Volume 64, Issue 3, 2020

Journal of Scientific Research

Institute of Science,

Banaras Hindu University, Varanasi, India.

National Conference on Frontiers in Biotechnology & Bioengineering (NCFBB 2020), JNTU Hyderabad, India

A Comparative Study of Methanolic and Hydro-Alcoholic Extracts of *Moringa Oleifera* Pods on Memory Enhancing Activity

M.Sandhya Rani*[1], Manogna. Chintalapati[1], and G.Krishna Mohan[1]

[1]Centre for Pharmaceutical Sciences, Institute of Science and Technology, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India. sandhyampharmphd@gmail.com, manognachintalapati@gmail.com, drgkmohan@gmail.com

Abstract: **The aim of the present study is to evaluate the neuroprotective activity of methanolic and hydro-alcoholic extracts of *Moringa oleifera* pods in scopolamine induced amnesia model. MEMO (Methanolic extract of *Moringa oleifera*) and HAEMO (Hydro-alcoholic extract of *Moringa oleifera*) were tested at the doses of 100mg/kg body wt and 400mg/kg b.wt. for the neuroprotective effect or memory enhancing activity in amnesia mice using elevated plus maze, t-maze methods for Neurobehavioral studies .The methanolic and hydro-alcoholic extracts at higher dose (400mg/kg) has shown significant improvement in cognition in normal and in amnesia group mice . Significant difference was observed in biochemical parameters by the use of higher doses of the both the extracts in treated amnesic animal groups, untreated animal groups and scopolamine group animals. Thus, the high doses of both MEMO and HAEMO has shown significant effect in learning and memory enhancing activity and so may be useful for Alzheimer's treatment.**

***Index Terms: Moringa oleifera*, Alzheimer's, Neurobehavioral, Neuroprotective, Memory enhancing.**

I. INTRODUCTION

Alzheimer's ailment is the Neurodegenerative illness, a general term of dementia, memory misfortune and other psychological capacities sufficiently genuine to meddle with day by day life. (Ganiyu O,2012). It is neither irresistible nor infectious, however is the absolute most basic reason for dementia - a condition that effects around 10 percent of those aged more than 65 and around 20 percent of those aged more than 75. Dementia is the term used to portray an overall decrease in every aspect of mental capacity. Around 50 percent of individuals with dementia are experiencing Alzheimer's disease (Dhanya et al 2016).

The utilization of home grown and characteristic concentrate in the treatment of AD has been expanded in the previous 10 years (Tian, J, 2010). Moringa oleifera has a place with family Moringaceae which is regularly known as Munaga. Moringa oleifera is one of the quickly developing deciduous trees generally of tallness up to 10-12m and trunk measurement up to 45cm. Pod of this plant is hanging, and resembles an earthy colored case which is three sided of around 20-45cm size which holds seeds of dim earthy colored globular with a distance across of about 1cm (Parotta, John A. 1993).

Past the employments of Moringa as a food, it is utilized as a characteristic plant development enhancer, because of zeatin in high content (Leone A, 2015). It tends to be utilized as calming, hostile to pain relieving, in treatment of skin ailments, used to treat hypoglycemia. (Nadkarni K M,1976)

Moringa oleifera is likewise utilized as anti-parasitic, genitor-urinary treatment, hysteria, anti-spasmodic, tumors and anthelementhic action. Notwithstanding this, the plant root is accounted for having mind tonic impact as mentioned in Indian Medicinal plants. (Kirtikar K.R,1975). The plant and pods are reported to contain the chemical constituents like alkaloids, glycosides, triterpenoids, steroids, flavonoids, and amino acids. The extracts and the chemical constituents have demonstrated the intense pharmacological exercises like antifertility, cardiovascular, antiulcer, against pyretic and CNS activity were observed. The leaves of Moringa oleifera were accounted for improving intensity of memory and furthermore utilized in diabetes (P.Sudhir Kumar,2010). In this context, the current investigation was meant to assess the memory improving

* Corresponding Author

DOI: 10.37398/JSR.2020.640306

Selection and Peer-review under responsibility of the Program Chairs.

capacity of methanolic and hydro-alcoholic concentrates of Moringa oleifera pods on scopolamine instigated amnesic models.

II. II MATERIALS AND METHODS

A. Materials

Moringa oleifera was locally available and collected from Nalgonda in the month of March and was authenticated by Scientist in-charge L. Rasingam, Botanical survey of India, Attapur, Hyderabad and the used chemicals in the biochemical estimation were of analytical grade

Preparation of Methanolic and Hydro-Alcoholic extracts of Moringa oleifera pods:

The pods of *Moringa oleifera* were gathered and completely washed with refined water and shade dried. The shade dried pods were made into coarse powder. The powdered pods were taken about 100 grams in maceration tanks with methanol (R. Ganguly,2008) and hydro-alcohol Chatchadasutalangka et al, 2013) solvents in each tank and macerated for around a week at room temperature. The extracts were concentrated utilizing Rota evaporator (Heidolph) and crude extracts were put away for the future examination.

B. Animal Experiment

The tests were performed following the CPCSEA rules Swiss albino mice were bought from Teena biolabs (Hyderabad) weighing around 20-25g. The study was completed subsequent to endorsement from ethical committee - CPCSEA/1657/ IAEC/CMRCP/COL-18/75. The mice were acclimatized for a week before beginning the neurobehavioral study under standard lab conditions (12 hrs light/dull cycle, at 25ºC ± 2 º C temperatures) and are taken care of diet and water.

Acute toxicity studies:

Standards Studies were done following OECD-423. Mice were starved for 4 hrs before dosing (OECD guideline,2001). The methanolic and hydro-alcoholic concentrates were delivered orally at a fragment of 2000 mg/kg b.wt and noticed that there is no destructiveness, changes in behaviour and mortality for 14 days.

The concentration of methanolic and hydro-alcoholic extracts were choosen according to the acute oral toxicity studies, 100mg/kg and 400mg/kg were selected and were orally given by utilizing water for infusion. Donepezil 3mg/kgb wt was managed in refined water. Amnesia was incited by managing Hyoscine (3mg/kg) ip dissolving in water for infusion. New medication arrangements were arranged each day prior dosing.

scheduled Experimental design:

In the current examination, the mice (male), were sorted into seven gatherings with six each and were exposed to two models.

Gathering I: Mice were given refined water in the portion of 10mg/kg orally for 7 progressive days.

Gathering II: were given Scopolamine Hydrobromide3mg/kg intraperitoneally (i.p) for 7 progressive days.

Gathering III: were given Donepezil 3mg/kg orally for 7 progressive days and after 60 min of last portion organization, Scopolamine (3mg/kg i.p) was infused to initiate amnesia.

Gathering IV, V, VI and VII: These gathering of mice were pre-treated orally with the extracts MEMO 100mg/kg (Gathering -IV), HAEMO 100mg/kg (Gathering -V), MEMO 400mg/kg (Gathering -VI), HAEMO 400mg/kg(Gathering -VII) individually for seven days continously and 60 min of the last portion organization, scopolamine (3mg/kg i.p) was infused to prompt amnesia and was assessed for memory maintenance after 30 mins of amnesia acceptance by utilizing different exteroceptive models.

1) Elevated plus maze:

Elevated plus labyrinth is utilized as an exteroceptive model to assess momentary memory in mice. EPM was structured of two open arms (16×5cm) and two encased arms (16×5×12cm) stretched out from a focal stage and the labyrinth was lifted to a tallness of 25 cm from the floor is utilized to contemplate the securing and maintenance of transient memory. On the seventh day, after half an hour of Hyoscine administration, each mouse was put towards one side of the open arm confronting ceaselessly from the focal stage, to quantify the procurement move inactivity time. The time taken by the creature to enter the encased arm with four legs is known as move inertness. The cutoff was 90seconds and if the creature didn't enter the encased arm inside the predefined time the mouse is permitted to investigate the labyrinth for one minute and put over into confine. Memory retention is analyzed after 24hrs i.e., on eighth day of dosing. Noteworthy decrease in move inertness time is a file of the improved memory. (Mani V, 2009)

2)T-Maze:

T-labyrinth filled in as the model to assess the memory in mice. To contemplate securing and maintenance of transient memory, T-labyrinth was structured as three arms stretched out from the middle. On the seventh day of dosing, after 30 min of Hyoscine infusion, each mouse was set towards the open arm one side confronting ceaselessly from the focal stage, to gauge the securing rate modification. The rate modification is characterized as the no. of potential triplets to the complete number of arm passages – 2 and rate esteem was determined by duplicating. Memory retention is inspected after 24 hrs. Critical decrease in rate modification is an improved cognition. (Hala FZ,2014)

C. Estimation of biochemical parameters

The creatures were relinquished on the eighth day after neurobehavioral examination and the entire mind was extracted out cautiously and flushed in 0.9 % NaCl to eliminate blood and homogenized in phosphate buffer (10%W/V), centrifuged at 15,375 x g at 4ºC for 20 min utilizing small scale rotator. The protein content in the supernatants was estimated by Lowry strategy (Lowry OH,1951)

1) Lipid peroxidation Assessment :

Recently organized 1ml of 10% Trichloro acetic acid was incorporated with 500µl of supernatant and the mix was set aside momentarily for half an hour and centrifuged at 5000 rotations per minute at 4ºC for 10 min. To 1ml of supernatant, 250µl of freshly prepared 0.33% TBA was incorporated and mixed well, and heated for 60mins at 95ºC and the chambers were speedily cooled under running fixture water and the pink concealing was scrutinized at 532 nm (Madhubabu G,2012) and lipid peroxides were estimated.

2) Assessment Catalase:

To 10µl of supernatant was mixed with 1ml of 30 mM H_2O_2 in 0.05M phosphate support and change in absorbance was checked at every 30sec for 3min (Madhubabu G,2014)

$K_{30}= (2.303/30)\times\log (A_1/A_2)$

Where A_1 is the high ebb OD value and A_2 is the low ebb OD value.

3) Assesment of AchE:

The entire mind AChE activity was assessed using Elman's technique with few adjustments. The mice were relinquished by cervical separation and minds were analyzed out, gauged and promptly positioned in super cooled saline. The gauged tissue was homogenized in 0.1 M phosphate buffer pH 8 (10% w/v) and centrifuged at 15,375 x g for 10 min. 400 µl aliquot of the supernatant was added to a blend of 2.6 ml phosphate support and 100µl of DTNB altogether blended and estimated at 412 nano meters. The steady optical density was recorded as the basal perusing. To this, 20µl of acetylthiocholine substrate was included and the adjustment in OD was recorded for a time of 10 min at 2 min span. The adjustment in the absorbance per min was resolved. The activity was determined utilizing following condition**.** (Ellman GL,1961)

$R= A/C_o \times 5.74 \times 10^{-4}$

Where, R is the rate in moles of substrate hydrolyzed/ min./ gram of brain tissue; A is the change in OD/ min and C_o is the original concentration of the tissue in mg/ml.

D. Statistical analysis

Certain evaluation was performed by one-way analysis of variance (ANOVA) trailed by Dennett's test. Attributes are permitted as Mean ± SEM and $p< 0.05$ was viewed as target and $p>0.05$ was non-monstrous.

III. RESULTS AND DISCUSSION

A. Experimental animals

The trials were performed by the rules of CPCSEA, New Delhi, India on Swiss albino mice of either sex, secured from Teena Biolabs (Hyderabad) gauging 20-25g. The investigation was done subsequent to getting endorsement from the Institutional animal ethical committee (approval no: CPCSEA/1657/IAEC/CMRCP/COL-18/75). Seven days before the neurobehavioral examination mice were adjusted under standard lab conditions and took care of pellet diet and water.

B. Acute toxicity studies

Both the extracts MEMO and HAEMO concentrates of 2000mg/kg divide were found to be shielded upto14 days and no mortality was seen during the treatment time span. The doses selected for the examination of neuroprotective effect in the organization of Alzheimer's ailment were 100 and 400mg/kg consistently.

C. Neurobehavioral studies

The mice demonstrated higher Transfer latency (TL) values on seventh day than on eighth day (after 24hr) showing hindrance in learning and memory because of scopolamine treatment. Donepezil (3mg/kg) pretreatment for 7 days diminished TL. On seventh day after 24 hrs i.e., on eighth day when contrasted with scopolamine gathering, showing improvement in both learning and memory. Scopolamine (3mg/kg) expanded TL essentially (in Fig 1) in mice on seventh day and eighth day when contrasted with normal gathering, showing hindrance of learning. MEMO 100 and 400mg/kg and HAEMO 100 mg/kg diminished TL on seventh day and eighth day in mice when contrasted with scopolamine gathering. Higher portion of MEMO and HAEMO 400mg/kg has essentially upgraded the learning and memory of mice by stamped decline in TL on seventh and eighth day when exposed to elevated plus labyrinth tests. The higher dosages of MEMO and HAEMO pretreatment for 7 days progressively ensured the mice against scopolamine instigated amnesia. The percentage alteration of the experimental animals was appeared in (Fig 2). The i.p infusion of scopolamine in mice increased the percentage alteration when contrasted and the ordinary benchmark group. The diminishing in rate change was demonstrated in the donepezil treated mice and MEMO and HAEMO treated gatherings on correlation with amnesia prompted gatherings, low portion of MEMO 100mg/kg and high portion of HAEMO 400mg/kg has indicated a huge reduction in percentage alteration.

D. Biochemical studies

The mice which are pre-treated with the Donepezil (3mg/kg), MEMO and HAEMO (100mg/kg) has showed significant

increase in antioxidant activity when stood out from scopolamine gathering. Administration of scopolamine (3mg/kg) extended the cerebrum thiobarbituric acid reactive substance level which was considered as an extension in the oxidation activity as a top priority when appeared differently in relation to that of control group of animals. Association of MEMO and HAEMO 100mg/kg and HAEMO 400mg/kg and Donepezil basically pivoted the Scopolamine incited increase as a main priority thiobarbituric acid reactive substance levels showed up in (Fig 3).

The mice which are pre-treated with Donepezil (3mg/kg) and MEMO and HAEMO 400mg/kg has demonstrated huge increment in antioxidant activity when contrasted with that of scopolamine gathering (Fig 4). Scopolamine organization brings about diminished mind catalase levels which were considered to bring about the expanded oxidation action in cerebrum when contrasted with that of control gathering of mice. The most minimal portion of MEMO and HAEMO 100mg/kg non essentially decreased the catalase levels. The organization of MEMO and HAEMO 400mg/kg and Donepezil has altogether turned around scopolamine prompted decline in cerebrum catalase levels. To decide the impact of MEMO and HAEMO extricates in synapse metabolic protein, AChE in the mind tissue was assessed and appeared in (Fig.5). Scopolamine infusion (3mg/kg; i.p) had altogether expanded the AChE action when contrasted and that of ordinary benchmark group. Among the treatment gatherings, the low portion of HAEMO (100mg/kg) treated mice, there was a noteworthy decrease in the compound levels when contrasted and the scopolamine gathering and high portion of MEMO and HAEMO 400mg/kg has additionally indicated the critical impact.

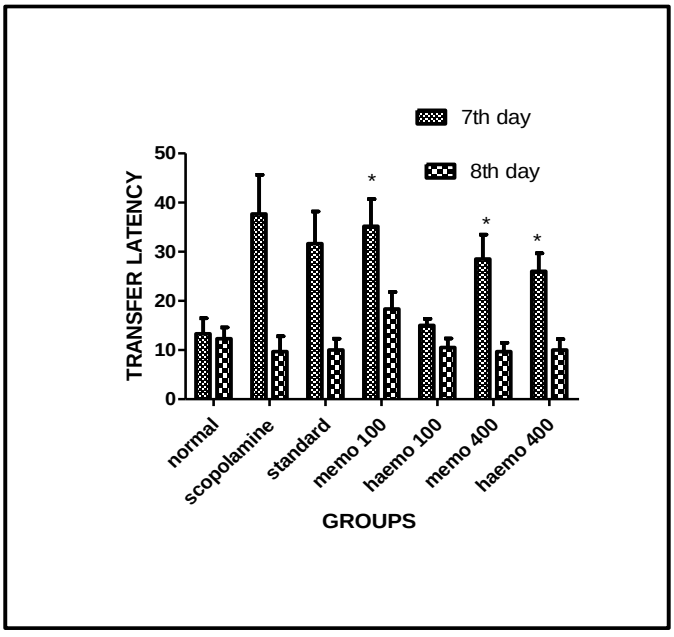

Figure 1: Effect of MEMO and HAEMO extracts on scopolamine instigated amnesia model in elevated plus labyrinth task in mice. Each gathering comprises of six mice (n =6). Qualities are communicated as Mean ± SEM.*p < 0.05 contrasted and scopolamine bunch are viewed as huge.

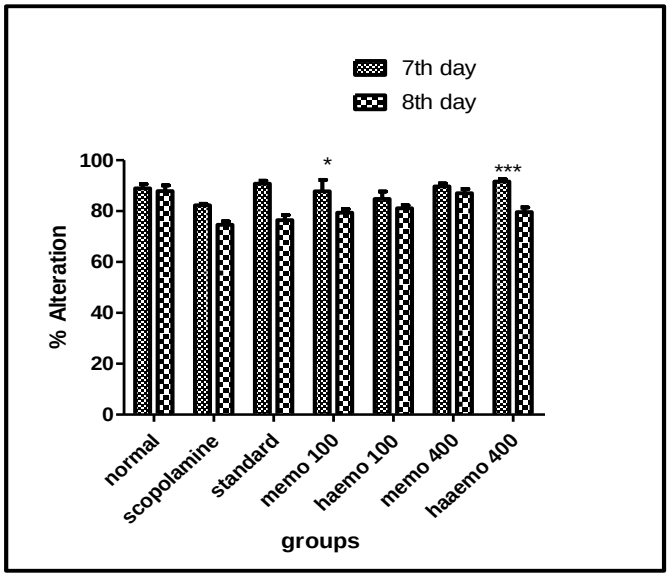

Figure 2: Effect of extracts of MEMO and HAEMO on scopolamine instigated amnesia model in T-labyrinth task in mice. Each gathering comprises of six mice (n =6). Qualities are communicated as Mean ± SEM. ***p <0.001,*p < 0.05 contrasted and scopolamine bunch are viewed as huge.

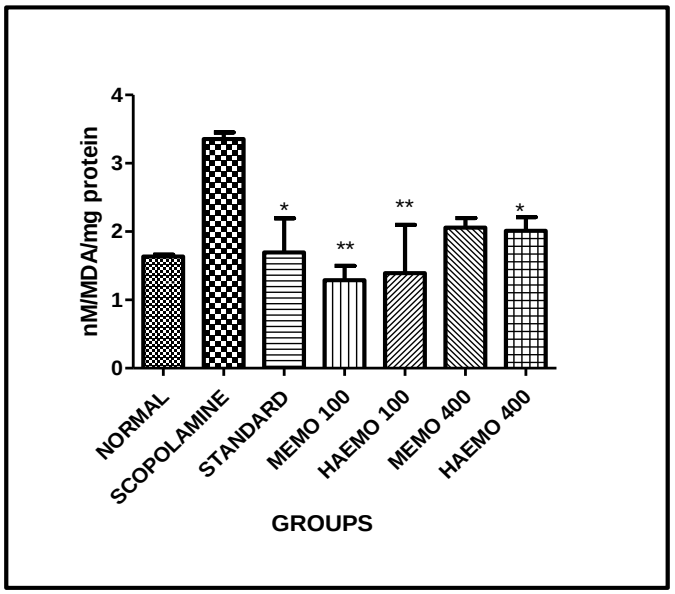

Figure 3: Effect of concentrates MEMO and HAEMO in scopolamine instigated amnesia model on thiobarbituric receptive species. Each gathering comprises of six creatures (n =6). Qualities are communicated as Mean ± SEM. **p < 0.01, *p < 0.05 contrasted and scopolamine bunch are viewed as huge.

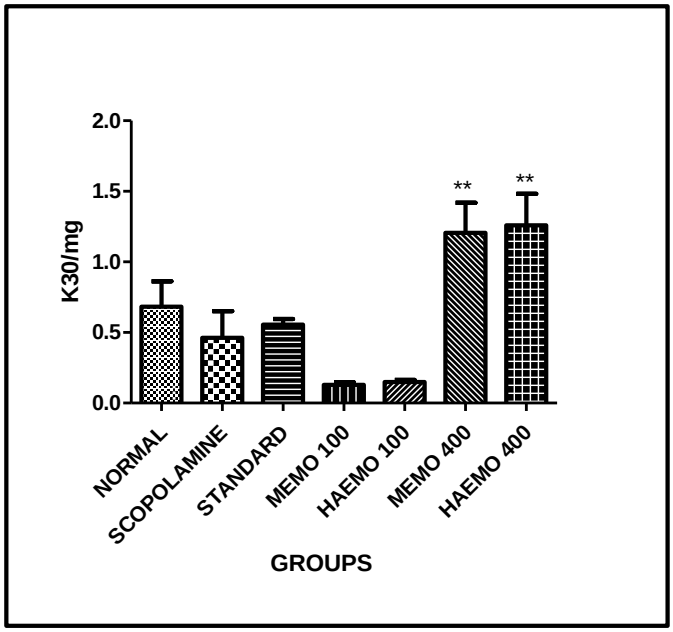

Figure 4: Effect of MEMO and HAEMO extracts in scopolamine instigated amnesia model on Catalase levels. Each gathering comprises of six mice (n =6). Qualities are communicated as Mean ± SEM. **p < 0.01, contrasted and scopolamine bunch are viewed as critical.

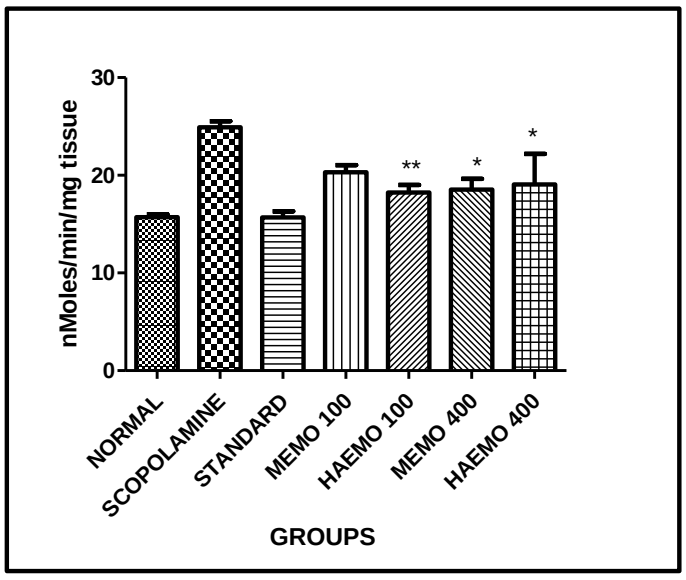

Figure 5: Effect of MEMO and HAEMO ectract in scopolamine prompted amnesia model on AChE levels. Each gathering comprises of six mice (n =6). Qualities are communicated as Mean ± SEM.**p < 0.01, *p < 0.05 contrasted and scopolamine bunch are viewed as noteworthy.

The major clinical sign found in Alzheimer's associated dementia fuses the progression of various scholarly deformations which interfere in step by step and master works. In Alzheimer's psyche, the cerebrum brokenness starts with neuronal injury, synaptic dissatisfaction and neuronal passing inciting memory shortcoming. Functional system of the cerebrum including learning and memory support was found to be connected with the cholinergic structure and Ach levels in the brain (Miwa JM,2011), (Dinesh Dhingra,2012)and the thickness of the neuronal cells accept a critical activity in memory retention. Therefore different methodology have been gotten to improve the cholinergic transmission, by extending the Ach combination, pre-synaptic acetylcholine release, and using the cholinesterase inhibitors (Robinson L,2011),(Musial A,2007)and the meds which overhaul the cholinergic limit can be used for Alzheimer's treatment.(Micheau J, 2011). Hence the current examination is expected to treat the Alzheimer's using the normal concentrates containing phytochemical constituents and the extract which is used in this work is used generally as a food. Scopolamine, obstructs the cholinergic hailing and produce memory and mental dysfunctions and in this manner lead to shortcoming in learning and memory (Souza AC,2013),(Kim SJ,2013) scopolamine is a nonselective muscarinic adversary. Scopolamine makes the oxygen free radicals at risk for the Alzheimer's contamination and it fabricates the oxidative weight. In the current examination, the scopolamine has extended the thiobarbituric acid reactive substances and reduced catalase protein levels. The association of the extracts MEMO and HAEMO in 2 measurements (100 and 400mg/kg) to mice for 7 dynamic days has reduced the oxidative concern just as prevented the scopolamine incited rise in oxidative damage by the diminished thiobarbituric destructive open substances and extended catalase levels when stood out from isolated control animals.

In the current assessment, association of MEMO and HAEMO extracts have improved learning and memory in both the models. The treatment of both the concentrates MEMO, HAEMO and Hyoscine exhibited an imperative augmentation in the scholarly introduction was assessed by Elevated plus maze and T-maze and decreased activity of the AchE in cerebrums of mice. It is expected that the enhancement of cholinergic development by raising the acetylcholine levels may be seen by lessened AchE activity which achieves extended cognitive activity. In this context, higher AChE block doesn't mean it gives better scholarly execution it induces that there should be cholinergic transmission and mental execution. It was in like manner seen that there is no mortality when extracts were given orally MEMO and HAEMO even with the higher bits (2000mg/kg). The extracts had no unsafe effect on the behavior of the mouse. New clinical studies are changing the AD therapy by shifting the focus to disease modification rather than symptom management.,(Kristina, 2019).If all the Research efforts are put together ,an effective medicine could be made for alzeimers patient in near future. (Konstantina G,2020)

CONCLUSION

The current investigation exhibits that the MEMO and HAEMO extracts of Moringa oleifera units methanolic and hydro alcoholic extract has demonstrated promising memory upgrading impacts because of its antioxidant property at all dosages however the most noteworthy portion has indicated more expected impact as a standard medication (Donepezil) against a scopolamine instigated psychological brokenness in mice and this powerful neuroprotective trademark is very much upheld by neurochemical discoveries. In this manner both the MEMO and HAEMO could be helpful in neurodegenerative issues of Alzheimer's sort.

ACKNOWLEDGEMENT

I sincerely thank Professor Abbulu Principal, of CMR college of Pharmacy Kandlkoya, Hyderabad, for providing necessary facilities to carryout this work and Associate Professor, M. Ragavendhra of Pharmacology Department in CMR college for his guidance and support during the complete period of work. I would like to place my special regards to L. Pravalika, Scholar of JNTU, Hyderabad for her help to accomplish my work successfully.

REFERENCES

Chatchadasutalangka, Jintanaporn Wattanathorn, Supaporn. (2013). Moringa oleifera mitigates memory impairment and neurodegeneration in animal model of age related dementia-Hindawipublishing corporation, Oxidative medicine and Cellular Longetivity, Volume Article id- 695936.

Dhanyaa k, Satish S, Karunakar Hedge, Shabaraya AR. (2016). Investigation on learning and memory enhancing activity of essential oil in Albiziajulibrissin flowers in experimental mice-Asian journal of biomedical and pharmaceutical sciences, 6(55), 11-15.

Dinesh Dhingra and Varun Kumar. (2012).Memory enchancing activity of Palmitine in mice using Elevated plus maze and Morris water maze. Advances in Pharmacological sciences. Volume Article ID 357368.

Ellman GL, Courtney KD, Valentino AJ, Featherstone RM.(1961). A new and rapid colorimetric determination of acetyl cholinestrase activity. Biochemical pharmacology7, 88-95.

Ganguly. R, D. Guha . (2008).Alteration of brain monoamines and EEG Wave pattern in rat model of Alzheimer's disease and protection by Moringa oleifera-Indian Journal of Medical research 128, 744-751.

Ganiyu, AdedayoOA,Ayodele JA.(2012).Inhibition of acetylcholinesterase activities and some pro-oxidant induced lipid peroxidation in rat brain by two varieties of ginger.Experimental and toxicological pathology,64(4),315-319.

HalaFZ,May A Abd-El-F, Amia SA. (2014).Naringenin protects against scopolamine-induced dementia in rats.bulletin of faculty of Pharmacy,Cario University, 52,15-25

Kim SJ, Lee JH, Chung HS, Song JH, Ha J, Bae H.(2013). Neuroprotective Effects of AMP activated protein kinase on scopolamine induced memory impairment. Korean Journal of Physiology and Pharmacology, 17,331-338.

Kirtikar K.R and Basu B.D. (1975). Indian Medicinal Plants, vol.11 Delhi: Jayyed Press

Leone A, Spada A, Battezzati A, Aristil J, Bertoli S.(2015). Cultivation, Genetic Ethnopharmacology, Phytochemistry and Pharmacology of Moringa oleifera leaves: An Overview. International Journal of Molecular Sciences,16(6): 12791-12835.

Lowry OH, Rosebrough NJ, Farr AN, Rendall RJ. (1951). Protein measurement with Folin Phenol reagent. The Journal of Biological Chemistry, 193, 265-275.

Madhubabu G, Yenugu S. (2012). Effect of continuous inhalation of allethrin-based mosquito coil smoke in the male reproductive tract of rats. Inhalation toxicology,24(3):143-152

Madhubabu G, Yenugu S. (2014). Allethrin induced toxicity in the male reproductive tract of rats contributes to disruption in the transcription of genes involved in germ cell production. Environmental toxicology,29(11),1330- 1345.

Mani V, Milind P. (2009). Antiamnesic potential of MurrayaKoenigii leaves. Phytotherapy Research, 23, 308-316.

Micheau J, Marighetto A. (2011). Acetylcholine and memory: A long, complex and chaotic but still living relationship. Behavioral Brain Research , 221,424-429.

Miwa JM, Freedman R, Lester HA. (2011).Neural systems governed by nicotinic acetylcholine receptors: Emerging hypotheses. Neuron,70,20-33.

Musial A, Bajda M, Malawska B. (2007). Recent developments in cholinesterases inhibitors for Alzheimer's disease treatment. Current Medicinal Chemistry, 14, 2654-2679.

Nadkarni K M. (1976). Indian Material Medica, Vol. Popular Prakashan, Bombay,

OECD Guideline. (2001) on acute oral toxicity (AOT) Environmental health and safety monograph series on testing and adjustment number 425.

Parotta, John A. (1993). "*Moringa oleifera* Lam. Reseda, horseradish tree. Moringaceae. Horseradish tree family ".USDA Forest service, International Institute of Tropical Forestry.

Robinson L, Platt B, Riedel G. (2011). Involvement of the cholinergic system in conditioning and perceptual memory. Behavioral Brain Research,221:443-465

Souza AC, Bruning CA, Acker CI, Neto JS, Nogueira CW. (2013). 2-Phenylethynyl butyltellurium enhances learning and memory impaired by scopolamine in mice. BehaviouralPharmacology, 24, 249 -54

SudhirKumar.P,Debasis Mishra, Goutam Ghosh, Chandra S. Panda-(2010). Medicinal uses and pharmacological properties of Moringa oleifera-International journal of Phytomedicine, 2210-216.

Tian, J., Shi, J., Zhuang's. et al. (2010). Herbal therapy: a new pathway for the treatment of Alzheimer's disease. Alzeimers research and Therapy 2, 30 .

Konstantia G Yiannopoulou and sokratis apapgeorgiou(2020) current and future treatments in alzeimers disease: An upadate, journal of central nervous system disease, v12

Kristina Nikl et al (2019), alzeimers disease: Current treatments and potential agents. Neurologus pharm;44(1);20-23.

***