humans and non-human primates. AD symptoms include decreases in ACh levels, the ACh-producing enzyme choline acetylcholine (CHAT) throughout the
cerebral cortex, and reduction in the basal forebrain in cholinergic neurons [38].

Mitochondrial Dysfunction hypothesis: Adenosine triphosphate (ATP), which is produced by mitochondria, is the primary source of energy for the cell [39]. To fulfil the cellular need for ATP, mitochondria, which are active organelles, engage in a variety of metabolic processes and oxidative phosphorylation (OXPH0S). They also support Ca2+ homeostasis and take part in apoptosis [40]. Age-related conditions and aging are complications of mitochondrial dysfunction, neurological conditions [41].

Oxidative stress hypothesis: Oxidative stress affects the activity and levels of critical enzymes like b-secretase (BACE) and g-secretase, which can change A production directly by increasing APP levels or indirectly by doing the same. Aβ is an oxidant, and by creating greater oxidative stress, it produces a positive feedback loop that affects APP levels and its proteolytic pathway [43]. Current research has identified certain neurotransmitters as being essential to the development of AD pathogenesis are-
Acetyl choline- ACh a neurotransmitter crucial for memory and learning, is present in lower concentrations and functions in patients with Alzheimer's illness.
The cholinergic theory of AD is supported by presynaptic cholinergic anomalies, including decreased acetylcholinesterase activity and the death of cholinergic neurons [47]. Because of this, the choline acetyltransferase enzyme's action, which catalyzes the conversion of choline and acetyl coenzyme A into ACh, is decreased to 35–50% of its typical level.

1.4 Risk factor [53, 54, 55]
Risk factor of AD-

1. Age- Old.
2. Gender- Female>male.
3. Life styles- physical inactivity.
4. Family history.
5. Smoking.
6. Depression.
7. Head injury.
8. Hypertension.
9. A high amount of cholesterol.
10. Genetics-APP, PS1, PS2, ApoE.

1.5 Diagnosis
Blood test- test amyloid β and tau in blood plasma.
Cerebrospinal fluid test- abnormal amyloid β levels.
For the routine assessment of AD, computed tomographic imaging (CT) or magnetic resonance imaging (MRI) are advised [56].
The most accurate diagnosis is made through histological examination of tissue samples from affected areas [57].

1.6 Treatment of AD
FDA approved drugs for symptomatic treatment of AD are-

Cholinesterase inhibitors-
Selective cholinesterase inhibitors- Galantamine, rivastigmine, and donepezil.

Non-selective cholinesterase inhibitions- Tacrine
NMDA receptors antagonists: Memantine [58, 59, 60].

2. PLANT PROFILE (*Rubus ellipticus*)

The plant *Rubus ellipticus* (Smith), commonly referred to as the Himalayan raspberry and Indian raspberry tree, belongs to the Rosaceae family. Diabetes, diarrhea, gastritis, wound healing, dysentery, antifertility, antibacterial, analgesic, and epilepsy are among the ailments for which a variety of plant components have been suggested to be helpful. The use of lead compounds, nutraceuticals, medicinal herbs, and spices as a source has been beneficial to traditional medicine [63].

Figure no. 02: *Rubus ellipticus* (a) Shrub (b) Flower (c) Fruit

Table 1: Taxonomical classifiacation of *Rubus ellipticus*

Domain	Eukaryotic
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Rosales
Family	Rosaceae
Genus	Rubus
Species	*Rubus ellipticus*

2.1 DISTRIBUTION AND HABITAT

The golden Himalayan raspberry, native to Southern China, Assam, India, Pakistan, Nepal, Tibet, Vietnam, Laos, Myanmar, The Philippines, Sri Lanka, and Thailand, originated in the temperate Himalayan region. It is a weed that grows well in the open grasslands and woodlands of the Himalayan Indian states, including Uttarakhand and Himachal, at elevations between 1,500 and 2,100 meters (4,900 and 6,900 feet). It is commonly observed in the local pine forests [64].

2.2 **CHEMICAL CONSTITUENTS**

This plant has a range of Polyphenols, flavonoids, anthocyanins, tannins, and terpenoids are examples of secondary metabolites. Chemicals discovered in this plant, such as the antioxidant vitamin C, kaempferol, gallic acid, and catechin, have been extensively examined for their potential health benefits. Rubus species include a wide an assortment of secondary metabolites, including as flavonoids, anthocyanins, tannins and phenolics. The primary substances identified or isolated from *Rubus ellipticus* are campesterol, rubinic acid, rubitic acid, kaempferol, stigmasterol, matairesinol, tocopherol, morin [65].

At least 19 chemical components have been discovered from several sections of *Rubus ellipticus*, including 02 flavonoids (5 and 6), 13 triterpenoids (7–19), and 04 phenolic compounds (1-4).

Using the Soxhlet type equipment and suitable solvents like ethanol, methanol, and hydroalcohol, these components have been extracted

2.3 Ethnomedicinal Uses

The genus Rubus provides farmers with both economic and medical opportunities. Its fruits help farmers in rural areas improve their economic standing by giving them more revenue without requiring investment [49]. As per traditional Tibetan medicine, the leaves and fruits of *Rubus ellipticus* have antibacterial, carminative, and tonic properties and can be utilized to treat many ailments, including diabetes, ulcers, pneumonia, and nausea [37,50,51].

The root bark is used as an emmenagogue and abortifacient, and to cure shattered bones, diarrhea, and dysentery [52]. An infusion of roots can be ingested to warm the stomach, and the plant's stalk is occasionally chewed to relieve stomach discomfort [53–56]. Due to the extensive use of its roots and fruits in traditional medicine, this plant is ranked among the top 10 therapeutic plants that can be eaten in the wild Nepal's Tanahun District.

Additionally, because of its flavour and color, *Rubus ellipticus* juice is used to make jams and squash [50].

2.4 Phytochemical Constituents

Rubus species contain a wide variety of secondary metabolites, including flavonoids, anthocyanins, tannins, and phenolics.

2.5 PHARMACOLOGICAL ACTIVITIES

Nineteen compounds have so far been cut off from different areas of *Rubus ellipticus*. However, none of the compounds been brought to the attention of exhibit biological activity.

- Antioxidant Activity
- Antimalarial Activity
- Antidiabetic Activity
- Antiproliferative and Anticancer Activity
- Anti-Inflammatory Activity
- Antifertility Activity
- Nephroprotective Activity
- Antiviral Activity
- Antipyretic Activity
- Effect on Central Nervous System (CNS)
- Antimicrobial Activity
- Wound Healing Activity
- Photocatalytic Activity

2.6 Plant part used
Leaves, Root, Fruit

3. METERIAL AND METHODS
3.1METHODS

3.1.1 Collection and Identification
3.1.2 Collection of plant

Fresh leaves of *Rubus ellipticus* were collected from Soham Plant Conservatory, The Mall Road, Shimla, Distt. H.P.

3.2.2 Plant Material

The authentication of *Rubus ellipticus* was confirmed by **Botantical Survey of India (BSI),** Dehradun, Uttarakhand, India after submission of Herbarium specimen of BSI. The voucher specimen no. is **BSI/NRC.Tech./Herb(Ident.)/2025/26/195**. The certificate is given in (Appendix 1)

3.2.3 Preparation of Methanolic extract of Leaves of *Rubus ellipticus*

Figure no 3: Extraction of *Rubus ellipticus* by Soxhlet apparatus

The leaves of *Rubus ellipticus* was washed clean, shade-dried and reduced to coarse powder in a mechanical grinder. Soxhlet apparatus was used using methanol and the extract obtained was evaporated at 45°C to get a semisolid mass. According to OECD guidelines dose was taken 200 mg/kg, 400 mg/kg orally. For additional research, the extracted material was refrigerated.

3.3.3 Experimental Design

A period of 7-8 days was allocated for the animals to acclimate in the lab where tests on rats are performed. Five groups of six albino rats each (vehicle, inducer, standard, and test) were created from the total population of rats. For this investigation, a total of 30 rats were required. Over the course of 21 days, the entire course of treatment was given.

* Group 1: (Normal control): Albino rats received 1ml/kg body weight of normal saline (0.9% NaCl) daily for 21 days through the orally route.
* Group 2: (Disease control): Albino rats received aluminium chloride at a dosage of 17 mg/kg, body weight daily for 21 days through the orally route.
* Group 3: (Standard group): Albino rats received a daily dose of 3 mg/kg of donepezil for 21 days. Additionally, daily for 21 days, they received aluminium chloride at a dosage of 17 mg/kg orally, 30 minutes prior to the trial.
* Group 4: (Test group 1): Albino rats received *Rubus ellipticus* (methanolic extract) at a dose of 200mg/kg/p.o for 21 days and they received aluminium chloride at a dosage of 17mg/kg orally, 30 minutes prior to the trial.
* Group 5: (Test group 2): Albino rats received *Rubus ellipticus* (methanolic extract) at a dose of 400mg/kg/p.o for 21 days and they received aluminium chloride at a dosage of 17 mg/kg orally, 30 minutes prior to the trial.

4. RESULT

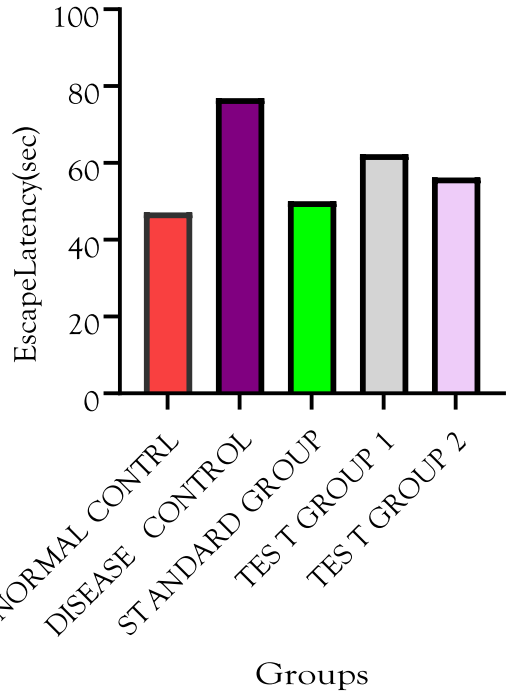
4.1 Effect of *Rubus ellipitus* on Aluminium Chloride induced amnesia in rats using Elevated Plus Maze

The Elevated plus Maze test was used to develop a more thorough understanding of the rat behavioral model related to external stimuli, allowing the measurement of transfer latency (TL) to be used to evaluate learning and memory processes. When the TL value dropped during the retention phase, memory performance had improved provided evidence of how REME improved amnesia brought on by Aluminium chloride. On the 20th and 21th days, rats treated with donepezil (3 mg/kg p.o.) or various doses of REME (200 and 400 mg/kg, p.o.) showed a dose-dependent decrease in TL. In comparison to the control groups, they also mitigated the effects of Aluminium chloride. With a high dose of REME, rats learned and remembered things better. Both REME and donepezil reduced TL days and successfully treated the amnesia brought on by Aluminium chloride, indicating a cholinergic mechanism was at play. The observed cognitive and memory improvement effects of REME in animals could partially be explained by the drug's induction of an increase in cortical muscarinic acetylcholine receptor capacity. A physiological reaction to make up for decreased cholinergic activity is the upregulation of muscarinic receptors in response to cholinergic antagonists like Aluminium chloride. In order to improve memory, it was proposed that TL might be decreased if the rats had prior experience entering the open arm. TLs were regarded as acquisition in the past and retrieval in the present, respectively.

Table 2: Effect of REME and other drugs employed on transfer latency (TL) of rat using elevated plus maze

Groups	Dose	Transfer latency (sec)
Normal control	1mg/kg body weight p.o	47.12±0.52
Disease control (Alcl3)	17mg/kg body weight p.o	76.89±1.25###

Donepezil + Alcl3	3mg/kg body weight p.o	50.01±0.79***
REME+ Alcl3	200mg/kg body weight p.o	62.27±0.69***
REME+ Alcl3	400mg/kg body weight p.o	56.18±0.81***



Graph 1: Shown effect of REME on escape latency of EPM at the aluminium chloride- treated rat

4.1 Effect of *Rubus ellipticus* leaves on Aluminium chloride induced amnesia in rats using Morris water maze

The escape latency time (ELT) was evaluated during the 18th through 20th days of the 21-day protocol schedule. In comparison to the untreated rats on day 18, there were no observable differences in the rats treated with aluminium chloride. Additionally, when compared to the rats that responded to aluminium chloride, the rats treated with donepezil did not show any appreciable differences. When compared to the rats given aluminium chloride treatment, the administration of REME at doses of 200, and 400 mg/kg, p.o. did not cause any appreciable changes in ELT in the treatment groups.

The Morris Water Maze (MWM) escape latency time (ELT) comparison data showed significant differences between the various treatment groups on the 19th, 20th, and 21th days.

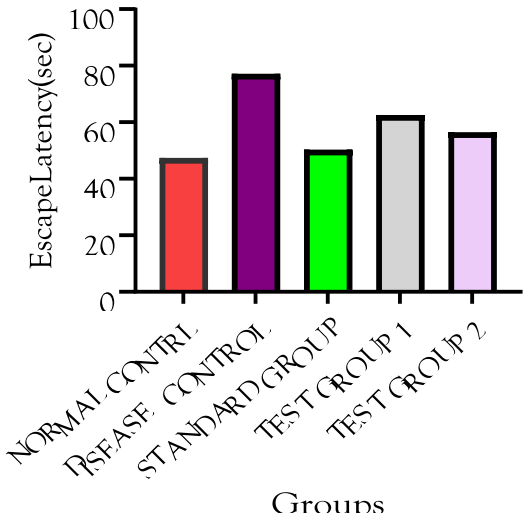
ELT was significantly higher in the aluminium chloride -treated rats than it was in the control animals. As opposed to the rats given aluminium chloride, those given Donepezil displayed a striking reduction in ELT. Additionally, when compared to rats given aluminium chloride, the administration of REME at doses of 200, and 400 mg/kg, p.o. showed a remarkable reduction in ELT. REME significantly reduced ELT when compared to rats given aluminium chloride and rats given ECEE at a dose of 400 mg/kg, p.o. These findings show a notable enhancement in learning in the REME treated rats.

The Time Spent in the Target Quadrant (TSTQ) was evaluated as a retrieval index in the Morris Water Maze on the 22th day of the protocol schedule (MWM). When compared to the control rats, the rats given aluminium chloride showed a significant drop in TSTQ. Furthermore, compared to rats treated with aluminium chloride, those treated with Donepezil showed improved memory. When REME was

given to rats at a dose of 200 mg/kg, p.o., it significantly increased TSTQ compared to the rats given aluminium chloride. Additionally, when compared to the rats under the control of aluminium chloride, the administration of REME at doses of 200 mg/kg and 400 mg/kg, p.o. indicated an improvement in memory function.

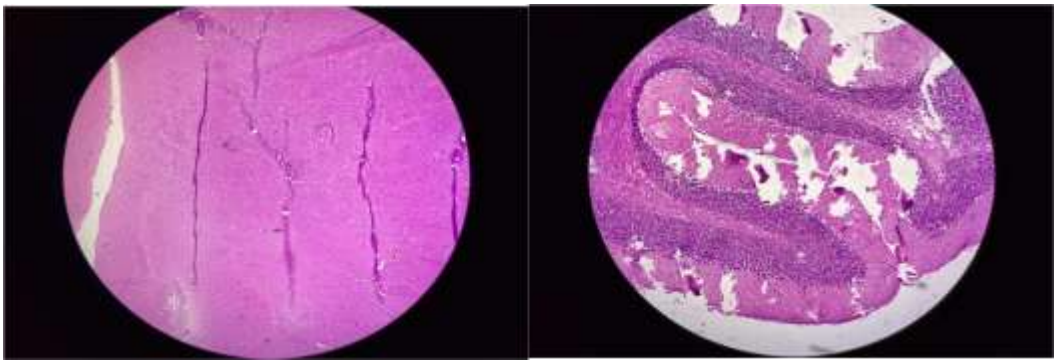
Table 3: Effect of REME and other drugs employed on transfer latency (TL) of rat using Morris Water maze

Groups	Dose	Transfer latency (sec)
Normal control	1mg/kg body weight p.o	31.12±0.1964
Disease control (Alcl3)	17mg/kg body weight p.o	12.38±1.817###
Donepezil + Alcl3	3mg/kg body weight p.o	35.62±1.932***
REME+ Alcl3	200mg/kg body weight p.o	22.39±2.0321** *
REME+ Alcl3	400mg/kg body weight p.o	27.20±1.992***

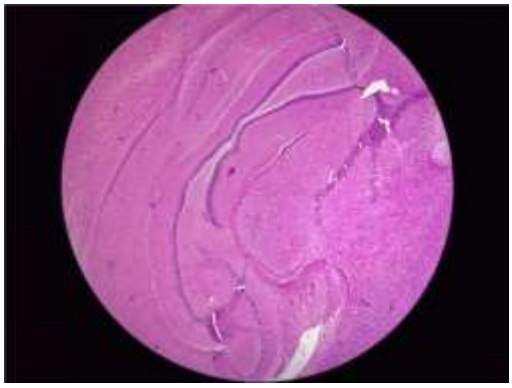


Graph 2: shown effect of REME on escape latency of MWM at the aluminium chloride- treated rat

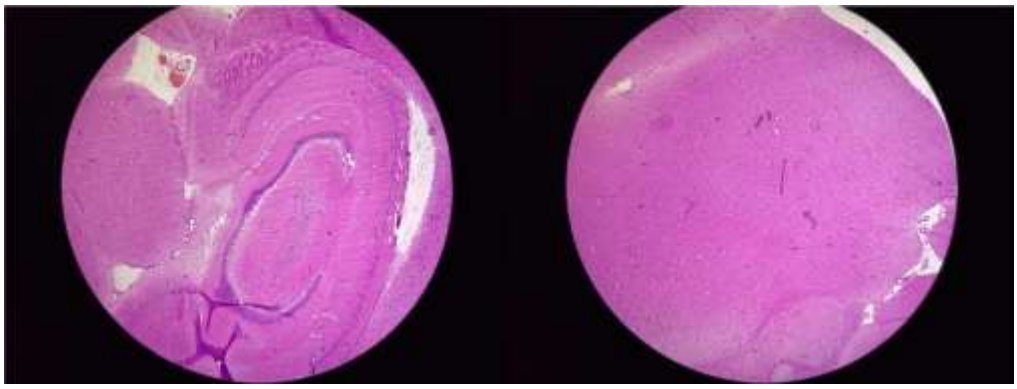
4.3 HISTOPATHOLOGICAL CHANGES:



Normal control Diseased control



Standard control



Test group 1 Test group 2

5. DISCUSSION

In the Indian medical system, *Rubus ellipticus*, commonly known as Himalayan raspberry.

However, until now, there has been no research conducted on its neuroprotective effects. Our recent study provides the first evidence that *Rubus ellipticus* exhibits an anti-amnesic effect on aluminium chloride-induced amnesia in rats. To evaluate this effect, we employed several screening methods including the Morris water maze, elevated plus maze tests. Furthermore, we conducted analyses on brain tissue homogenates to assess the levels of neurochemicals.

In the elevated plus maze task, a reduction in retention latency was noted in the treatment group, indicating an improvement in memory performance. Conversely, the aluminium chloride treated group showed an increase in retention latency compared to the normal group, suggesting a decline in memory function. The treatment group receiving the higher dose of REME (400mg/kg) exhibited superior performance compared to the aluminium chloride -treated group, indicating a neuroprotective effect against aluminium chloride -induced memory impairment.

Administering at a dose of REME 400mg/kg orally for 21 days successfully reversed the learning deficits induced by aluminium chloride when compared to the other groups. To validate the effects of REME, Rats spatial learning was evaluated using the Morris Water Maze (MWM) test.

The results showed that rats treated with aluminium chloride take longer to get to the secret platform, indicating memory impairments in this spatial task. However, rats treated with REME demonstrated a remarkable reduction in escape latency, which had been prolonged by the administration of aluminium chloride. Additionally, REME exhibited a notable improvement in cognitive performance, as evidenced by a significant decrease in the escape latency time (ELT). It is worth noting that the MWM test is commonly used to investigate changes in the central cholinergic system related to spatial learning and memory. The animals would have improved their spatial memory if they had spent more time during the training session in the target quadrant where the platform had been previously put. This would suggest that the animals had learned from their past experiences with the MWM test.

In this study, aluminium chloride -treated rats exhibited a decrease in time spent in the target quadrant (TSTQ), whereas rats treated with REME (400mg/kg) showed a significant increase in TSTQ. These findings suggest that ECBE effectively mitigated the behavioural changes induced by chronic administration of aluminium chloride, alleviating memory and cognitive impairments in the rats.

In the current study, Acetylcholinesterase (AChE) activity in the hippocampus was found to significantly increase when rats were given aluminum chloride. This increase in AChE activity led to a decreased concentration of acetylcholine, a neurotransmitter associated with cognitive functions. Consequently, the induction of amnesia was observed in the rats. However, rats that were pre-treated with donepezil or REME at a dose of 400mg/kg exhibited a significant decrease in AChE activity. The concentration of acetylcholine increased significantly as a result of this decrease in AChE activity. This restoration of acetylcholine levels is believed to contribute to the improvement of cognitive functions.

Recent studies have consistently reported that memory impairments, particularly in aluminium chloride-induced dementia in rats, are closely associated with oxidative damage. Clinical research that connects oxidative stress to the etiology of Alzheimer's disease lends more credence to this. Neuronal membranes, which are rich in long chain polyunsaturated fatty acids, are particularly susceptible to oxidative damage due to the high rates of signal transfer and continuous generation of reactive oxygen species (ROS) during normal metabolism and neuronal activity. The brain, which utilizes a significant amount of oxygen, is prone to lipid peroxidation induced by free radicals. Lipids and proteins, essential components of cell membranes, are particularly vulnerable to oxidative modification in neurodegenerative disorders. Extensive evidence supports the role of lipid peroxidation and protein oxidation in the loss of membrane integrity, which is a crucial factor in accelerated aging and age-related neurodegenerative disorders. Oxidative stress has been implicated in the pathogenesis of AD in humans. In the present study, the administration of aluminium chloride in rats significantly induced lipid and protein peroxidation while reducing antioxidant defence, indicating increased oxidative stress. Malondialdehyde (MDA), a byproduct of lipid peroxidation and a sign of the production of free radicals, demonstrated a significant rise in rats given aluminum chloride injections, suggesting widespread lipid peroxidation. To evaluate the effect of REME at a dose of 400mg/kg on brain lipid peroxidation, MDA levels were assessed. The results demonstrated that aluminium chloride -induced MDA levels were significantly reduced in a dose-dependent manner by REME, suggesting that lipid peroxidation has decreased.

In the current study, oral administration of REME, at a dose of 400mg/kg for a period of 21days demonstrated improvement in memory performance in rats. This was evident from the reduced transfer latency and improved spatial learning values compared to the normal group. REME treatment also resulted in a decrease in central cholinesterase activity, indicating it's ability to inhibit the breakdown of acetylcholine. Moreover, REME administration led to a reduction in lipid peroxidation levels, reflecting its antioxidant properties. Additionally, the mice were shielded against memory impairments brought on by aluminum chloride by a 21-day pretreatment with REME.

This suggests that REME possesses neuroprotective effects, potentially safeguarding against memory impairment.

6. CONCLUSION

This experimental study aimed to assess the impact of *Rubus ellipticus* on cognitive decline induced by aluminium chloride in Albino Wistar rats. The administration of aluminium chloride via orally route was found to cause neurotoxicity by generating harmful free radicals and reducing acetylcholine levels in the brain through the inhibition of muscarinic cholinergic receptors. Aluminium chloride is commonly employed in animal experiments to investigate cognitive deficits. However, in this study, it was observed that the detrimental effects of aluminium chloride were significantly mitigated in the test groups. *Rubus ellipticus* exhibited a dose-dependent effect in preventing cholinergic dysfunction, neurodegeneration, oxidative stress, and memory impairment induced by aluminium chloride. Overall, *Rubus ellipticus* demonstrated the potential to alleviate aluminium chloride- induced memory impairment.

Furthermore, both the Donepezil and *Rubus ellipticus* extract (REME) groups exhibited shorter escape latency times and better spatial learning memory compared to the aluminium chloride group. The decline in AChE levels observed in the Donepezil and REME (400mg/kg) groups suggests the restoration of acetylcholine levels in the brain, as supported by the data. REME was found to reduce AChE levels and enhance the antioxidant defence system. Based on these findings, we conclude that REME shows promise in improving memory-enhancing activity and wants further investigation.

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