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EVALUATION OF *ANETHUM GRAVEOLENS* EXTRACT ON MEMORY IMPAIRED MICE

Neeraj Kumar*, Chetna Dhiman, Preeti Kothiyal
Department of Pharmaceutical Sciences, Shri Guru Ram Rai Institute of Technology and Science, Dehradun, Uttarakhand, India.

Abstract:
Objective:*The objective of this study was to evaluate the effect of Anethum graveolens (Dill) extract on scopolamine induced learning and memory impairment in mice. The antioxidant property of Anethum graveolens was evaluated.*
Material and methods: *A total of 36 mice (25-30 g) were randomized into 6 equal groups. Memory enhancing activity of Anethum graveolens in amnesic mice was investigated by using Elevated plus maze and Morris water maze. AchE activity, SOD and lipid peroxidation of brain homogenate were performed in control/ scopolamine/ standard / Anethum graveolens leaves extract treated mice.*
Result:*Administrationof Anethum graveolens leaves extract significantly treated the learning and memory impairment induced by scopolamine. The effects were evaluated with the help of Morris water maze and Elevated plus maze. The study showed the significant reduction in AchE activity, increased activity of brain antioxidant enzyme such as superoxide dismutase and also reduced the increased activity of lipid peroxidation. The effects observed were dose dependent; the high dose of Anethum graveolens extract (400 mg/kg, p.o.) was most potent to show the action against learning and memory impairment.*
Conclusion: *Anethum graveolens leaves extract has potential effect on learning and memory impairment produced by scopolamine and may have beneficial effect in the treatment of Alzheimer's disease and amnesia.*

Keywords: *Anethum graveolens,AchE, Piracetam, scopolamine and antioxidant.*

Corresponding Author:
Dr. Neeraj Kumar
Assistant Professor
Department of Pharmaceutical Sciences,
Shri Guru Ram Rai Institute of Technology and Science,
Patel Nagar, Dehradun, Uttarakhand, India
Email id: neeraj_sidana2007@rediffmail.com

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INTRODUCTION

Alzheimer's disease is slowly or gradually progressive dementia affecting both (1) cognition (process of acquiring knowledge and understand thought & sense), (2) behavior (conducts oneself toward others) [1].

Alzheimer's disease also deals with synaptic dysfunction and diffuse neuronal loss, it is a very most common form of dementia[2]. AD is an irreversible neurodegenerative disorder characterized by the fibrillary tangles and neutritic plaques [3,4].

The cause for most Alzheimer's cases is still unknown except for 1% to 5% of cases where genetic differences have been identified [5].

Several hypotheses explains the cause of the disease: Genetics inheritence of Alzheimer's disease, based on reviews of twin and family, ranges from 49% to 79% [6,7]. Around 0.1% of the cases are familial forms with autosomal (not sex linked) dominant inheritance, having onset before age of 65[8]. This form of the disease is called as early onset Familial Alzheimer's disease. Cholinergic hypothesis is the oldest hypothesis based on which current available drug therapies are prescribed [9]. Which postulates that AD is caused when the synthesis of neurotransmitter acetylcholine is reduced. The cholinergic hypothesis has not maintained widespread support [10]. Amyloid hypothesisis based on the deposition of extracellular amyloid beta (A_β) [11, 12]. A specific isoform of apolipoprotein, APOE4, also collaborate in the of cause Alzheimer's disease. Apolipoproteins generates the breakdown of beta amyloid, which leads to excess amyloid buildup in the brain [13]. The tau hypothesis proposes that the abnormalities in tau protein, initiate the disease process [12]. The theory postulated, hyperphosphorylated tau begins to pair with other threads of tau. Finally, leading to the formation of neurofibrillary tangles inside nerve cell bodies [14].

Long-term treatment of non-steroidal anti-inflammatory drugs (NSAIDs) reduced chances of developing AD. [15]. Evidence also supports the notion that NSAIDs can reduce inflammation related to amyloid plaques [15]. They do not appear to be useful as a treatment. Hormone replacement therapy, may increase the risk of dementia [16].

The genus named anethum is derived from greek word 'aneeson' or 'anethon', which means strong smelling. *Anethum graveolens*is sole species of the genus Anethum, a variant occur in India called as Indian dill or sowa cultivated as a cold weather crop throughout Indian subcontinent, Malaysian archipegalo and Japan[17,18].

Constitutes essential oils, fatty oils, moisture (8.39%), protein (15.68%), carbohydrates (36%), fibre (14.8%), ash (9.8%) and mineral elements such as calcium, potassium, magnesium, phosphorus, sodium, vitamin A and niacin. Fruits of *Anethum graveolens* contain 1-4% essential oil comprising of major compounds: carvone (30-60%), limonene (33%), α- phellandrene (20-61%), including pinene, diterpene, dihydrocarvone, cineole, myrcene, paramyrcene, dillapiole, isomyristicin, myristicine, myristin, apiol [18].

*Anethum graveolens*is used as ingredient in gripe water to treat colic pain in babies [19]. Seeds are aromatic, carminative, mildly diuretic, galatogogue, stimulant and stomachic [20,21]. The volatile oil helps in increasing appetite, treat gas and improves digestion [22]. Also helps in improving bad breath, intestinal spasms, helps to settle colic. It helps in stimulating milk flow during lactation; hence it is given to cattle. Also treat urinary complaints, piles and mental disorders[23]. It is generally used as a spice, flavouring agent and seasoning agent in food such as pickles, salads etc. it helps in inhibition of growth of several bacteria hence it is used as preservative [24].

Piracetam (sold under many brand names) is a nootropicdrug in the racetams group, with chemical name *2-oxo-1-pyrrolidine acetamide*. It shares the same 2-oxo-pyrrolidone base structure with pyroglutamic acid. Piracetam is a cyclic derivative of GABA (gamma-Aminobutyric acid). Presently piracetam is used in many European countries, Asia and South America. Piracetam's mechanism of action, as with racetams in general, is not fully understood. The drug influences neuronal and vascular functions and influences cognitive function without acting as a sedative or stimulant [24].

Piracetam is a positive allosteric modulator of the AMPA receptor. It is hypothesized to act on ion channels or ion carriers, thus leading to increased neuron excitability. GABA brain metabolism and GABA receptors are not affected by piracetam [25].

It has been found to increase blood flow and oxygen consumption in parts of the brain, but this may be a side effect of increased brain activity rather than a primary effect or mechanism of action for the drug [25].

Piracetam improves the function of the neurotransmitter acetylcholine via muscarinic cholinergic (ACh) receptors, which are implicated in memory processes. Furthermore, piracetam may have

an effect on NMDA glutamate receptors, which are involved with learning and memory processes. Piracetam is thought to increase cell membrane permeability. Piracetam may exert its global effect on brain neurotransmission via modulation of ion channels (*i.e.*, Na^+, K^+). It has been found to increase oxygen consumption in the brain, apparently in connection to ATP metabolism and increases the activity of adenylate kinase in rat brains. But in the brain, it also increases the permeability of the mitochondria of some intermediaries of the Krebs cycle [25].

MATERIALS AND METHODS

Plant material

The leaves of *Anethum graveolens* were collected from Roorkee, Uttarakhand.

Animals

Albino mice weighing 25-30g were procured from departmental animal house of Shri Guru Ram Rai Institute of Technology and Science, Patel Nagar, Dehradun.

Animals were acclimatized in the departmental animal house facility and housed in polypropylene cages with husk bedding (renewed every 48 hrs.), under 12:12 hours lightdark cycle at 25º C ± 5º C. and were fed with standard Commercial pellet diet and water *ad libitum.*

The protocol were approved by Institutional animal ethics committee and were carried out in accordance with the CPCSEA (264/PO/ReBi/S/2002/CPCSEA).

Methodology

Collection and authentication of plant:

The leaves of shrub *Anethum graveolens* were collected from Roorkee, Uttarakhand.

The authentication of *Anethum graveolens* was confirmed by Botanical Survey of India (BSI), Dehradun after submission of herbarium.

Extraction

Collected fresh leaves were separated from desirable materials and washed with water before letting it stand under the sun for a week. The dried leaves were coarsely powdered with the help of a grinder.

Air dried powder was taken in organic solvent (ethanol) in a conical flask, plugged with the cotton wool and then keep on stirring, after 24 h, the supernatant was collected and the solvent evaporated to make the final volume one-fourth of original volume and stored at 4° Celsius[26].

Experimental induction of learning and memory impairment

Scopolamine (0.4 mg/kg) was used in the present study for induction of Amnesia.

Experimental Protocol

Group 1- Normal control group- normal saline was administered for 21 days.

Group 2- Memory impairment induced by Scopolamine (0.4mg/kg i.p) on first day.

Group 3- Standard group treated with Piracetam (200mg/kg i.p) for 21 days.

Group 4- Test group (scopolamine induced) was administered with *Anethum graveolens* (100mg/kg, p.o) for 21 days.

Group 5- Test group (scopolamine induced) was administered with *Anethum graveolens* (200mg/kg p.o) for 21 days.

Group 6- Test group (scopolamine induced) was administered with *Anethum graveolens* (400mg/kg p.o) for 21 days.

Behavioral Models

Morris water maze

MWM is a circular pool having diameter 60 cm and height 25 cm, mainly used for mice. MWM was filled to a depth of 20 cm with opaque water made up from milk or nontoxic white dye. The temperature of the maze maintained at 25°C. Then the pool was divided into four equal quadrants (Q1, Q2, Q3 and Q4) using a thread or string. A hidden platform, painted with white top surface (6 cm × 6 cm) was placed 1 cm below the surface of water in one quadrant (Q4 in the present study) of the pool. Every mice was subjected to 4 consecutive time trials each day as per scheme mentioned in table, a gap was given between each the trial was 5 min [27].

Day 1	Q1	Q2	Q3	Q4
Day 2	Q2	Q3	Q4	Q1
Day 3	Q3	Q4	Q1	Q2
Day 4	Q4	Q1	Q2	Q3

Data was collected on basis of two trials: Acquisition and RetrievalTrial

Elevated plus maze

It is an exteroceptive behavioral model for the evaluation of learning and memory. The EPM apparatus for mice contains two open arms i.e 16 cm × 5 cm and two enclosed arm i.e 16 cm × 5 cm × 15 cm. The elevated plus maze is elevated at 25 cm height from the floor.

Mice was placed at one end of the open arm, facing toward opposite from the centre of EPM (on first day of experiment). For each mice of all groups, transfer latency (TL) was recorded at first day of experiment. On second day same procedure was followed for TL (Retrieval). If the animal was not able enter into covered arms within 90 sec then it is pushed into one of the enclosed arm and the TL was recorded at 90 sec [28].

Biochemical Parameters

All biochemical parameters were performed in the brain homogenate after the evaluation of Morris Water Maze and Elevated Plus Maze.

Preparation of brain homogenate

All mice were sacrificed by cervical dislocation and brain were removed through breakdown of temporal bone and rinsed with ice cold saline (isotonic) solution. Brain tissue samples were homogenized in ice cold phosphate buffer (0.1 M & having pH 7.4) and the volume of phosphate buffer was maintained 10 time the weight of the brain tissue[29].

Following are the biochemical parameters which were used in the study.

- Estimation of brain cholinesterase activity according to the Ellman G F *et al*.
- Estimation of lipid peroxidation or MDA according to the Ohkawa*et al*.
- Estimation of superoxide dismutase according to the Mishra *et al*.

Estimation of brain cholinesterase activity: According to the Ellman G F *et al* [30,31].

Principle

The brain cholinesterase activity was measured by providing an artificial chemical, acetylthiocholine (ATC). After the cleavage of ATC, thiocholine was formed with acetic acid allowed to react with 5, 5'-dithiobis - (2nitrobenzoic acid) (DTNB), yellow colour anion was formed (Thionitrobenzoic acid). The concentration of thionitrobenzoic acid was detected using UV spectrophotometer at 412 nm.

Procedure

Cuvette containing 2.6 ml phosphate buffers, add 0.4 ml of brain homogenate and 100 µl of DTNB. The content of cuvette was mixed thoroughly and the absorbance was measured at 412 nm in the spectrophotometer i.e basal reading. After this 20 µl of ATC was added and change in absorbance was noted down.

Estimation of lipid peroxidation

Lipid peroxidation levels were estimated by the Ohkawa*et al* method [32].

Thiobarbituric acid (TBA) reaction is done in this method. 2- thiobarbituric acid reactive substance (TBARS) are naturally present in biological livings which increase in concentration in response to oxidative stress.

Principle

One molecule of MDA reacts with two molecule of TBA under acidic condition and form MDA – TBA adduct i.e pink colored. Absorbance was measured at 535 nm in spectrophotometer.

Procedure

Taken 2 ml of brain homogenate, add 2 ml of 30% of trichloroacetic acid then add 0.8% thiobarbituric acid reagent in a test tube. Keep test tube in cold water for half an hour. After this process homogenate was centrifuged at 3000 RPM for 15 min, supernatant was separated out and absorbance was noted down at 535 nm against blank.

Estimation of superoxide dismutase

SOD was estimated according to Kono method.

Principle

This method is based on principle of the inhibitory effect of SOD on the reduction of nitroblue tetrazolium (NBT) dye by superoxides radical which are formed by the auto oxidation of hydroxylamine hydrochloride [32].

Procedure

Cuvette containing 1.3 ml of NaOH buffer + 500 µl NBT and the reaction was started by the addition of 100 µl hydroxylamine hydrochloride. After 2 or 3 min 70 µl enzyme extract was added. Increase in absorbance at 540 nm was noted after % inhibition in the rate of NBT reduction.

Statistical Analysis

The statistical analysis was carried out using prism graph pad 7 software. All values were represented as mean ± SEM. Multiple comparision between different groups was performed using one way analysis of variance followed by Tukey's test for all behavioral test and biochemical evaluation except escape latency in Morris water maze. In Morris water maze two way analysis of variance was used followed by Bonferroni's test. Difference level for statistical significant result, $P<0.05$ was considered.

RESULTS

Phytochemical profile of *Anethum graveolens* ethanolic extract

Percentage yield of extract

Ethanolic extract of *Anethum graveolens* Weight of dried leaves of *Anethum graveolens* = 960 gm

Weight of extract obtained = 59.2

$$\% \text{ yield} = \frac{\text{wt. of extract obtained}}{\text{wt. of dried leaves taken}} \times 100$$

% yield of *Anethum graveolen* sethanolic extract = 6.16%

Pharmacological study

Behavioral estimation

Effect of *Anethum graveolens* leaves extract (AGE) on Transfer Latency (TL) of scopolamine treated mice in Elevated plus maze (EPM)

Treatment with scopolamine showed significant (P<0.001) increase in TL time when compared to control group. Ethanolic extract of *Anethum graveolens* leaves (100 mg/kg, 200 mg/kg and 400 mg/kg) and standard significantly (P<0.001) reduce TL time when compared to disease control group. The effect of AGE 400 mg/kg was noticed to be comparable to standard treated group. Therefore, AGE treated groups was not effective as standard treated group.

Effect of *Anethum graveolens* leaves extract (AGE) on Escape Latency and time spent in target quadrant (TSTQ) of scopolamine treated mice in Morris water maze (MWM)

Treatment with ethanolic leaves extract of *Anethum graveolens* (100, 200 and 400 mg/kg p.o) significantly (P<0.001) decrease ELT time and increase TSTQ when compared to disease control group. The effect of AGE 400 mg/kg was noticed to be comparable to standard treated group.

Biochemical estimation

Effect of *Anethum graveolens* leaves extract on brain AchE activity of scopolamine treated mice

Treatment with scopolamine showed significant (P<0.001) increase in brain AchE activity when compared to control group. The group treated with standard showed significant (P<0.001) decrease in AchE activity when compared to scopolamine treated group where as a significant (P<0.001) decrease in AchE activity was observed in the AGE (400 mg/kg) treated group. On the other hand the group treated with AGE (100 & 200 mg/kg) showed less significant (P<0.01) effect.

Effect of *Anethum graveolens* leaves extract on level of SOD of scopolamine treated mice

Scopolamine treated group showed significant (P<0.001) decrease in SOD level when compared with control group. Whereas, standard treated group showed significant (P<0.001) increase in activity of SOD level when compared to scopolamine treated group. On the other hand AGE (100 mg/kg) treated group showed significant (P<0.001) increase in SOD level when compared to standard treated group. The most potent effect was shown by the AGE (400 mg/kg).

Effect of *Anethum graveolens* leaves extract on lipid peroxidation of scopolamine treated mice

Lipid peroxidation study revealed that scopolamine treated group showed significant (P<0.001) increase in MDA level when compared to control group. Standard and AGE (400 mg/kg) treated group were able to prevent the elevated MDA level, showed significant (P<0.001) decrease in MDA level when compared to Scopolamine treated group. The AGE (100 & 200 mg/kg) also showed significant effects.

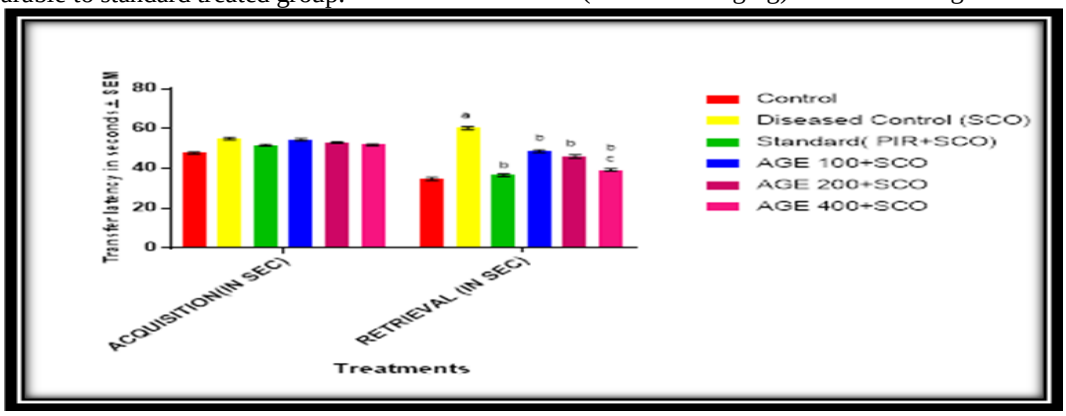

Fig 1: Transfer latency of mice on elevated plus maze (Acquisition and retrieval in seconds)

Each group (n=6) represents mean± standard error mean (SEM)

a= p≤0.001 versus control

b= p≤0.001 versus diseased control

c= p≤0.01 versus AGE 100+SCO

The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 1 way ANOVA and Tukey's test.

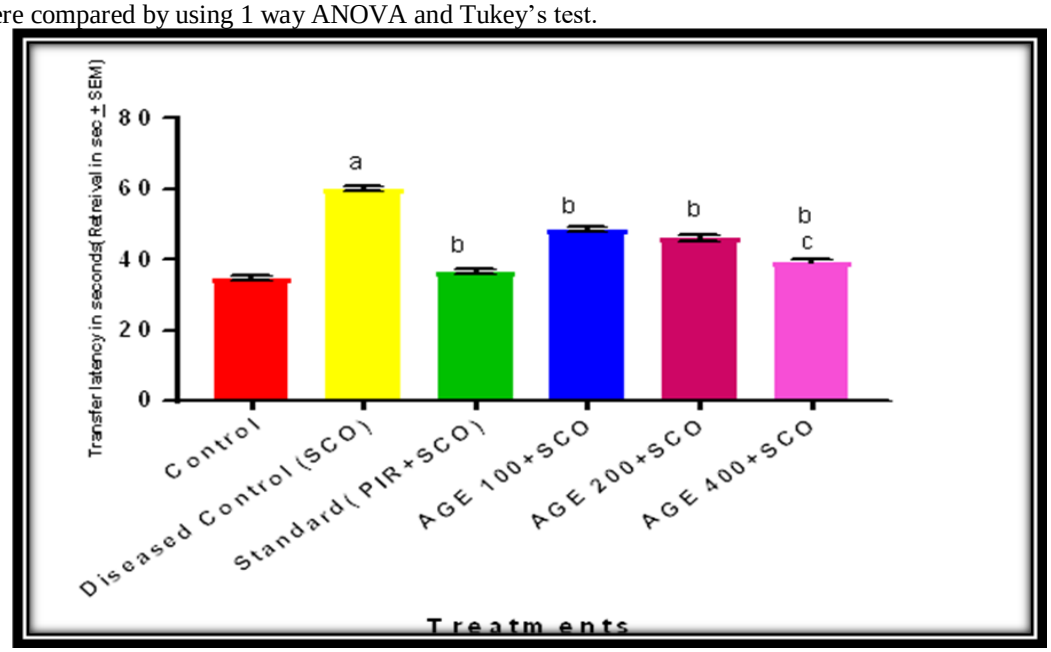

Fig 2: Transfer latency of mice on elevated plus maze (Retrieval in sec ± SEM)

Each group (n=6) represents mean ± standard error of means (SEM)
a= p≤0.001 versus control
b= p≤0.001 versus diseased control
c= p≤0.01 AGE 100+ SCO
The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 1 way ANOVA and Tukey's test.

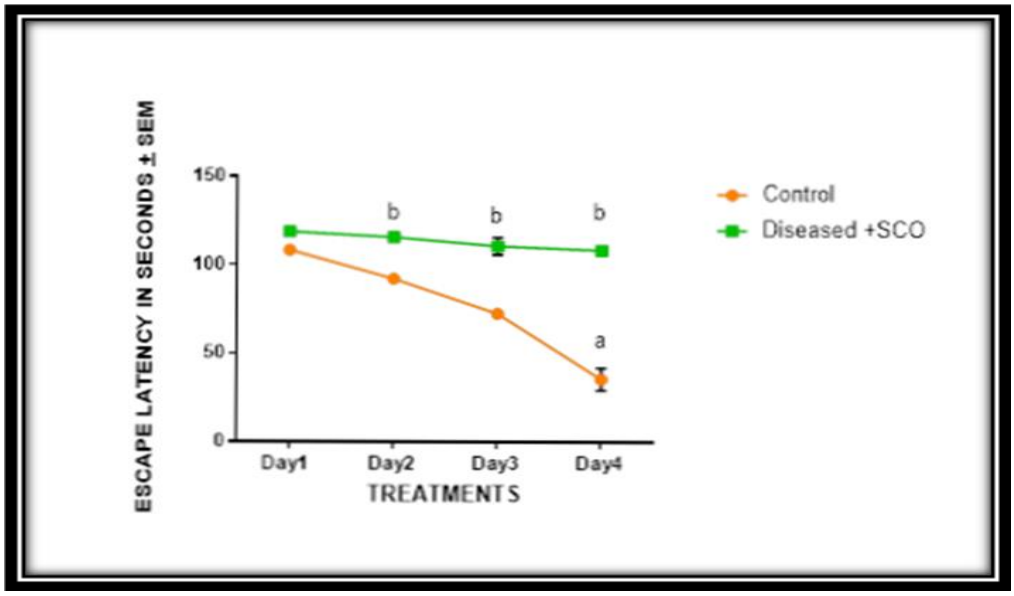

Fig 3: Effects of scopolamine on Escape Latency (ELT) during Acquisition Trials in Morris Water Maze on mice

Each group (n=6) represents mean ± standard error of means (SEM)
a= p≤0.001 versus ELT on first day of control group
b= p≤0.001 versus ELT on same day of control group

The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using way2 ANOVA and Tukey's test.

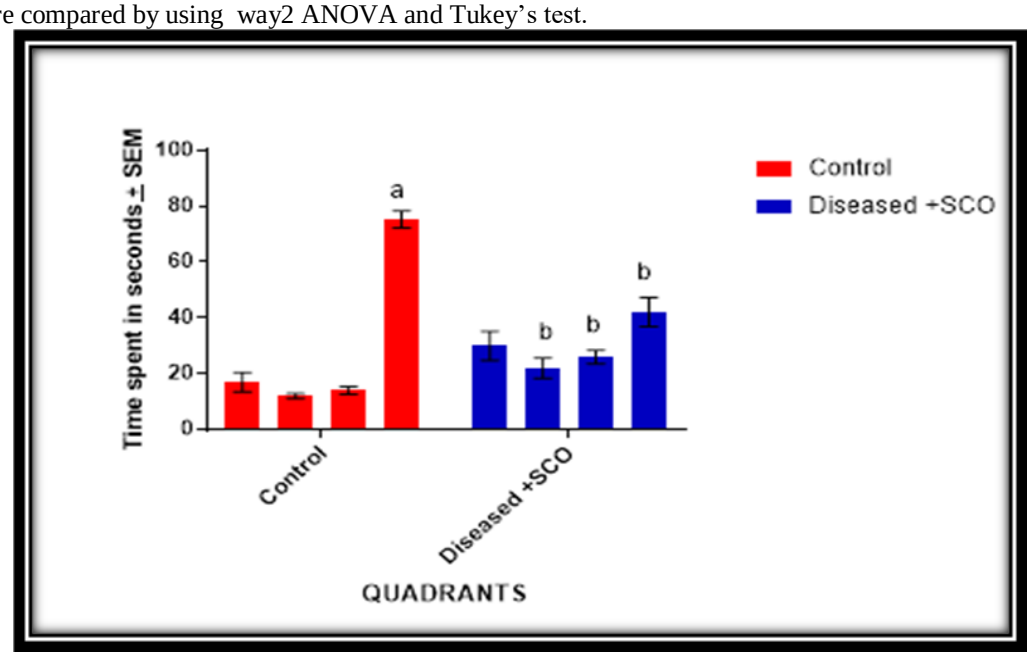

Fig 4: Effect of scopolamine on time spent in target quadrant during retrieval trial in morris water maze.
Each group (n=6) represents mean ± standard error of means (SEM)
a= p≤0.001 versus other quadrant in same group
b= p ≤0.001 versus time spent in target quadrant in control group
The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 2 way ANOVA andTukeys's test.

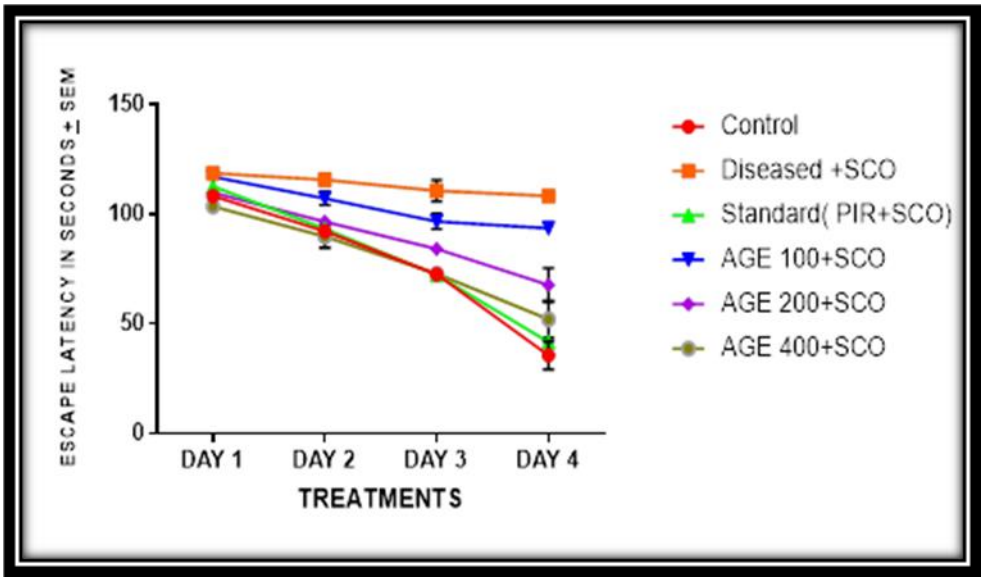

Fig 5: Escape latency (day 1 to day 4) on Morris water maze in seconds on mice
Each group (n=6) represents mean ± standard error of means (SEM)
a= p≤0.001 versus control
b= p≤0.001 versus diseased control
The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 2 way ANOVA and Bonferroni's test.

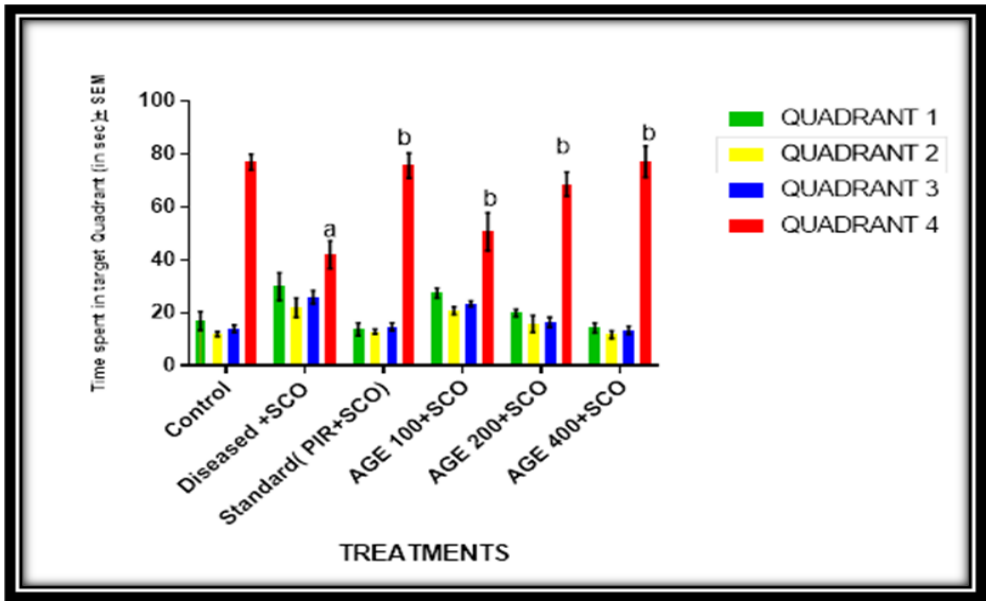

Fig 6: Effect of *Anethum graveolens* on time spent on target quadrant during retrieval trial in Scopolamine treated mice on morris water maze.

Each group (n=6) represents mean ± standard error of means (SEM)

a = p≤0.001 time spent in other quadrant versus control group in Q1

b = p≤0.01 time spent in target quadrant i.e Q4

The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 2 way ANOVA and Bonferroni's test.

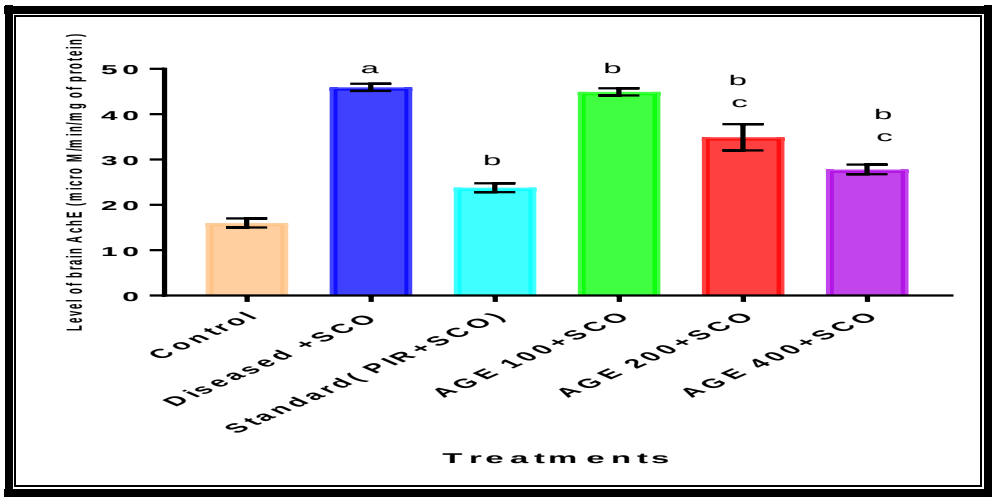

Fig 7: Effect of *Anethum graveolens* leaves extract on brain cholinesterase activity in scopolamine treated mice

Each group (n=6) represents mean ± standard error of means (SEM)

a= p≤0.001 versus Control Group

b= p≤0.001 versus Diseased Control Group

c= p≤0.001 versus AGE + SCO Group

The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 1 way ANOVA and Tukey's test.

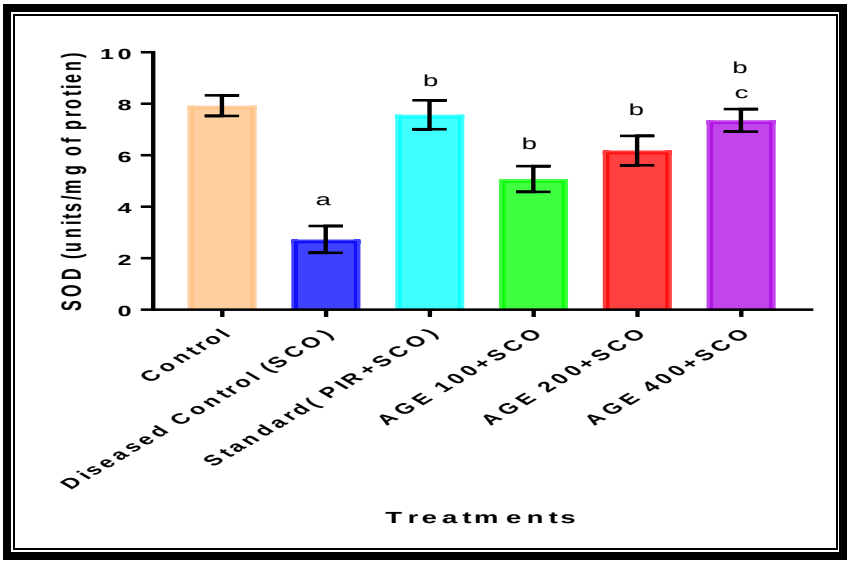

Fig 8: Effect of *Anethum graveolens* extract on level of superoxide dismutase in scopolamine treated mice.

Each group (n=6) represents mean ± standard error of means (SEM).
a= p≤0.001 versus Control Group
b= p≤0.001 versus Diseased Control Group
c= p≤0.01 versus AGE 100+SCO
The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 1 way ANOVA and Tukey's test.

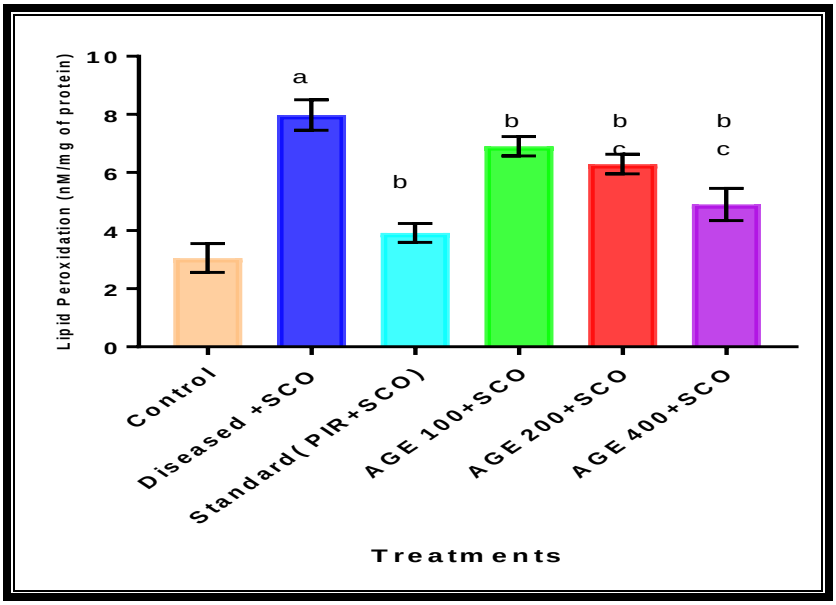

Fig 9: Effect of *Anethum graveolens* leaves extract on lipid peroxidation in scopolamine treated mice

Each group (n=6) represents mean ± standard error of means (SEM)
a= p≤0.001 versus Control Group
b= p≤0.001 versus Diseased Control Group
c= p≤0.001 versus AGE + SCO Group
The statistical analysis was carried out prism graph pad 7 software. All values are represented as mean ± SEM (n=6). Results were compared by using 1 way ANOVA and Tukey's test.

DISCUSSION

Alzheimer's disease is slowly and gradually leads to progressive dementia which affect both

(1) Cognition i.e. process of acquiring knowledge and understand thought & sense and

(2) Behavior i.e. conducts oneself toward others[1].

Learning is explained as the act of obtaining novel or making certain changes to existing knowledge, behavior and skill. Learning is basically a long term change in mental representation i.e. mental imagery of things that are latest or old seen or sensed by sensory organ and enhance due to experience [2].

Memory is known as the process in which the information which is being captured is encoded, stored and retrieved.

Learning and memory impairment are closely related to the cholinergic hypothesis. The level of Ach (messenger in the brain) decrease severely in the brain and simultaneously nerve ending and brain cell are also damaged and some structural changes are also takes place in brain [23].

Oxidative stress also plays a fundamental role in the learning and memory impairment. Oxidative Formation of Aβ amyloid precursors in AD leads to induction of lipid peroxidation and generates reactive oxygen & nitrogen species which contains unpaired extra electron. This extra unpaired electron needs other molecule for their stable configuration. During this process extra molecule binds with another molecule and form free radical (high energy electron) and this free radical helps in alteration of the molecule to which they are attached and finally cause cellular and molecular damage leading to AD.

The most widely used nootropics i.e. Racetams drugs act as AMPA modulator. After the administration of Piracetam it is believed it will help in (1) reduction of free radicals which cause oxidative leading to cholinergic damage, (2) modulation of central neurotransmitter like Ach and glutamate, (3) positively allosteric modulation of AMPAR.

Scopolamine helps in induction of significant impairement in the hippocampus dependent memory, after the administration of scopolamine on 21st day they cause cholinergic dysfunction through elevation in the level of Acetylcholiensterase and reduction in the level of Ach in brain and they cause competitive blockage of the muscarinic receptor, hence scopolamine induces neurotoxicity or learning and memory impairment.

The plant *Anethum graveolens* is rich in flavones and flavanoids, these flavanoids and antioxidants are well known for antioxidant potential, hence shows significant potential effect on learning and memory impairement.

Elevated plus maze and Morris water maze test are incorporated model for evaluation of learning and memory which is extensively accepted. Mice took lesser seconds in transfer latency (Retrieval) in comparison to transfer latency (acquisition), it means standard and AGE showed better result on retrieval day. In morris water maze, after the administration of standard and AGLE there is significant reduction in escape latency time and also increase time spent in target quadrant on 5th day.

Evaluation of Brain AchE activity

The level of AchE rises in Alzheimer's disease. In the hypothesis it is assumed that learning and memory impairment is linked to degradation of cholinergic system. Therefore the approach for treatment of Alzheimer's disease mainly includes the increase in level of Ach in the brain region.

The present study postulated a significant increase in AchE in mice treated with scopolamine. A significant decrease in acetylcholinesterase level has been recorded in the mice treated with AGE especially in 400 mg/kg dose. Thus the ethanolic extract of *Anethum graveolens* leaves is known to inhibit the rise in acetylcholinesterase level in brain.

Superoxide Dismutase

Synthesis of free radicals or the reactive oxygen species can cause damage of the cell and tissue of the brain which leading to neuronal death. The main antioxidant that prevents the generation of new free radical species is Superoxide Dismutase. Hydrogen peroxide was covered from SOD into non harming molecules.

The present study concludes that the oxidative stress is induced by incorporation of scopolamine on 21st day. In mice, scopolamine decreases the level of SOD. After the administration of Piracetam and *Anethum graveolens* showed significant increase in SOD.

Lipid peroxidation

When the level of lipid peroxidation is increased in brain it can cause brain neuronal damage. The decrease in antioxidant defence of brain and/or increase in free radical generation deteriorates the balance between the prooxidant and antioxidant regulation which leads to oxidative stress and finally cell death.

The oxidative stress is produced by scopolamine is linked to the increased amount of lipid peroxidation. The administration of ethanolic extract of *Anethum graveolens* in scopolamine treated mice showed potential action in reducing the oxidative stress. This indicates that *Anethum graveolens* leaves extract has potent antioxidant property against the oxidative stress induced by increased level of lipid peroxidation.

CONCLUSION

The aim of the present study was to evaluate the therapeutic potency of *Anethum graveolens* on scopolamine induced learning and memory impaired mice. Evaluation was based on the following parameters.

The phytochemical constituents in ethanolic extract of *Anethum graveolens* were found to be glycoside, flavones, alkaloids, carbohydrate, tannins, terpenoids and phenols. Disease induced mice which were treated with scopolamine, showed a significant increase in the AchE activity. Whereas, increased activity was reversed when the group is treated with the *Anethum graveolens* extract and Piracetam (standard). Decrease in the AchE activity by AGE may be directly or indirectly related to the learning and memory dependent on cholinergic system of body.

After administration of scopolamine, disease control mice showed decrease in free radical scavenging enzyme SOD. On the other hand after when the mice were administered with AGE, free radical scavenging enzyme restored significantly.

In present study treatment by *Anethum grvaeolens* decreases the lipid peroxidation level. Hence, with the evaluation of all these parameters the following study concludes that AGEhave a potential role in management of learning and memory impairment.

REFERENCES

1.Dipiro Joseph T. 2005. Pharmacotherapy. A Pathophysiologic Approach. Chapter 63- Alzheimer's disease. 6thed. The McGraw hill companies 1158.
2. http://www.alz.org.com. 15-03-2017.
3.Larry R. Squire. Memory system of brain: A brief history and current perspective. Neurobiology of learning and memory, 2014: 171-177.
4.Fatimah M. Mitochondrial dysfunction and Alzheimer's disease; 2008.
5.Reitz, Christiane; Mayeux, Richard. Alzheimer disease: Epidemiology, Diagnostic Criteria, Risk Factors and Biomarkers". Biochemical Pharmacology, 2014; 88 (4): 640–51.
6.Alzheimer's Disease. Lancet, 2006; 368: 387–403.
7.Genome-wide association studies in Alzheimer disease. Archives of Neurology, 2008; 65(3): 329–34.
8.Selkoe DJ. Translating cell biology into therapeutic advances in Alzheimer's disease. Nature, 1999: 399
9.Martorana, Alessandro; Esposito, Zaira; Koch, Giacomo. Beyond the cholinergic hypothesis: do current drugs work in Alzheimer's disease. CNS neuroscience & therapeutics. ISSN 1755-5949, 2010; 16 (4): 235–45.
10.Shen ZX. Brain Cholinesterases: II. The Molecular and Cellular Basis of Alzheimer's Disease. Medical Hypotheses, 2004; 63(2): 308–21..
11.Apolipoprotein E, Dementia, and Cortical Deposition of Beta-amyloid Protein. The New England Journal of Medicine, 1995; 333(19): 1242–47.
12.Alzheimer-type Neuropathology in Transgenic Mice Overexpressing V717F Beta-amyloid Precursor Protein. Nature, 1995; 373(6514): 523–27.
13.The Role of Tau Phosphorylation and Cleavage in Neuronal Cell Death. Frontiers in Bioscience, 2007; 12: 733–56.
14.Long term hormone therapy for perimenopausal and postmenopausal women. The Cochrane Database of Systematic Reviews, 2012; 7: 45-50.
15.Heamalatha S et al. Pharmacognostical, pharmacological, investigation on AnethumGraveolens. Research Journal of Pharmaceutical Biological and Chemical Sciences, 2011; 2(4): 564.
16.Kaur G.J, Arora D.S. J Med Plant Res, 2010; 4(2): 087-094.
17.https://en.wikipedia.org/wiki/.anethumgraveolens. 5-11-2016
18.Sharma R. Argotechniques of Medicinal Plants. New Delhi. Daya Publishing House, 2004: 3-8.
19.Duke J A. Handbook of Medicinal Herbs. London. CRC Press, 2001: 42.
20.Nair R. Chanda S. Antibacterial activities of some Medicinal plants of the western region of India. Turk J Biol, 2017: 231.
21. S.Jana And G.S.Shekhawat, Anethumgraveolens: Indian Traditional Medicinal herb and spice. Pharmacognosy Review, 2010; 4(8): 179-184.
22.http.//www.recetam.noo.org.com. 24-4-2017
23.Malykh&Sadaie. Drugs. Piracetam and Piracetam-Like Drugs. From Basic Science to Novel Clinical Applications to CNS Disorders, 2010; 70(3): 287-312.
24.Hsieh MH. Et al. Ceftriaxone reverses deficit of behaviour and neurogenesis in an MPTP- induced rat model of Parkinson's disease dementia. Brain Research, 2017: 129-138.
25.VivekSharma ,Subrahmanya GS and Ashok Kumar G. The effect of Minocycline on oxidative stress and memory deficits in aged rats. International journal of pharmac, 2012: 73.
26.Habidur Rahman. Inhibition of acetylcholinestrase and antioxidant activity are mostly used mechanism of NardostacysJata Mansi in sleep deficiencyAlzhiemer's mice model. IJPPR, 2011: 1809-1815.
27.R.Yogendra. Evaluation of antioxidant and AChE inhibitory activity of Punicagranatum in scopolamine treated rats. IJPPR, 2012: 115-125.
28.Kono et al. Measurement of SOD level. J Boil Chem, 2013: 270-274.
29.Bhosle V, Rama K. Anticonvulsant and antioxidant activity of aqueous leaf extract of Desmodiumtriflorum in mice. BJP, 2013; 23: 1807-1812.
30.Khandelwal K.R. Practical Pharmacognosy. 3rd ed. NiraliPrakashan. Pune, 1996.
31.Tiwari P. and Kumar S. Pharmaceutical screening and extraction. International pharmaceutical sciences, 2011: 98-106.
32.Tiwari P. and Kumar S. Pharmaceutical screening and extraction. International pharmaceutical sciences, 2011: 101-106.