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## Anti- Alzheimer's Activity of Methanolic Extract of *Tamarindus Indica Leaves*: in-Vivo Study

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**ABSTRACT: Objective:** To determine the **anti- alzheimer's activity** of methanolic extraction of *tamarindus indica leaves* by morris water maze test.

Materials and methods: Leaves of tamarindus indica was collected, dried and crushed. The leaves were extracted with methanolic by using soxhlet apparatus at 60°C of extraction. After the extraction phytochemical screening were performed. The methanolic extract leaves of tamarindus indica was studied at dual dosage level (250mg/kg and 500mg/kg, in p.o. administration) in rats by using MWM model. The animals are shared into 5 groups and every group contain 6 rats. Group I: The control group received oral administration of water. Group II received an i.p. admin of scopolamine (0.5 mg per kg) for negative control. Group III: Rats oral administration of Donepezil standard (2.5 mg per kg p.o) and AD caused by toxic agent (scopolamine). Set IV: Rats receive a low dosage of extract (250 mg/kg) orally, and Alzheimer's disease was created using scopolamine. Group V: Animals receive a high dosage of extract (500 mg/kg) orally and produced Alzheimer's using scopolamine.

Memory enhancer activity action of methanolic extract of *tamarindus indica* was estimated by MWM apparatus test. Methanolic extracts of *tamarindus indica* leaves were investigated for Alzheimer protective activity in the MWM. Commonly utilized MWM to assess memory enhancer in animals. These demonstrated dose-dependent decline in EL time while increase in TSTQ.

**Results:** Phytochemical investigation of *tamarindus indica m*ethanol excerpt exposed the existence of alkaloids, flavonoids, triterpenoids, chemicals. Administration of Donepezil (2.5 mg/kg p.o.) produced a significantly decrease the Alzheimer's behaviour when matched by control treated group. Admin of *tamarindus indica* extract (250mg/kg & 500mg/kg) to rats significantly decrease the Alzheimer's like behaviour when matched through Donepezil cured group and it was found that extract dose 500mg/kg show higher anti-Alzheimer activity than 250mg/kg dose of excerpt of *tamarindus indica*.

**Conclusion:** Results suggest that leaves of *tamarindus indica* possess significantly anti-Alzheimer activity.

**KEYWORDS:** *Tamarindus indica*, Donepezil, anti-Alzheimer, MWM.

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#### I. ALZHEIMER'S DISEASE

AD are long-lasting neurodegenerative disorder these are commonly starts gradually and characterized by difficulty in remembering recent events. It is characterized by short term memory loss, poor thinking ability.

#### Dementia:

Dementia has developed as a worldwide healthiness concern. Rendering to the WHO 2022 roadmap for dementia investigation, an expected 55.2 million people worldwide are suffered. Incidence amongst persons above oldness of 60 differs via geography, through Southeast Asia at 2.9%, Europe at 6.5%, and other regions ranging from 3.1% to 5.7%. Dementia is charming more communal in general, yet it is decreasing in certain high-income countries. By 2030, the predictable number of persons through dementia would have risen to 78 million. AD, is most common form of dementia, follows alike epidemiological tendencies and constitutes an crucial and rising global warning [1]. These illness initiates gradually and get worse over time. Alzheimer's illness is primarily defined by dementia, which is marked by a worsening in mental functions such as memory, praxis, and orientation. Quick sickness symptoms include





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short time memory damage, failure to learn new things, mood changes, trouble locating words, disremembering designations, and misplacing stuff. Patients through Alzheimer's illness usually exhibit defeat, aggression, and irritability. In severe cases, people become completely incontinent, forget their memories, and lose track of period and place. Antioxidants, for sample, are desirable kinds for together inhibition and management because they can stop the radical chain reaction, reducing ROS formation. This species have likewise been demonstrated to improve the efficacy of predictable managements when utilized in conjunction. Scopolamine, an antimuscarinic medication, increases AChE action in cortex and hippocampus via effectively. Scopolamine causes cerebral blood flow to decrease due to cholinergic hypofunction. Scopolamine also produces ROS, Long-lasting scopolamine admin caused severe histological abnormalities in cerebral cortex, containing neuronal death [2].

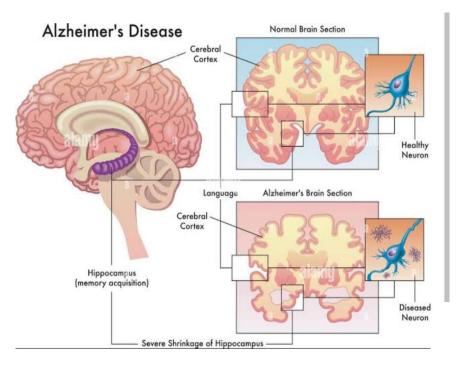


Figure 1. Alzheimer's illness

#### 1.1. Types of AD:

#### 1.1.1. Quick-Onset AD:

Progresses beforehand oldness of 65. Often, but not always, associated with a genetic component. Symptoms can appear more rapidly than in late-onset cases.

#### 1.1.2. Late-Onset AD:

The greatest communal form, developing after age of 65. While hereditary issues can show a role, lifestyle and environmental factors are also considered influential.

#### 1.1.3. Familial Alzheimer's Disease (FAD):

A unusual, genetic syleaves of Alzheimer's. Triggered via specific gene mutations that are passed down through families. Often, individuals with FAD develop signs at a younger age than persons through late-onset Alzheimer's[3].

#### 1.1.4. Other Presentations and Subtypes:

**Posterior Cortical Atrophy (PCA):** It mostly affects the back and upper-rear parts of the brain, influencing visual processing and spatial awareness. Early signs may include issues with vision, reading, and spatial judgment.

❖ Logopenic Aphasia: Involves damage to language areas of the brain, leading to speech difficulties, such as long pauses and labored speech.





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❖ Frontal Variant Alzheimer's Disease: Impacts the frontal lobes, causing problems with planning, decision-making, and social behaviour.

#### 1.1.5. Stages of Alzheimer's Illness:

- \* Mild Alzheimer's: Memorial harm, trouble with familiar tasks, and variations in mood and personality are common.
- ❖ Moderate Alzheimer's: Worsening memory, confusion, difficulty recognizing loved ones, and changes in behavior like hallucinations or paranoia.
- \* Severe Alzheimer's: Inability to communicate, complete dependence on others for care, and physical decline[4].

#### 1.1.6. Mixed Dementia:

A combination of Alzheimer's illness and another type of dementia, utmost usually vascular dementia.

#### 1.2. Causes of AD:

#### 1.2.1. Protein Abnormalities:

Amyloid Plaques: Beta-amyloid protein fragments cluster calm, forming plaques that disturb communiqué among head cells

**Tau Tangles:** Tau proteins twist into tangles within neurons, interfering with the transportation of nutrition and other vital particles.

#### 1.2.2. Genetic Factors:

**Quick-onset Alzheimer's:** Rare cases of quick-onset Alzheimer's (affecting individuals in their 30s to mid-60s) can be caused by specific gene mutations passed down through families.

**Late-onset Alzheimer's:** While most cases are not solely caused by genetics, certain genes like APOE4 can rise the threat of increasing the disease future in lifespan[5].

#### 1.2.3. Age:

Age is the utmost substantial hazard reason for Alzheimer's illness. The threat of increasing the illness doubles around each 5 yrs. afterward age of 65[6].

#### 1.2.4. Lifestyle and Environmental Factors:

- > Cardiovascular Health: Situations alike hypertension, great cholesterol, hyperglycemia, and fatness can growth the risk.
- ➤ Physical Inactivity: Lack of exercise is linked by a advanced risk.
- Food: An unhealthy diet can contribute to the risk.
- Smoking and Alcohol Misuse: These habits can increase the risk[7].
- ➤ Head Injuries: Traumatic brain injuries can accelerate development of Alzheimer's, particularly in individuals with genetic predispositions. [8].

#### 1.3. Signs and symptoms of AD:-

- ➤ Memory damage: Disremembering recent actions, discussions, or arrangements.
- > Disorientation: Difficulty understanding time and place.
- > Communiqué complications: Trouble discovery the accurate words or subsequent discussions.
- ➤ Mood variations: Charming simply disturbed, nervous, or unhappy.
- > Difficulty with regular tasks: Suffering by each day activities, such as showering, dressing, or cooking.
- > Disorientation in familiar places: Receiving lost in acquainted environments or having trouble understanding directions.
- ➤ Changes in behavior: Becoming more suspicious, agitated, or aggressive.
- Loss of coordination: Trouble with balance, movement, or coordination.
- ➤ Difficulty with speech: Trouble speaking or understanding language.
- > Sleep disturbances:
- > Appetite changes:
- ➤ Wandering:
- ➤ Personality changes[9]





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#### II. METHODOLOGY

#### 2.1. Assembly of herb resources:-

Plant was picked for proposal view of its customary, phytochemical profile was assembled from wild source, Azamgarh, Uttar Pradesh.

#### 2.2. Authentication of plant:-

Section of Botany, B.H.U. Varanasi, India, permitted the plant was set at the herbarium of BHU Varanasi.

#### 2.3. Requirements:-

Table No. 1.: Requirements:-

| Instruments        | Chemicals                        | Drugs     |  |
|--------------------|----------------------------------|-----------|--|
| Incubator          | Mayer's, Wagner's, Scopolamine   |           |  |
| * Hot air oven     | Shinoda, Benedict test           | Donepezil |  |
| ❖ Weighing balance | Hager's, Molisch's test reagents |           |  |
| * Condenser        | Lead acetate                     |           |  |
| * Desiccator       | Biuret , methanol Reagents and   |           |  |
|                    | Distilled Water                  |           |  |
| * Grinder          | Ninhydrin                        |           |  |
| * MWM apparatus    | Foam test, Methanol Reagents and |           |  |
|                    | Distilled Water                  |           |  |
| <b>❖</b> Syringe   | Ferric chloride test             |           |  |
| ❖ Oral cannula     | Keller-killiani test             |           |  |

#### 2.4. Preparation of extracts:-

Powdered (300g) leaves of the plant was dried with methanol (60-80° C), and then completely extracted with methanol using soxhlet apparatus at 60°C for 48 hour. Extract was filtered on whatman No. 1 filter paper. Solvent was completely removed under reduced pressure in a rotator vacuum evaporator to get a powdery mass. The concentrated extract was stored in vacuum desiccators for further use

#### 2.5. Experimental Animals:-

For this experiments utilize wistar albino rats weighing 140-190 gms. Using cages made of poly (a total of 38 x 23 x 10 centimeters) with paddy husk as bedding was arrangement for all rats treatment groups. Organization Temperature of  $25\pm2^{\circ}$ C, comparative humidity of  $50\pm5$  percent rats housed. Monitored light (12 h dim / 12 h sunny period). Fresh water ad libitum, fed using normal pellet nutrition allowed to all animals. The experiments was performed Animals ethics guidelines of "Institutional Animals Ethics Committee".

**Table No. 2. Grouping of Animals:** 

| Sr. No. | Groups   | No. of Animals |
|---------|--|----------------|
| 1       | Normal control given free excess of water p.o. | 6              |
| 2       | Negative (Scopolamine 0.5 mg per kg i.p.)      | 6              |
| 3       | Standard (Donepezil 2.5 mg per kg p.o.)        | 6              |
| 4       | Test-1 (METI 250 mg per kg p.o)                | 6              |
| 5       | Test-2 (METI 500 mg per kg p.o)                | 6              |

Note: Scopolamine 0.5 mg per kg admin all (Except normal control).

#### 2.6. MWM assessment (Scopolamine-induced Alzheimer's disease ) in rats:

The device was made up round pond 45 cm overall height, one hundred centimeters total circumference) via a flat inside superficial. Pool was full with opaque water  $(22 \pm 2^{\circ}\text{C's})$  at a standing height of thirty centimeters. and separated into 4 quadrants of equivalent zone, labeled 1, 2, 3 and 4. A 29 cm × 6 cm platform was put one cm lower than water level in the center of one of four quadrants. Position of platform remained constant through trial. Trial began on day ten





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of management period, when animals were permitted to swim for 120 seconds lacking the platform to acclimate. Throughout following 4 days, every rat was given four 120-second learning test with a 60-second intertrial gap. For every learning test, animal was located in the water, fronting puddle wall diagonally contrary the quadrant where the platform was stored. For each experiment, the escape latency time was calculated using the time it took rat to identify submerged platform. If some of the rats were incapable to identify the platform within 120 seconds, they were absorbed to it and allowable rest for 60 seconds, at which point escape latency time was noted as 120 seconds. On day 15 (24 hours following last learning trial), platform was detached from pool, and memory retention was assessed via a probing trial session. Every animal was placed in water diagonally opposed target quadrant and given 60 seconds to swim and discover The region in which scaffolding was formerly positioned. Time spent by the rat in target region were measured. [10].

Normal control given free excess of water oral. Negative control (Scopolamine 0.5 mg per kg i.p.) Standard (Donepezil 2.5 mg per kg p.o.) Test-I (METI 250 mg per kg p.o) Test-I (METI 500 mg per kg p.o)

Note: Scopolamine 0.5 mg per kg admin all (Except normal control)

#### All Agents are administered for 15 days.

#### 2.7. Statistical investigation:-

The records was examined with BioStat Pro (version 5.9.8). Results for every group are provided as mean  $\pm$  SEM. The statistical differences were examined utilizing a one-way ANOVA, tracked by Tukey-Kramer examination. Examinations with P < 0.05 remained measured statistically significant.

- \*\*\* showed p < 0.001
- \*\* showed p < 0.01
- \* showed p < 0.1
- \* are utilized towards compare standard and experiment groups to illness control set. Investigational data were collected since everything creatures various assemblies, documented, and charted on a broadsheet utilizing an MS Excel application toward create graphs.

#### III. RESULT

#### 3.1. Phytochemical Screening:-

*Tamarindus indica* exposed the existence of alkaloids, flavonoids, **tannins**, **Protein**, **Amino acid** and **glycosides**. In order to address the existence of various phytochemicals such as alkaloids, flavonoids, **tannins**, **Protein**, **Amino acid** and **glycosides** etc

**Table No. 3:** Preliminary phytochemical investigation of *Tamarindus indica*.

| Sr.No. | Phytochemicals | Test name            | Observation                | Result |
|--------|----------------|----------------------|----------------------------|--------|
| 1.     |                | Mayer's test         | Yellowish or white ppt.    | ++     |
|        | Alkaloids      | Wagner's test        | Yellow or brown ppt.       | ++     |
|        |                | Hager's test         | Yellow crystalline ppt.    | ++     |
| 2.     |                | Lead acetate         | Yellow colour              | ++     |
|        | Flavonoids     | Alkaline reagent     | Yellow fluorescence        | ++     |
|        |                | test                 | White ppt.                 | ++     |
|        |                | Gelatin test         |                            |        |
| 3.     | Tannins        | Ferric chloride      | Blackish blue colour       | ++     |
| 4.     | Saponin        | Foam test            | No foam formed             |        |
| 5.     | Glycosides     | Keller-killiani test | Reddish brown layer formed | ++     |
| 6.     | Protein        | Biurate test         | Pink or violet colour      | ++     |
| 7.     | Amino acid     | Ninhydrin test       | Dark purple                | ++     |
| 8.     | Carbohydrate   | Benedict's test      | No ppt.                    |        |
|        |                | Molisch's test       | No ppt.                    |        |





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#### 3.2. Study Against Alzheimer's:

#### **MWM Test:**

Throughout development periods (days 11 to 14), scopolamine cure caused considerably higher EL than controls; however, these outcome was minimized by co-admin of test preparation. On days 2-4 (cure days 12-14) of the acquisition sessions, escape latencies were significantly lesser in control cluster than on day 1 (treatment day 11), but No in Scopolamine-treated animals. This variance were recovered in animals treated through both Scopolamine and test preparation. On day 15, during the probe experimental session, Scopolamine-cured animals spend substantially fewer period Swim into desired area than controls, whereas animals co-administered via test preparation and Scopolamine spent more time within the selected area compared to sickness norms.

**TABLE 4. :** Outcome of methanolic excerpts leaves of *tamarindus indica* on EL period in scopolamine-produced AD in rats.

| Group Name                   | Escape Latency Period (Sec.) |                      |                      |                      |
|------------------------------|------------------------------|----------------------|----------------------|----------------------|
|                              | Day 11 <sup>th</sup>         | Day 12 <sup>th</sup> | Day 13 <sup>th</sup> | Day 14 <sup>th</sup> |
| Normal (Water) oral          | 83.23 + 2.12                 | 74. 83 + 0.54        | 53.25 + 0.76         | 24.33 + 0.88         |
| Negative scopolamine         | 96.5 + 1.58#                 | 82.75 + 0.76#        | 62.75 + 0.77#        | 34.83 + 2.11         |
| (0.5 mg per kg) i.p.         |                              |                      |                      |                      |
| Standard Donepezil(2.5mg/kg) | 78.03 + 4.11***              | 52.23+0.75***        | 24.91+0.72***        | 12.20+ 1.23 ***      |
| oral                         |                              |                      |                      |                      |
| Test-I (100 mg/kg) oral      | 82.25 + 0.58**               | 66.17+1.79***        | 39.5 + 0.47***       | 20.75 + 0.53***      |
| Test-II (250 mg/kg) oral     | 73.92 + 0.72***              | 53.33+0.57***        | 35.83+1.53***        | 16.17 + 0.53***      |

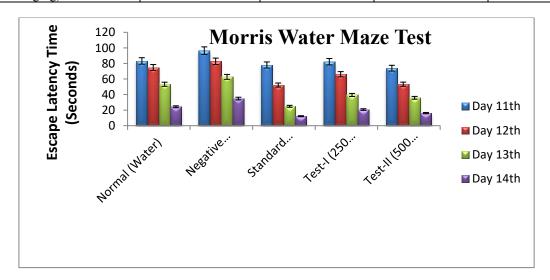


Figure no. 2. Result of methanolic excerpts of leaves of *tamarindus indica* on EL period in scopolamine-produced AD in rats:

**Table no. 5.** Result of methanolic extracts leaves of *tamarindus indica* on TSTQ in scopolamine prompted AD in rats:

| Group Name                        | TSTQ (sec.)  |
|-----------------------------------|--------------|
| Normal (Water) oral               | 11.23 + 0.6  |
| Negative scopolamine              | 6.66 + 0.74  |
| (0.5 mg per kg) i.p.              |              |
| Standard Donepezil(2.5mg/kg) oral | 21.22+ 1.21  |
| Test-I (250 mg/kg) oral           | 12.33 + 0.74 |
| Test-II (500 mg/kg) oral          | 16.66 + 0.6  |





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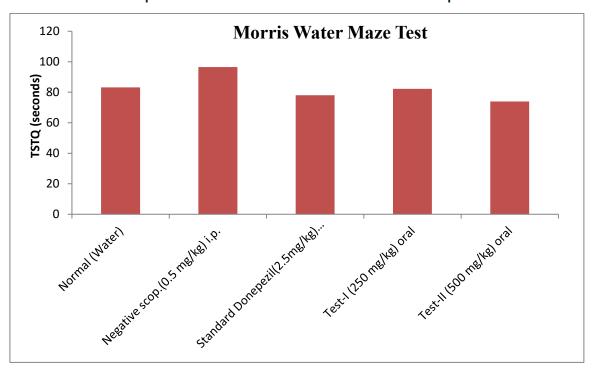


Figure no.3. Result of methanolic extracts leaves of tamarindus indica on TSTQ in scopolamine produced AD in rats:

#### IV. DISCUSSION

AD is a deteriorating Mental condition these reasons memory harm and mild mental weakening, ultimately progressing to dementia. Congenital irregularities, neurofibrillary tangle formation, inadequate amyloid progenitor processing, mitochondrial inadequacies, neurotropic factor insufficiency, trace element neurotoxicity, dynamism metabolic rate flaws, and oxidation impairment remain just a rare of causes of Alzheimer's disease. Acute memory loses, incapability to acquire anything novel, mind fluctuations, trouble Learning words, ignoring individualities, as well as a mistake items remain wholly signs of previous illness. Alzheimer's sufferers frequently exhibit frustration, aggression, and irritability. However, the anti-Alzheimer activity of the methanolic excerpt of tamarindus indica leaves (250 and 500 mg/kg oral) was tested using MWM test, which is recommended when the experiment agent decline in escape latency time and an increasing in time spent in the target quadrant. Standard drug (Donepezil) has long been used as a anti-Alzheimer, and it is as well commonly used in behavior pharmacology as a reference chemical for potentially anti-Alzheimer compounds. However, rats cured by 250 mg per kg body wt. of plant excerpt displayed a significant reduction in EL time and an increasing in TSTQ. There are still several studies being conducted on cures that can inhibit or at least significantly alter the course of AD, similarly Famous is "disease-modifying therapies." Examine for novel treatments This comprises both harmless plus in effect combat alongside AD has already necessitated the participation of numerous researchers and thousands of willing volunteers. Methanolic extracts of Tamarindus indica leaves were investigated for Alzheimer protective activity in MWM trial. MWM method is commonly utilized to assess Directional memory and learning in animals. This demonstrated a dose-dependent reduction in EL period plus increase in TSTO.

#### V. CONCLUSSION

The current study's findings show that methanolic extracts of *Tamarindus indica* leaves can help inhibit or cure AD by drastically lowering Acetylcholinesterase stages in the brain. A primary phytochemical examination of methanolic extracts of *Tamarindus indica* leaves exposed the attendance of alkaloids, flavonoids, **tannins**, **Protein**, **Amino acid** and **glycosides** chemicals.





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The current study concluded that methanolic extracts of *tamarindus indica* leaves have anti-Alzheimer action via improving spatial memory, as well as a substantial rise in beginning of achievement and a decrease period of action and retrieval time when matched to negative control, therefore explanatory its Alzheimer protective action, which could be due to the existence of alkaloids, flavonoids, **tannins**, **Protein**, **Amino acid** and **glycosides**. Further research is recommended to categorize the active phytochemicals and demonstrate their method of action.

#### VI. ACKNOWLEDGMENT

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