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ABSTRACT

This study intends to explore the neuroprotective and memory-enhancing properties of *Myristica malabarica* (MM) leaf extracts on diabetic-induced cognitive decline rats. The models of Y maze and Morris water maze were selected for nootropic activity and neuroprotective properties were deliberate by assessing the levels of Ach, malondialdehyde (MDA), superoxide dismutase (SOD), nitric oxide (NO), catalase (CAT) and glutathione hormone (GSH) in diabetic rat brains. Significantly improved memory and learning with 100 mg/kg ($P < 0.01$) and 200 mg/kg ($P < 0.001$) of EAMM (L) and MAMM (L) in Y maze and Morris water maze models. Significant effect was observed in all the extracts with two doses when compared with diabetic control on day 75. The levels of AChE ($P < 0.001$), MDA ($P < 0.01$), and NO ($P < 0.05$) were decreased significantly and significantly raised ($P < 0.01$) levels of SOD, CAT, and GSH with MAMM (100 and 200 mg/kg) compared with disease control. Further studies on MM leaf are needed as evidence of cognitive impairment in defense against diabetes has been shown to expose its mode of action.

Keywords: Acetylcholinesterase, malondialdehyde, *Myristica malabarica*, neuroprotective, nootropic

INTRODUCTION

According to the International Diabetes Federation-Diabetes Atlas indicated that currently, 387 million people are existing with diabetes. It is anticipated to escalate to 592.8 million by the year 2035. Diabetes mellitus (DM) is a polymorphic disease, outlined by increased levels of blood glucose (hyperglycemia) due to proportionate inadequacy of insulin or resistance of tissues to insulin.[1]

Alzheimer's disease (AD) is a neurodegenerative common form of dementia that disrupts intellectual functioning because of irrevocable impairment of neuronal processes. The epidemiological data disclose that 47 million people are estimated to be affected with dementia worldwide and the predominance of AD, that is, 60–80% is more in people over 65 years of age.[2]

The epidemiological studies reveal that cognitive impairment is the common problem of diabetes[3] where in 20–70% of patients with DM accounted for cognitive deterioration, and currently 60% are at risk.[4] The different phases of cognitive dysfunction have been accompanying with diabetes, exaggerated cognitive structures, prognosis with aging, and altered fundamental mechanisms.[5] Earlier studies in patients have stated that the extensive collection of diabetes-associated cognitive derangements might give rise to cognitive complaints and led to mild-to-severe forms of dementia.[6] Numerous interplays of mechanisms including vascular injury, inflammation, insulin resistance, and depression are also

hazarding for cognitive derangement in DM patients.[7] These records also have testimonials from various animal models where severe cognitive dysfunctions are observed in diabetic animals.[8]

The AD brain is also interpreted as a decline in cholinergic neurotransmission and a rise in oxidative stress.[9] The pre-eminent reasons of oxidative stress in Alzheimer's patients are due to escalation of the end products of lipid peroxidation, such as malondialdehyde (MDA) and a decrease in antioxidant enzymes: Glutathione hormone (GSH) and superoxide dismutase (SOD).[10] The reduction in cholinergic transmission seems to be the prime reason for dementia. The cardinal therapeutic strategies against AD are acetylcholinesterase inhibitors (AChEi), show its action by enhancing the cholinergic transmission, and thereby increase the availability of acetylcholine in the neuronal synapse.[11] AChEis were not so successful because of their adverse reactions on liver (hepatotoxicity) and their limited efficacy.[12]

Myristica malabarica Lam (*Myristicaceae*) is a perennial tree about 25 m tall. It is known as Malabar nutmeg or kaatuhjathi and found widely in the Western Ghats Forest Area of India. *Myristica malabarica* (MM) seed and seed aril are used as a spice in Indian foods to improve the taste and aromatic flavor. In Ayurveda, aril is used for many conditions related to vata such as, bronchitis, burning sensation, cough, and fever.[13] The fat extracted from seed of MM is used to treat analgesics, indolent ulcers, myalgia, rheumatism, sprains, and sores. The plant is also used for antioxidant, antidiabetic,[14] anti-ulcer,[15] anti-inflammatory,[13] analgesic,[13] sedative,[13] hypnotic,[13] and antimicrobial actions.[13]

This plant retains great medicinal properties (E.g., Antioxidant and anti-inflammatory) which are important for the treatment of AD. The plant was reported to contain the various phytoconstituents with biological activities such as 3-tetradecoyl-brenzcatechin, Malabaricone A, Malabaricone B, Malabaricone C, Malabaricone D, Biochanin A, prunetin, and silymarin.

The present study was conducted in strength to interpret the mode and mechanisms of action of this plant extract by utilizing streptozotocin (STZ)-induced diabetic rats as a model. Administration of low dose of STZ, accountable for the moderate β-cell destruction and this partial destruction effects β-cells to stow a lesser amount of insulin causing in glucose tolerance like the human form of T_2D. Datusalia and Sharm[16] postulated the development of cognitive dysfunction (15 w after induction of diabetes) in Sprague Dawley rats using high fat diet, 2 w and a relatively high dose of STZ (35 mg/kg), which may depict more of a Type 1-diabetes associated cognitive impairment in human. Hence, the intent of the present study was to explore the nootropic and neuroprotective effect of petroleum ether (PE), ethyl acetate (EA), and methanolic (MA) leaf extract of MM learning and memory enrichment in STZ-induced rat of cognitive impairment and brain oxidative stress including elevated plus, Y maze, and Morris water maze models were used to assess the levels of cognition. Acetylcholine levels, total nitrites and antioxidant enzymes (SOD, lipid peroxide (Thiobarbituric acid reactive substances [TBARS]), catalase [CAT], and GSH) levels in brain were also measured to demonstrate.

MATERIALS AND METHODS

Identification of Plant Material

MM leaves were gathered in the month of December 2018 from the Thiruvananthapuram, Kerala, it is authenticated by Dr. V. Chelladurai, Botanist, Tirunelveli.

Chemicals

Piracetam (Alkem Laboratories Ltd), Metformin (Cipla Pharmaceuticals), Diagnostic Kits (Bio Lab, India), MDA, SOD, CAT, GSH, and STZ were purchased from Sigma Aldrich, USA.

Selection and Maintenance of Animals

Rats of Wistar strains of either sex were chosen, and the weight variation should be 150 ± 50 gms that were purchased from Hyderabad. All are acclimatized for a week and sustained underneath typical research laboratory environments. The food preferred toward for animals regular pellet diet and water *ad libitum*.

Extract Preparation

The plant material was exposed to extraction by means of soxhlation for 72 h by increasing the polarity of solvents such as PE, EA, and MA. The Whatman filter paper was used for filtration and then concentrated beneath a vacuum. Finally, dry and the extracts remained reserved in pasteurized containers and frozen till usage.[17]

Phytochemical Study

Selected plant extracts were used to investigate the phytochemical constituents which are used by the standard method described by Khandelwal, 2008.[17]

Acute Toxicity Study

According to the OECD guidelines, 423 evaluate the lethal dose of extracts in the acute phase. In each step, three animals were selected in the acute toxicity study. Initial doses were selected which are 5, 50, 300, and 2000 mg/kg body weight *p.o.*[18]

Development of Disease (DM)

DM was induced with 55 mg/kg of STZ given to animals through the i.p route of administration. The disease was confirmed 48 h after STZ administration by measuring blood glucose level that was estimated by GOD-POD enzymatic method. Animals that contain blood glucose levels >250 mg/dl deliberated as diabetic and selected for the future studies.[19,20]

Nootropic Activity

The MM was used to test nootropic activity using rats which were recommended by Lucian *et al*.,[21] Morris *et al.,*[22] and Tuzcu and Baydas.[23] The designated animals were allocated

into ten groups ($n = 6$) and pretreatment on day 57 and post-treatment on day 71.

Group I:	**NC (2% Sodium CMC)**
Group II:	DC (55 mg/kg)
Group III:	DC+metformin (10 mg/kg, p.o)
Group IV:	DC+piracetam (5 mg/kg, p.o)
Group V:	DC+PEMM (100 mg/kg)
Group VI:	DC+PEMM (200 mg/kg)
Group VII:	DC+EAMM (100 mg/kg)
Group VIII:	DC+EAMM (200 mg/kg)
Group IX:	DC+MAMM (100 mg/kg)
Group X:	DC+MAMM (200 mg/kg)

Y Maze Test

Y-maze test used for instant reminiscence was measured through extemporary change behavior. Animal was positioned on termination of one arm and permitted to passage quickly over the maze. Time boundary remained stable to 8 min; therefore, each period finished 8 min later. An arm admission was calculated once the back legs of the rat remained entirely inside the arm. Spontaneous change behavior was clear as admission into entirely three arms on successive selections. The animals were skilled for 5 days and % spontaneous changes restrained on day 71 and 75.[22]

Morris Water Maze Test

On day, one rat was educated to swim for 60 s in the nonexistence of the stage. Throughout 4 consecutive days, rats remained assumed the probationary session through the stage. If rat locates the stage, allowed remaining continuously it intended for 10 s. The rat does not find, placed again for some time, and now detached on the platform. Once last trial probationary sessions, rats stayed separately exposed to investigation test session, the stage remained detached as of the pool and might swim for 120 sec to examine aimed at it. On day 71, animals were tested for latency time that was determined.[23]

Neurochemical Study

After the treatment, rats remained for decapitate through cervical disruption and the brain was insulated and weighed. The collected brain was cleaned by ice-cold saline and distinguished by 20 mg of the fleshy tissue per ml in cool phosphate buffer (pH 7.4). The homogenates remained centrifuged at 800 rpm for 5 min to distinct the nuclear debris. The gained supernatant remained then used for this study.[18]

AChE Estimation

It is designed to assess AChE level by method of Ellman's *et al*.[24] An aggregate of 0.4 ml supernatant was mixed with 2.6 ml phosphate buffer pH 8 and 100 µL of 5,5'-dithiobis-(2-nitrobenzoic acid) and absorbance was estimated at 412 nm by a spectrophotometer. The 20 µL of acetylthiocholine-iodide was added and the variations in absorbance were noted down for 10 min at interims of 2 min. Alteration in the absorbance per minute was consequently measured.[25]

TBARS Assay

TBARS levels are key for MDA formation, it is a finale invention of lipid peroxidation as per the method of Wills, and it is expressed in MDA/mg of protein.[26]

Nitric Oxide (NO) Levels

Greiss reagent (500 µl) mixed with supernatant fluid (100 µl) and absorbance was estimated at 546 nm. Nitrite levels were estimated by means of a typical curve on behalf of sodium nitrite and stated as ng/mg of protein.[27]

SOD Levels

To 100 µl of supernatant, 1 ml of sodium carbonate, 0.4 ml of nitroblutetrazolin, and 0.2 ml of ethylene diamine tetra acetic acid were added and absorbance was estimated at 560 nm as per the method of Green and conveyed in µg/mg of protein.[28]

CAT Levels

Claiborne (1985) method was used for the estimation of CAT levels in all treated groups. As per the method, 100 µl of supernatant mixed with 1.9 ml of phosphate buffer and absorbance was recorded at 240 nm and stated as µg/mg of protein.[29]

Glutathione (GSH) Levels

GSH levels were estimated in all experimental groups as per the method of Jollow. The GSH levels were estimated at 412 nm and stated as ng/mg protein.[29]

Analysis of Results

The results were analyzed by one-way ANOVA followed by Dunnett's multiple comparison tests using Graph pad prism 5.0 and $P < 0.05$ should be considered as significant.

Histopathological Studies

The animals remained anesthetized by urethane (1.2 g/kg, i.p) and the brain was isolated later opening the skull and the tissue of hippocampal was separated at 0–5°C. Using the normal saline, the tissue was cleaned and processed distinctly meant for histological explanations; the constituents were secure in 10% buffered neutral formalin for 48 h. Paraffin segments were taken at 5 µm width treated in alcohol-xylene series and were discolored with hematoxylin-eosin dye. The pieces were inspected microscopically for histopathological variations particularly in the hippocampus and in the cortex.

Drug-likeness

The phytoconstituents present in the plant were identified from the literature and their structures along with other details like canonical SMILES notation and in Chi key from the NCBI PubChem database. The compounds were subjected for drug-likeness screening in the Swiss ADME server of the Swiss Institute of Bioinformatics. The SMILES notation of each compound was incorporated into the server submission page and run the simulation in web. Typically, the output page displays the several parameters such as physicochemical,

lipophilic, hydrophilic, pharmacokinetic properties, and drug-likeness based on Lipinski rule of 5 and others.

RESULTS

Phytochemical Study

The results exhibited MA extract consist of the bioactive compounds such as glycosides, phenols, alkaloids, flavonoids, and tannins [Table 1].

Toxicity Study

In this study, 2000 mg/kg MM extract does not show any mortality due to 100 and 200 mg/kg body weight were chosen for the further studies.

Nootropic Study

Effects of MM extracts on spontaneous alterations (% SA) in Y-Maze

In diabetic controls, percent of spontaneous alteration was significantly ($P < 0.001$) decreased in the retention trial once equated with control. The Group-IV (5 mg/kg) and X (200 mg/kg) shows significantly ($P < 0.001$) rise in % spontaneous alterations. Group-VI, VIII (200 mg/kg), and IX (100 mg/kg) shows significantly increase the ($P < 0.01$) % spontaneous alterations and also Group-III (10 mg/kg), V and VII (100 mg/kg) treated diabetic animals showed significant ($P < 0.05$) increase in % spontaneous alterations. All the results were compared diabetic controls [Table 2].

Effects of MM Extracts on Transfer Latency (TL) in Morris Water Maze

During the training session, no changes in TL were observed. In retaining trial of diabetic controls, the TL was generate to be ($P < 0.001$) augmented when compared to controls. All the treated groups except Group-III significantly ($P < 0.001$) decrease the TL in the retention trial. All the results were compared diseased animals [Table 3].

AChE Estimation

In diseased controls, AchE efficacy was significantly increased ($P < 0.001$) when compared with normal controls, suggesting cholinergic dysfunction. The Group-IV (5mg/kg) and X (200 mg/kg) shows significantly ($P < 0.001$) decreases activity. Group -VI, VIII (200 mg/kg), and IX (100 mg/kg) cured groups displayed significantly ($P < 0.01$) decreases activity and also Group-V and VII (100 mg/kg) cured diabetic animals exhibited significantly ($P < 0.05$) decreases enzymatic activity whereas Group-III (10 mg/kg) showed insignificant effect [Table 3]. All the results were compared with diabetic controls.

Effects of MM Extracts on TBARS

In diabetic controls, TBARS remained significantly ($P < 0.001$) increased while compared to normal controls. Group-IV (5 mg/kg) and X (200 mg/kg) shows significantly ($^bP < 0.001$) reduce the MDA levels. In Group-VI, VIII (200 mg/kg), and IX (100 mg/kg) treated diabetic animals also showed significantly ($^bP < 0.01$) decreases MDA levels and also Group-V and VII (100 mg/kg) treated diabetic animals showed significant ($^bP < 0.05$) decreases MDA levels whereas Group-III (10 mg/kg) also showed insignificantly decrease the MDA levels [Table 4]. All the results were compared with diabetic controls.

Table 1: Preliminary phytochemical evaluation of various mm extracts

Specific Test (Leaf)	PEMM	EAMM	MAMM
Tests for Carbohydrates			
Molisch's Test	–	+	+
Fehling's Test	–	+	+
Benedict's Test	–	+	+
Barfoed's Test	–	–	+
Tests for Proteins			
Biuret Test	–	–	+
Million's Test	–	–	+
Ninhydrin Test	–	–	+
Tests for Steroids			
Salkowski's Reaction	+	+	–
Liebermann-Burchard reaction	+	+	–
Tests for Glycosides			
Borntrager's test (*Anthraquinone*)	+	+	+
Foam Test (*Saponin*)	–	–	+
Shinoda Test (*Flavonoid*)	–	–	+
Tests for Alkaloids			
Dragendorff's test	–	–	–
Mayer's test	–	–	+
Hager's test	–	–	–
Wagner's test	–	–	–
Tests for Tannins and Phenolics			
5% FeCl3 solution	–	–	+
Lead acetate solution	–	–	+
Potassium dichromate solution	–	–	+
Dilute iodine solution	–	–	–

Effects of MM Extracts Total NO Levels

In Group-II, the NO intensities remained significantly ($P < 0.001$) increased while compared to normal controls. All the treated groups (III-X) showed significant decreases ($^bP < 0.001$) in NO levels. All the results were compared diabetic controls [Table 4].

Effects of MM Extracts on SOD, CAT, and GSH Levels

The results showed a significant ($P < 0.001$) reduction in SOD, CAT, and GSH amount in Group-II when compared to control.

Table 2: Effects of mm extracts on spontaneous alterations (%) in rectangular maze arm and transfer latency in Morris water maze of diabetes-induced cognitive decline model

Groups	Dose (mg/kg)	% SA (Rectangular maze)		TL (Morris water maze)	
		71st day	75th day	71st day	75th day
Group-I	-	32.46±1.28	32.30±2.16	51.60±2.55	46.23±2.38
Group-II	55	46.14±1.50	39.43±2.50***	76.92±3.46	52.54±4.88***
Group-III	10	42.62±1.72	46.31±3.35*	62.39±3.52	61.62±3.35^{ns}
Group-IV	5	41.65±1.51	53.96±3.45***	57.65±3.93	42.52±2.20***
Group-V	100	42.74±1.48	46.62±2.88*	61.53±3.46	49.65±3.14***
Group-VI	200	43.17±1.89	48.34±3.84**	58.24±3.30	43.52±2.26***
Group-VII	100	45.08±1.20	47.55±2.67*	62.36±3.18	45.49±3.32***
Group-VIII	200	42.25±2.13	49.20±3.41**	59.25±3.42	42.61±2.58***
Group-IX	100	41.80±1.80	49.47±2.90**	60.42±3.66	47.69±3.90***
Group-X	200	44.48±2.32	51.59±3.62***	57.38±3.25	41.52±2.62***

Results represented as mean±SEM (n=6), ***P<0.001, **P<0.01, *P<0.05

Table 3: Effects of mm extracts on ache activity of diabetes-induced cognitive decline models

Groups	Dose (mg/kg)	AchE levels (μM/min/mg of protein)
Group-I	-	4.47±0.37
Group-II	55	6.23±0.58 ***
Group-III	10	6.56±0.53
Group-IV	5	4.00±0.34***
Group-V	100	5.26±0.36*
Group-VI	200	5.03±0.58**
Group-VII	100	5.12±0.42*
Group-VIII	200	4.84±0.47**
Group-IX	100	4.81±0.42^{b}**
Group-X	200	4.18±0.60***

Results represented as mean±SEM (n=6), ***P<0.001, **P<0.01, *P<0.05

All the treated groups (III-X) showed significant improvement in SOD ($P < 0.001$), CAT ($P < 0.001$), and GSH ($P < 0.001$) levels. All the results were compared with diabetic controls [Table 4].

Effects of MM Extracts Total NO Levels

In Group-II, the NO levels were significantly ($^{a}P < 0.001$) increased when compared with normal controls. All the treated groups (III-X) showed significant decreases ($^{b}P < 0.001$) in NO levels. All the results were compared with diabetic controls [Table 4].

Histopathological Studies

In normal control animal's brain sections display normal architecture of neuronal cells in hippocampus, it indicates normal structure (a) [Figure 1]. In disease control, neuronal cells were damaged which are neurotoxic to the neuronal cell (b). In the treatment with low doses and metformin displays the cells with neurotoxic with worsened cells and edema ongoing (c, e, and g). High dose and piracetam pretreated animals show less damaged neuronal cells and retaining to normal architecture of the control brain (d, f, h, I, and j).

Drug-likeness

The list of phytoconstituents selected and their corresponding results are shown in the Table 5 and the structures were given in Figure 2. From the literature, few compounds were identified and the trivial phytoconstituents were exempted from the evaluation. From the evaluated compounds, all the compounds have passed the Lipinski rule of 5 and were shown to possess a minimum of two hydrogen bond donor groups, three hydrogen bond acceptors, which reveal that the plant consists of phytoconstituents having drug likeness properties.

DISCUSSION

In patients with diabetes, the incidence of dementia is increasing twice with the process of aging.[30] This decrease in cognitive decline is compensated significantly with the administration of the extract. There was no registered evidence that MM can show significant in cognitive function till date. The experimental animals used were intra cerebroventricular STZ-induced dementia of AD type produced in animals.[31] Here, numerous mechanisms, which elucidate in what way diabetes, might raise the hazard of dementia with micro and macrovascular problems.

MM described toward obligate antidiabetic, antioxidant, and anti-inflammatory properties responsible for observed nootropic activity. The large number of plants was chosen in the management of memory decline. The previous investigations stated that the treatment with MM extracts significantly reduced the sugar in the treatment animals. The MM leaf extract was studied for antioxidant, sedative, hypnotic analgesics, and for rheumatism. Therefore, it was supposed value to explore the efficacy of MM on memory impaired investigational animals beside through its part in oxidative damage and AChE effect.

There are various reports of the neuroprotective properties; its active alkaloid component helps in the

Table 4: Effect of mm extracts on total nitrites, MDA, CAT, SOD, and GSH levels of diabetes-induced cognitive decline models

Groups	Dose (mg/kg)	Total nitrites (ng/mg of protein)	MDA Levels (M/mg of tissue)	CAT (µg/mg of protein)	SOD (µg/mg of protein)	GSH (ng/mg of protein)
Group-I	-	116.31±0.43	23.18±0.46	5.28±0.42	107.26±0.45	14.53±0.78
Group-II	55	236.42±1.06***	44.35±2.25***	2.51±0.45***	46.92±2.62***	3.24±0.04***
Group-III	10	161.41±0.49***	40.28±2.32*	3.36±0.30***	96.66±1.09***	11.64±0.63***
Group-IV	5	216.12±0.87***	36.42±0.24***	3.88±0.88***	97.45±0.59***	10.36±0.56***
Group-V	100	201.42±0.94***	43.57±1.94*	3.24±0.43**	81.42±1.34**	8.52±0.06**
Group-VI	200	154.47±1.15***	39.02±2.25**	3.44±0.58***	86.62±1.28***	9.58±0.81***
Group-VII	100	190.54±0.82***	43.99±1. 25*	3.35±0.54***	84.53±1.46***	9.67±0.08***
Group-VIII	200	150.19±1.02***	39.14±1.34**	3.55±0.69****	92.73±1.39***	10.12±0.73***
Group-IX	100	180.74±0.44***	40.62±1.48**	3.46±0.65***	89.56±1.41***	9.92±0.09***
Group-X	200	164.45±1.23***	37.31±1.23***	3.77±0.80***	94.74±1.53***	10.64±0.61***

Results represented as mean±SEM (n=6), ***P<0.001, **P<0.01, *P<0.05

Table 5: Drug-likeness properties of the selected phytoconstituents

S. No	Name of structure	MW	Hydrogen bond acceptors	Hydrogen bond donor	Log P	Ro5
1	3-Tetradecoyl-brenzcatechin	320.47	3	2	4.86	0
2	Malabaricone A	326.43	3	2	4.81	0
3	Malabaricone B	342.43	4	3	4.36	0
4	Malabaricone C	358.43	5	4	3.93	0
5	Malabaricone D	370.44	6	5	3.68	0
6	Biochanin A	284.26	5	2	2.44	0
7	Prunetin	284.26	5	2	2.43	0
8	Silymarin	482.44	10	5	1.59	0

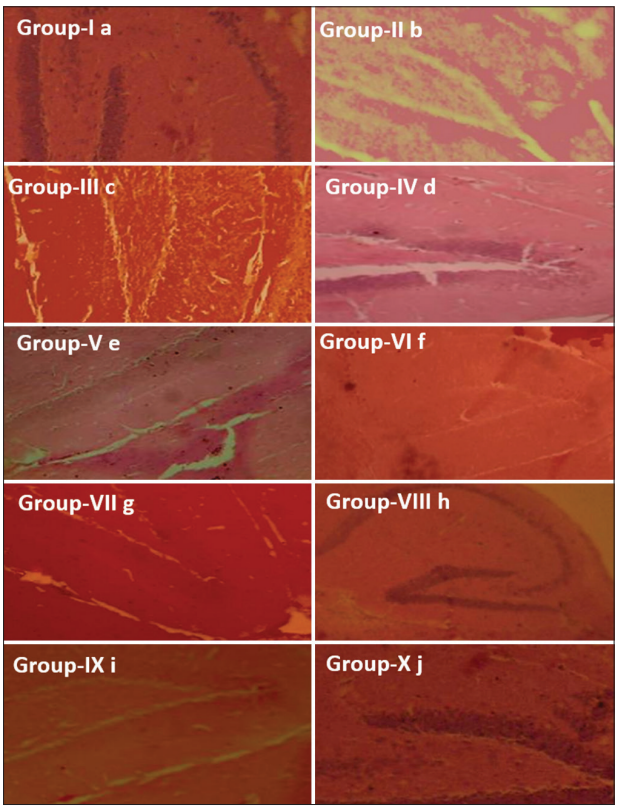

Figure 1: Histopathological studies of *Myristica malabarica* leaf extracts on hippocampal tissue

management of epilepsy along with associated mood disorders and memory related problems.[32] Outcomes of the present investigation exhibited significant enhancement in spatial reference memory and TL, suggesting of memory enhancing effect of MM in all treated animals. Oxidative damage in brain creates oxygen radical such as superoxide anion, hydroxyl radical, and hydrogen peroxide, action on polyunsaturated fatty acids in brain, in that way proliferating the lipid peroxidation. The chief antioxidant and oxidative free radical hunting enzymes such as GSH, SOD, and CAT show a significant part to decrease oxidative stress in the brain.[33] The MM strength obligates defensive result contrary to diabetes produced memory impairment due to diminished oxidative stress. The antioxidant properties of the MM extracts improve the memory in the disease control animals.

The acetylcholine is metabolized by AChE enzyme and one of the greatest effective therapeutic approaches for the AD is AChE inhibitors.[34] In the present study, it observed a significant increase in AChE action in diseased rats. The management through MM diminished rise in AChE action in diabetic animal's brain. Therefore, the management with MM improved memory impairment, cholinergic malfunction, decreased oxidative damage, and NO in the diabetic condition which might catch medical use in giving neuronal shortfall in the patients of diabetes. From the above result, it was concluded that diabetes-induced cognitive decline was improved by the treatment with MM leaves in rats

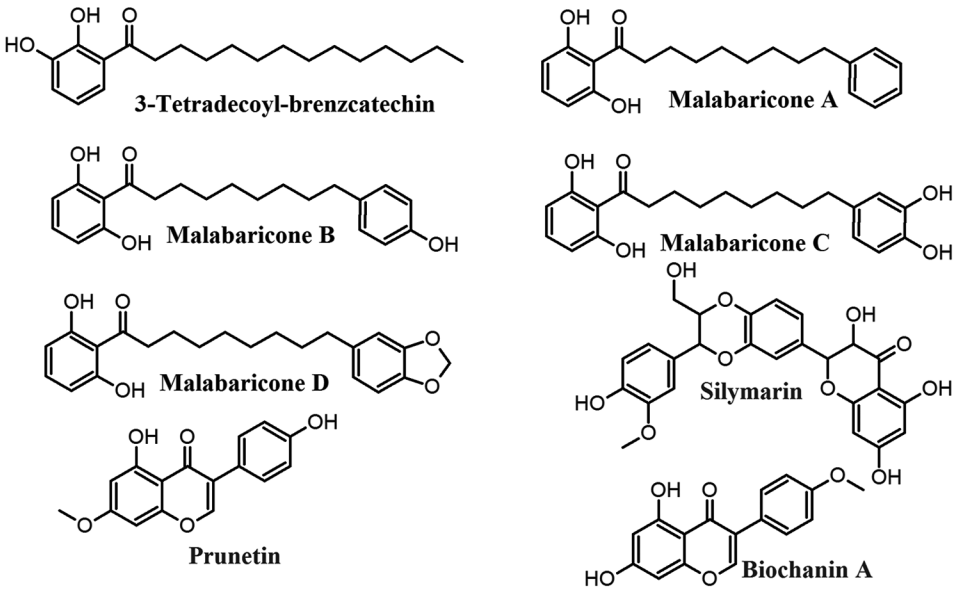

Figure 2: Chemical structures of reported phytoconstituents

CONCLUSION

Our results strongly show that the leaves of MM can significantly enhance the cognition by reducing TL time. In case of Morris water maze and Y maze, the neuroprotective effect is observed by inhibiting AChE enzyme and by inducing the free radical scavenging property. Although the pre-eminent evidence should be laid down in the forthcoming years to justify, the plant possesses the activity or not.

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