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Research Article

ROLE OF MORINGA OLEIFERA ON BRAIN ELECTRICAL ACTIVITY IN COLCHICINE INDUCED EXPERIMENTAL RAT MODEL OF ALZHEIMER'S DISEASE: POSSIBLE INVOLVEMENT OF ANTIOXIDANTS

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ABSTRACT

Objectives: The present study was designed to undertaken the role of *Moringa oleifera* (MO) on brain electrical activity in colchicine induced experimental rat model of Alzheimer's disease (AD) with possible involvement of antioxidants.

Methods: The antioxidant enzyme activities such as, superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH) and lipid peroxidation (LPO) level were studied in different parts of the brain such as Cerebral cortex (CC), Cerebellum (CB), Caudate nucleus (CN), Pons and Medulla (PM) and Midbrain (MB) in MO treated colchicine induced experimental Alzheimer's rat model. Electroencephalographic recordings were also examined throughout this study.

Key findings: MO significantly increased the superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) level in CC, CB, CN, MB and PM and significantly decreased the lipid peroxidation (LPO) level. After intracerebroventricular (ICV) infusion of colchicine, it significantly decreased the occurrence of alpha wave activity and significantly increased the occurrence of spike wave discharges in colchicine induced experimental rat model of AD as compared to that of control and MO treated colchicine treated experimental rat model of AD.

Conclusions: MO protects rat neurons against oxidative stress as is evidenced from our results of LPO, CAT, SOD, GSH and EEG activities possibly by vitamin E, C and beta carotene which are present in MO leaf extract.

Keywords: *Moringa oleifera*, Colchicine, Alzheimer's disease, Superoxide dismutase, Catalase, lipid peroxidation.

INTRODUCTION

Neurodegenerative diseases constitute a heterogeneous group of brain disorders leading to dementia such as in Alzheimer's disease (AD). They share in common the neurofibrillary degeneration affecting neurons of the central nervous system, process that include decrease in cholinergic transmission, higher sensitivity to oxidative stress, alterations in the cytoskeleton and neuronal death [1-2]. AD is one of the most common type of dementia disorders affecting the elderly, characterized by the formation of two main protein aggregates; senile plaques and neurofibrillary tangles**.**

Alzheimer's disease (AD) is a progressive neurodegenerative disorder, which is associated with excessive loss of memory [3-5]. It has been shown that AD afflicts about 8-10% of the population over 65 years of age and its prevalence doubles every 5 years thereafter [6]. In animals, it has been observed that central administration of microtubule disrupting agents can result in cell death associated with cognitive impairment, which resemble the microtubule dysfunction in AD [7-10]. Recently colchicine has been shown to be neurotoxic and to destroy certain neural cells selectively [11-12]. Colchicine, as a microtubule-disrupting agent [13] produces marked destruction of hippocampal granule cells, mossy fibers and septohippocampal pathways (SHC; a cholinergic link between medial septum and vertical limb of the diagonal band).

Moringa oleifera (Moringaceae) or MO, commonly known as Drumstick tree in English, is cultivated throughout India, mainly in West Bengal. Leaves have been also reported to possess hypotensive, antispasmodic, diuretic abortifacient and anti-microbial properties. Seed oil and gum plays a vital role in the treatment of rheumatism and dental caries. Flower possesses antibacterial, anti-ulcer, anti-tubercular, antiviral, anti-fertility, depressant, anti-inflammatory and anti-cancer property [14]. A number of Indian medicinal plants have been used for thousands of years in the traditional system of medicine (Ayurveda) for the management of neurodegenerative diseases such as Alzheimer's disease (AD). Some of these plants (rasayana) have already been reported to possess strong antioxidant activity [15]. MO leaves contain vitamins and antioxidants. It contains good amount of proteins, minerals, essential amino acids, vitamin A, vitamin C, vitamin B complex and a high content of vitamin E [16]. These compounds not only have antioxidant property but also have memory facilitating effect [17].

There is substantial evidence that oxidative stress is a causative or at least ancillary factor in the pathogenesis of major neurodegenerative diseases including Alzheimer's disease [18-19]. It has been suggested that Alzheimer's disease may be linked to diet, with reduced risk associated with diets high in antioxidants [20]. A number of in vitro studies have shown that antioxidants, both endogenous and dietary, can protect nervous tissue from damage by oxidative stress. Vitamin E was found to prevent cell death (apoptosis) in rat neurons subjected to hypoxia followed by oxygen reperfusion [21]. Both vitamin E and β carotene were found to protect rat neurons against oxidative stress from exposure to ethanol [22]. Recently it was shown that the protein responsible for the uptake of vitamin E is in fact present in brain cells of patients suffering from vitamin E deficiency or disease associated with oxidative stress [23].

Electrodes may be applied over the scalp of an individual and the electrical activity of the underlying bone may be recorded thereby. Such a record is called Electroencephalogram, and the machine, Electroencephalograph. Alpha, Beta, Delta and Theta waves may appear in EEG. Beta waves are of 10-30 Hz frequency and low amplitude and are seen particularly in the frontal region of normal person. Delta waves (high amplitude but frequency about 1 or 2 Hz) and Theta waves (low amplitude 4-7 Hz frequency) may be seen in some stages of normal sleep. Theta waves are seen prominently in Alzheimer's disease. A maximum number of spike wave discharges are seen in an AD patient.

Different treatment strategies have been explored to prevent or slow the progression of AD. Pharmacological treatment of AD is based on the use of acetylcholinesterase (AchE) inhibitors and the NMDA antagonist, memantine which have beneficial effects of cognitive, functional and behavioural symptoms of the disease. Treatment with various AchE inhibitors including *tacrine* (1,2,3,4-tetrahydro-9-aminoacridine; COGNEX), *donepezil* (ARICEPT) [24],

rivastigmine (EXCELON) and *galantamine* (REMINYL) have been shown in clinical studies to improve cognitive, functional and behavioural symptoms of AD [25-27]. The side effects of *donepezil, rivastigmine, tacrine* and *galantamine* are nausea, vomiting, diarrhea, insomnia etc. For adverse side effects there has been renewed interest in alternative therapies. MO containing high level of vit A, C, E has no side effects.

Based on this report, the present study was designed to undertaken the role of MO on brain electrical activity in colchicine induced experimental rat model of AD with possible involvement of antioxidants.

MATERIALS AND METHODS

Animal used and Maintainance

Twenty-four male Holtzman strain adult albino rats weighing between 200-250gm were selected throughout the experiment. The rats were kept in standard laboratory conditions (room temperature 27±1^{0}C, humidity 60% and 12h light/dark cycle) in accordance with **'Institutional Ethical Committee'** rules and regulations. They were allowed free access to standard laboratory diet, which supplemented the necessary proteins, carbohydrates and minerals. Drinking water was supplied ad libitum. Body weight of the rats were recorded every day and maintained in the laboratory throughout the experimental period. Also the animal's health was evaluated by checking the breathing for wheezing or rattling, the presence of mucus around the eyes, the presence of blood in the urine, the condition of fur and rapid and large changes in body weight or food intake. Before the experiment, the rats were allowed to get accustomed to laboratory conditions (for seven days) during which their motor behavior, food and drinking habits, micturation and fecal output were noted for future comparison. The behavioral procedure was carried out between 12:00 and 14:00 h.

Preparation of water extract from leaves of MO

Fresh, Young, healthy leaves of MO were shaded, dried and grinded with the help of on electrical grinder to get a free flowing powder. This powder was subjected to extraction with water at room temperature for 24 hours. The extract obtained was filtered through Whatman filter paper and vacuum dried at 40^0-50^{0}C to get a dry powder, which was dissolved in double distilled water for final use [28].

Treatment

The control animal was treated with normal saline. The MO leaf extract was given orally through orogastric cannula at the standard dose of 250mg/kg b.w. for fourteen consecutive days (between 10:00 and 11:00 hrs). The dose was standardized in the laboratory.

After fourteen days, the animals were sacrificed by cervical dislocation and the different parts of the brain like Cerebral cortex (CC), Cerebellum (CB), Caudate nucleus (CN), Pons and Medulla (PM) and Midbrain (MB) were isolated for antioxidant estimation.

Grouping of Animal

The animals were divided into four groups.

1.Control rats

2.Colchicine induced Alzheimer's rat model

3.Control rats treated with MO leaf extract

4.Colchicine induced Alzheimer's rat model treated with MO leaf extract.

Preparation of experimental Alzheimer's model by colchicine

Prior to surgery, all the animals were subjected to overnight fasting though drinking water was not withdrawn. The rats were anaesthetized with anesthetic ether (Kobra Drugs Ltd, India). The anaesthetized animals were placed on stereotaxic-instrument (INCO, India Ltd.) equipped with a custom-made ear bar, which prevents the damage of the tympanic membrane. Head was fixed in such a position that lambda and bregma sutures were in the same horizontal plane by introducing the incisor bar properly attached to the mouth. For aseptic surgery, absolute alcohol or rectified spirit was applied. The scalp was incision in the midline and the pericranial muscles and fascia were retracted laterally. After retracting the nuchal musculature the overlying bone was drilled at the specific loci in the lateral ventricle following the coordinanates of the stereotaxic atlas [29](Coordinates for the lateral ventricles were: 0.6 mm posterior to bregma, 1.8 mm lateral to the midline and 2.7 mm below the cortical surface). After two-trephine hole was burred in the skull, the subjects were infused through a 10 µl Hamilton syringe with 15 µgm of colchicine in 5 µl of artificial CSF (ACSF; in mM: 147 Nacl, 2.9 Kcl, 1.6 Mgcl2, 2.2 Dextrose and 1.7 Cacl2) in the lateral cerebral ventricles bilaterally. A total volume of 10 µl was delivered to the injection site and the injection cannula was left in place for 2-3 min following infusion. After injecting colchicine the trephine hole was covered with gel foam and sterile bone wax and skin and muscle were sutured back separately. Neosporin powder was sprayed over the wound site as antiseptic measure. Also, Penicillin or PCN (10,000 IU) were injected on the day of the operation and for the next two consecutive days. 2-3 ml of freshly prepare dextrose solution was intraperitoneally (i.p) injected to maintain blood volume. Dilute food was supplied on the day of operation.

Postoperative care

After surgery, all aseptic measures and care were taken for feeding until recovery from surgical stress. Penicillin or PCN (10,000 IU) was given post operatively to all animals for 3 consecutive days by intramuscular (i.m) route. After 3 days of surgery, experiment was started and continued routinely until sacrificed. Similar procedure was repeated thrice, each at an interval of two days.

Electroencephalographic (EEG) study

For Electroencephalography or EEG recordings, rats were anesthetized with Pentobarbitone sodium (40 mg/kg i.p). Each rat was placed in a stereotaxic apparatus. Bipolar electrodes were implanted on the surface of the sensorimotor cortex through trephine hole. A reference electrode was also implanted over the frontal bone. EEG recordings from conscious rats were recorded from day 3-5 after ICV injection of colchicine using an 8 channel Electroencephalogram. Recording session lasted for 5 hours without interruption. Animal's behavior was critically checked for movement artifacts in the recordings [30-31].

Biochemical Estimation

Tissue preparation

Rats were sacrificed by cervical dislocation on day fourteen immediately after behavior study. The Cerebral cortex (CC), Cerebellum (CB), Caudate nucleus (CN), Pons and Medulla (PM) and Midbrain (MB) were dissected out. The tissues were weighed and homogenized in ice-cold phosphate buffer and prepared for biochemical estimation.

Estimation of SOD, CAT, GSH and LPO level

Superoxide dismutase (SOD) was estimated by the method of Mishra and Fridovich (1972) [32]; Roy et al., (2007) [5], Catalase (CAT) activity was estimated by the method of Cohen *et al.* (1970) [33]; Roy et al., (2007) [5]Reduced glutathione (GSH) level was measured according to the method of Das and Roy (2012) [34] and Lipid peroxidation (LPO) level was estimated by the method of Bhattacharya *et al.* (2001) [35]; Roy et al., (2007) [5].

Statistical analysis

The data were expressed as MEAN ± S.E.M. and were analyzed statistically using one way analysis of variance (one way ANOVA) followed by multiple comparison ***'t'*** test. In addition to this, two-tailed Student't' test was performed to determine the level of significance between the means. Difference below the probability level 0.05 was considered statistically significant.

RESULTS

Fourteen days after intracerebroventricular (ICV) infusion of colchicine, the electroencephalographic study (EEG) was done and the SOD, CAT, GSH level and LPO level were estimated.

The normal EEG wave pattern showed predominance of low voltage fast waves or β waves in normal saline treated control rats. Pretreatment with MO leaf extract at a dose of 250 mg/kg body weight, it significantly increased the occurrence of α wave activity which persisted for more than five hours. After intracerebroventricular (ICV) infusion of colchicine, there was an increase in the occurrence of spike wave discharges. In MO pretreated colchicine treated experimental rat model of AD, there was a markedly decline in the occurrence of spike wave discharges along with an increase in the occurrence of α wave activity in comparison with colchicine treated experimental rat model of AD. The result is shown in Plate 1.

There was a sharp decrease ($p<0.001$) in SOD activity in CC, CB, CN, MB and PM in the colchicine treated group as compared to the control group. The SOD activity was significantly ($p<0.001$) increased in MO treated control group rather than control group in CC, CB, CN, MB and PM. MO significantly ($p<0.001$) increased SOD activity in MO pretreated colchicine treated group rather than colchicine treated group in CC, CB, CN, MB and PM. The result is shown in Table-1.

There was a sharp rise ($p<0.001$) in lipid peroxidation level in CC, CB, CN, MB and PM in the colchicine treated group as compared to the control group. The LPO level was significantly ($p<0.001$) decreased in MO treated control group rather than control group in CC, CB, CN, MB and PM. MO significantly ($p<0.001$) decreased LPO levels in MO pretreated colchicine treated group rather than colchicine treated group in above mentioned parts of the brain. The result is shown in Table-2.

There was a sharp decline ($p<0.001$) in CAT activity in CC, CB, CN, MB and PM in the colchicine treated group as compared to the control group. The CAT activity was significantly ($p<0.001$) increased in MO treated control group rather than control group in CC, CB, CN, MB and PM. MO significantly ($p<0.001$) increased CAT activity in MO pretreated colchicine treated group rather than colchicine treated group in above mentioned parts of the brain. The result is shown in Table-3.

There was a sharp decrease ($p<0.001$) in GSH level in CC, CB, CN, MB and PM in the colchicine treated group as compared to the control group. The GSH level was significantly ($p<0.001$) increased in MO treated control group rather than control group in CC, CB, CN, MB and PM. MO significantly ($p<0.001$) increased GSH level in MO pretreated colchicine treated group rather than colchicine treated group in above mentioned parts of the brain. The result is shown in Table-4.

Table 1: Changes in SOD activity in different brain areas (CC, CB, CN, MB and PM) of MO pretreated colchicine (15µg/ 5 µl of ACSF) induced Alzheimer rat model.

	SOD (% inhibition unit)				
	CC	**CB**	**CN**	**MB**	**PM**
Control	12.43±0.13	12.52±0.07	11.42±0.14	12.64±0.10	12.47±0.09
Colchicine	24.94±0.16***	27.83±0.16***	26.61±0.12***	28.88±0.15***	24.40±0.13***
MO	8.99±0.05***	6.79±0.07***	6.27±0.17***	8.73±0.11***	5.82±0.13***
MO+Colchicine	15.12±0.21#	18.55±0.14#	19.22±0.09#	17.28±0.24#	19.13±0.03#

Values are mean ± SEM, n = 6;***p < 0.001 when compared with control group. #p < 0.001 when compared with colchicine treated group. Data were analyzed statistically using one-way ANOVA Test followed by multiple comparison t – test.

Table 2: Changes in LPO level in different brain areas (CC, CB, CN, MB and PM) of MO pretreated colchicine (15µg/ 5 µl of ACSF) induced Alzheimer rat model.

	LPO (nmol of TBARS/gm mol of tissue)				
	CC	**CB**	**CN**	**MB**	**PM**
Control	5.25±0.04	4.64±0.03	4.17±0.05	4.31±0.03	5.57±0.09
Colchicine	12.57±0.12***	11.36±0.12***	10.48±0.11***	8.99±0.04***	12.62±0.12***
MO	1.97±0.02***	1.49±0.15***	2.16±0.04***	2.15±0.04***	1.95±0.03***
MO+Colchicine	8.60±0.12#	7.55±0.10#	5.68±0.07#	5.33±0.06#	7.54±0.12#

Values are mean ± SEM, n = 6; ***p < 0.001 when compared with control group. #p < 0.001 when compared with colchicine treated group. Data were analyzed statistically using one-way ANOVA Test followed by multiple comparison t – test.

Table 3: Changes in CAT activity in different brain areas (CC, CB, CN, MB and PM) of MO pretreated colchicine (15µg/ 5 µl of ACSF) induced Alzheimer rat model.

	CAT (% inhibition unit)				
	CC	**CB**	**CN**	**MB**	**PM**
Control	14.63±0.11	13.95±0.13	13.14±0.03	13.38±0.11	13.13±0.11
Colchicine	24.30±0.16***	22.42±0.16***	20.53±0.10***	25.85±0.15***	21.15±0.04***
MO	8.13±0.14***	7.98±0.07***	5.74±0.07***	9.89±0.02***	8.37±0.17***
MO+Colchicine	18.66±0.05#	16.36±0.11#	16.55±0.03#	20.45±0.07#	15.44±0.04#

Values are mean ± SEM, n = 6; ***p < 0.001 when compared with control group. #p < 0.001 when compared with colchicine treated group. Data were analyzed statistically using one-way ANOVA Test followed by multiple comparison t – test.

Table 4: Changes in GSH level in different brain areas (CC, CB, CN, MB and PM) of MO pretreated colchicine (15µg/ 5 µl of ACSF) induced Alzheimer rat model.

	Reduced glutathione (µg/g of tissue)				
	CC	**CB**	**CN**	**MB**	**PM**
Control	50.34±0.53	48.68±0.35	46.16±0.28	44.59±0.28	40.23±0.39
Colchicine	2.57±0.41***	4.45±0.01***	3.21±0.05***	2.44±0.12***	2.24±0.37***
MO	58.58±0.27***	54.41±0.33***	55.56±0.40***	56.58±0.42***	51.44±0.48***
MO+Colchicine	18.95±0.06#	23.56±0.12#	31.33±0.29#	25.55±0.43#	18.46±0.15#

Values are mean ± SEM, n = 6;***p < 0.001 when compared with control group. #p < 0.001 when compared with colchicine treated group. Data were analyzed statistically using one-way ANOVA Test followed by multiple comparison t – test.

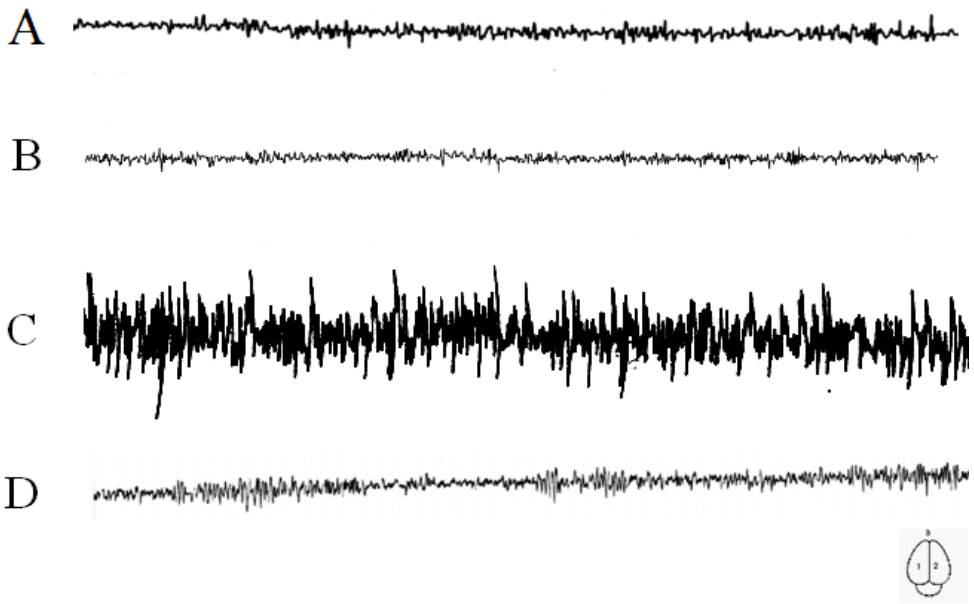

Fig. 1: Electroencephalographic (EEG) recordings.

A: Control model: predominance of low voltage first waves or β waves.

B: MO treated model: occurrences of α wave activity was increased.

C: Colchicine treated model: occurrences of spike wave discharges was increased and occurrences of α wave activity was decreased.

D: MO pretreated colchicine treated model: occurrences of spike wave discharges was decreased and occurrences of α wave activity was increased.

DISCUSSION

In our present study, we have tried to find out the role of MO on the frequency of α waves and spike wave pattern in colchicine induced experimental rat model of AD with the possible involvement of antioxidants. The normal EEG wave pattern showed predominance of low voltage fast waves or β waves in normal saline treated control rats. Pretreatment with MO leaf extract at a dose of 250 mg/kg body weight, it significantly increased the occurrence of α wave activity which persisted for more than five hours. After intracerebroventricular (ICV) infusion of colchicine, there was an increase in the occurrence of spike wave discharges. In MO pretreated colchicine treated experimental rat model of AD, there was a markedly decline in the occurrence of spike wave discharges along with an increase in the occurrence of α wave activity in comparison with colchicine treated experimental rat model of AD. These findings can be explained by alterations of the lipid peroxidation (LPO) level and the antioxidant enzyme activities such as SOD, CAT and also the GSH level in different brain regions.

Intracerebroventricular (ICV) infusion of colchicine causes it to bind with tubulin which is the structural protein of microtubule and thereby generates more and more reactive oxygen species (ROS) leading to neurodegeneration and ultimately produces a condition akin to AD or produces experimental AD model which is histopathologically characterized by the extracellular deposition of senile plaques. Free radicals play a crucial role in the pathogenesis of AD. The LPO is determined by the balance between the production of oxidants and the removal and scavenging of those oxidants by antioxidants [36-38]. Lipid peroxidation can be used as an index for measuring the damage that occurs in membranes of tissue as a result of free radical generation [39-40]. In our present study, ICV infusion of colchicine, it significantly increased the LPO level. The results of significant elevation of LPO level in colchicine treated experimental Alzheimer's group indicates increased free radical generation in the colchicine treated rat group which was supported by Veerandrakumar and Gupta, 2002 [41]. The LPO level was significantly decreased in MO treated group rather than control group. So, from the results of LPO level, it may be concluded that MO, the storehouse of vitamin E, C and β-carotene, provides antioxidant protection on colchicine induced oxidative stress through the changes of LPO level.

Endogenous antioxidant status in colchicine induced experimental Alzheimer's rat model was evaluated here by noting the activities of CAT, SOD and GSH as these are the important biomarkers for scavenging free radicals [42]. Generally SOD catalyzed to scavenge excess superoxide anions and convert them to H_2O_2 [40]. Biphasis fluxes of SOD activities are common and an increase or decrease may relate to the presence of excess superoxides [43]. The level of SOD was found to be decreased in the colchicine treated group rather than control, MO treated and MO pretreated colchicine treated experimental groups. Inhibition of SOD activity in colchicine treated group may be a consequence of decreased de novo synthesis of SOD protein or irreversible inactivation of enzyme protein from increased free radical generation resulting from ICV infusion of colchicine. Santiard et al., 1995 [44], supported this line of reasoning. The SOD activity significantly increased in MO treated control group rather than control group. This increase in the levels of SOD in control, MO treated control and MO pretreated colchicine treated experimental AD groups is possibly due to the increased de novo synthesis of SOD protein or irreversible activation of enzyme protein from decreased free radical generation.

The primary role of CAT is to scavenge H_2O_2 that has been generated by free radicals or by SOD in removal of superoxide anions and to convert it to water [45]. The level of CAT was found to be significantly decreased in the colchicine treated group rather than control, MO treated control and MO pretreated colchicine treated experimental groups. CAT activity was significantly increased in MO treated control group rather than control group. The increase in the CAT activity in MO pretreated colchicine treated experimental AD group is possibly due to excess H_2O_2 production resulting from SOD inhibition.

Glutathione is an endogenous antioxidant, which is present majorly in the reduced form within the cells. It prevents the hydroxyl radical generation by interacting with free radicals. During this defensive

process, reduced glutathione is converted to oxidized form under the influence of the enzyme glutathione peroxidase (GPX). The GSH level was significantly decreased in colchicine treated experimental group rather than both of control and MO pretreated colchicine treated experimental group. The decreased level of reduced glutathione in colchicine treated experimental group seen in our study indicates that there was an increased generation of free radicals and the reduced glutathione was depleted during the process of combating oxidative stress [46-47]. The GSH level was significantly increased in MO treated control group rather than control group. The increase in the level of GSH in MO pretreated colchicine treated experimental AD group rather than colchicine treated experimental AD group is possibly due to the activity of vitamin C, E and β carotene that is present in MO leaf.

From the results of EEG activities in our study, this has probably been possible either from the low level of ROS production or through a rapid dissolution of ROS that has further been strengthened from the elevated activities of important antioxidant defense enzymes CAT and SOD, studied in this experiment. Literature study has shown that the MO contains high level of vitamin E, C and β-carotene that protects rat neurons against oxidative stress possibly through the presence of both vitamin E and β carotene. Because vitamin E (α tocopherol and other tocopherol) is the most potent antioxidant that can break the propagation of free radical chain reactions in the lipid part of biological membranes.

The conclusion reached is that there is an increased sensitivity to oxygen free radicals, which could be due to either a decrease in free radical defenses (as in a decrease in SOD activity) or an increase in free radical formation in colchicine treated experimental rat model of AD compared to that of MO pretreated colchicine treated experimental rat model of AD. Thus this study clearly shows a deficit in the antioxidant enzyme in colchicine induced experimental rat model of AD and suggests that the mechanism of neuronal cell death may be from a failure to protect against free radical damage which in turn possibly increased occurrence of the spike wave discharges and simultaneously decreased the occurrence of α wave activity. An increase in free radical activity could lead to increased neuronal cell death, the hallmark of AD [48,3,49]. Thus the overall differences among the control, BH treated control, colchicine treated experimental rat model of AD group and MO pretreated colchicine treated experimental rat model of AD group assays offer a possible cause for AD. In our present study it appears that increased oxidative stress is unable to induce brain antioxidant activity resulting in markedly increase in lipid peroxidation. Pretreatment with MO leaf extract possibly decreased oxidative stress by increasing the antioxidant enzyme activity resulting in markedly decrease in LPO level and thereby significantly decreased the occurrence of spike wave discharges and simultaneously increased the occurrence of α wave activity.

CONCLUSION

It may be inferred from the present results MO protects rat neurons against oxidative stress as is evidenced from our results of LPO, CAT, SOD, GSH and EEG activities possibly by vitamin E, C and beta carotene which are present in MO leaf extract.

Thus the findings are that the aqueous leaf extract of this plant results significant neuroprotection in the level of antioxidant status in CC, CB, CN, MB and PM after a certain period of ICV infusion of colchicine induced oxidative stress without causing any general and metabolic toxicity. From this point of view, it may be proposed that further research on this field is essential to find out other active ingredients present in the MO leaf extract and their specific role by which the therapeutic importance may be evaluated and the outcome of which can be utilized in the protection of AD.

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