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WHOLE PLANT EXTRACTS OF *MENTHA ARVENSIS* AMELIORATES ANTIDEPRESSANT ACTIVITY IN ALBINO MICE

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ABSTRACT

The present study was designed to evaluate antidepressant activity of aqueous and methanol extracts of *Mentha arvensis*. DPPH, Hydroxyl and Nitric Oxide radical scavenging test techniques were used to investigate preliminary in-vitro antioxidant activity. Then, antidepressant efficacy was investigated in mice models using locomotor tests, forced swim tests, and tail suspension tests at dose levels of 125, 250, and 500 mg/kg. The reference drug, fluoxetine, was administered orally at a dosage of 10 mg/kg. The findings showed that, aqueous and methanol extracts of *Mentha arvensis* have promising anti-oxidant activity. The antidepressant effect of the aqueous and methanol extracts of *Mentha arvensis* was found to be excellent and in a dose-dependent. In conclusion, *Mentha arvensis* plant extracts exhibited significant antioxidant and antidepressant activity.

Keywords*: -* *Mentha arvensis*, antidepressant, anti-oxidant, forced swim test, tail suspension test, fluoxetine

INTRODUCTION

Depression is a severe public health concern that affects millions of individuals throughout the world. Severe depression often leads to suicidal tendencies, with approximately 0.8 million people committing suicide each year (1). Disturbances in neurotransmitter function, notably serotonin, noradrenaline, and dopamine, are a primary cause of depression. According to several scientific studies, a decrease in brain serotonin is one of the most important etiological elements in the development of depression. Serotonine reuptake inhibitors (SSRIs), which enhance serotonin's extracellular availability, are the most often prescribed antidepressant medicines. It's also been suggested that the noradrenergic and dopaminergic systems are involved, and that they work in unison with the serotonergic system (2). In individuals with significant depression, changes in brain monoamine neurotransmitters such as norepinephrine, serotonin, and dopamine have been reported.

It has been suggested that oxidative stress has a role in the development of depression. According to research, patients with significant depression have poor antioxidant enzyme activity, such as superoxide dismutase and glutathione peroxidase, as well as increased lipid peroxidation, according to research (3). Antidepressant therapy dramatically increases antioxidant enzyme levels and reduces lipid peroxidation in patients (4-7). As a result, lipid peroxidation and the response of antioxidant enzymes appear to be linked to the onset of serious depression. In light of this, the antioxidant activity of MA extract was assessed utilising several test techniques.

Several antidepressant compounds are available in the market including serotonergic, noradrenergic and/or dopaminergic systems, requires to consume for longer periods to get relief; however chronic usage leads to severe side effects. Medicinal plant remedies might be a viable alternative to antidepressant medication. In Indian traditional system of medicine, herbs or herbal based products are widely used to treat depressive disorders. Medicinal plants such as *Withania somnifera, Bacopa monniera, Hypericum perforatum, Cordyceps sinensis*, and *Perilla frutescens* etc have been reported to have antidepressant activity (2, 6). *Mentha arvensis* is an indigenous plant belongs to the family Lamiaceae commonly known as '*Pudina*' and '*Mint*' in English has been studied extensively for different pharmacological activities such as antiseptic, diuretic, antispasmodic, stimulant, stomachic, carminative, emmenagogue, expectorant and tonic. It is useful in the disease of liver, spleen, asthma, pains in the joints. The dried plant is refrigerant, stimulant. It is useful in jaundice and given to stop vomiting (8). Furthermore, the anti-depressant effect of the plant MA has yet to be

thoroughly verified. Therefore, the present work was designed to investigate the antidepressant activity of '*Mentha arvensis'* using locomotor test, tail suspension test and forced swim test in the experimental animals.

MATERIALS AND METHODS

Collection of Plant material

The plant material was collected from the local market, Mumbai and authenticated by Dr Ganesh Iyer, Department of Botany, Ruia College Matunga, Mumbai. The voucher specimen (No. 2010/01) was submitted in the herbarium of the Institute. The whole plant material was washed properly and air dried under shade. After drying, the plant material was grinded to a fine size.

Preparation of plant extract

The plant material was defatted with petroleum ether and then successively extracted with methanol using soxhlet extractor. The aqueous extract of plant material was prepared by maceration technique. Both the extracts were filtered through vacuum filter and the filtrates were concentrated in vacuum evaporator. Dried extracts were used for the further studies.

Experimental animals

Swiss albino mice of either sex weighing between 20-25 g were used in the study. The animals were procured from Haffkine Biopharmaceuticals, Parel, Mumbai and housed in polypropylene cages at an ambient temperature of 25±1 $^{\circ}$C, with a 12:12 h light and dark cycle. They had free access to standard pellet diet and water *ad libitum*. Animals were acclimatized for at least one week before using them for experiments and exposed only once to every experiment. The experimental protocols were approved by the Institutional Animal Ethical Committee (IAEC) of Institute of Chemical Technology, Mumbai.

Determination of anti-oxidative components

Quantitative determination of total flavonol, phenolic content and flavonoid were carried out (9).

Total phenolic content

Total phenolic content of aqueous and methanol extracts of *Mentha arvensis* was estimated from gallic acid calibration curve as described by method of Nagmoti D et al (10). 1.0 ml diluted Folin and Ciocalteu's reagent (1:1) was added to 100 µl of different concentration of gallic acid (2-10 µg/ml). Test extracts of 100 µl at the concentration of 10 mg/ml were added to the mixture and incubated for 5 min. After that, Na_2CO_3 (7%) was added to each test tube,

followed by 90 min incubation at room temperature. Absorbance of the samples were taken at 750 nm using a UV-Visible spectrophotometer (SHIMADZU UV-1650PC) and compared to a gallic acid calibration curve. The total phenolic content is expressed as gallic acid equivalent (GAE) in milligrams per gram of dry extract. The data is presented as the average of triplicate analyses.

Total flavonol content

Rutin equivalents were used to calculate total flavonol content, which was represented as mg rutin acid/g of extract. The calibration curve was constructed using different concentrations of Rutin (0.5-0.015 mg/ml) in ethanol with a total volume of 2 ml. In ethanol, a 20 mg/ml aluminium trichloride solution was made and added to each test tube, followed by 6 ml sodium acetate (50 mg/ml) and incubation for 2.5 hours at 20 °C. Instead of Rutin, 2.0 ml (10 mg/ml) extract in ethanol was used for the test sample. Each tube's absorbance was measured at 440 nm (9).

Total flavonoid content

Total flavonoid content of MA-ME and MA-AQ was studied by slightly modified technique of Tunalier et al (9). To 1.0 ml of various concentration of Rutin and test sample (10 mg/ml), 1.0 ml of Aluminium trichloride (20 mg/ml) in ethanol was added and volume was made up to 25 ml with ethanol. All the test tubes containing reaction mixture were incubated at 25 °C for 40 min and absorbance was read at 415 nm. Blank samples were prepared from 1.0 ml plant extract and one drop acetic acid, and diluted to 25 ml. All determinations were carried out in triplicate and the mean values were used.

***In- vitro* anti-oxidant activity**

DPPH radical scavenging activity

The antioxidant activity of the plant extracts was determined by 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) radical scavenging assay method (10). A 0.5 ml methanolic solution of the plant extracts at various concentrations (50-1000 µg/ml) was added to 0.5 ml of 0.1 mM methanolic solution of DPPH and incubated in dark environment for 30 min at 25°C. At 517 nm, the absorbance of the reaction mixture was measured spectrophotometrically. As a control, a 0.1 mM DPPH solution in methanol was employed. Radical scavenging activity was represented as the inhibition percentage of free radical by the sample and was calculated using the formula

$$\% \text{ inhibition} = \frac{(\text{Abs control} - \text{Abs test})}{(\text{Abs control})} \times 100 \qquad \text{--------- equation (1)}$$

Nitric oxide radical scavenging activity

Plant extracts' nitric oxide radical scavenging ability was measured in terms of nitric oxide radical produced from sodium nitroprusside. The Griess reaction detects nitrite ions produced by the reaction of sodium nitroprusside with oxygen. In brief, aqueous solution of sodium nitroprusside (1.0 ml; 10 mM) in phosphate-buffered saline (pH 7.4) was mixed with 1 ml of test extracts at various concentrations (50-1000 µg/ml) dissolved in methanol. Control was processed in similar condition except test sample. The reaction mixture was incubated at 25°C for 30 min. After incubation, 1 ml of solution was withdrawn and mixed with 1 ml of Griess reagent (1% sulphanilamide, 2% phosphoric acid and 0.1% naphthyl ethylenediamine dihydrochloride). The absorbance of the pink chromophore produced during the diazotization of the nitrite with sulphanilamide and the subsequent coupling with naphthyl ethylenediamine dihydrochloride was measured at 546nm (10). All the tests were performed in triplicate. Percentage inhibition was calculated using equation 1.

Hydroxyl radical scavenging activity

The modified Klein et al (11) and Dhir A (12) et al. methods were used to examine the hydroxyl radical-scavenging activity of MA-ME and MA-AQ. A test sample of 50 -1000 µg were taken in test tubes. Then, 1 mL of iron EDTA solution (0.13% ferrous ammonium sulfate and 0.26% EDTA), 0.5 mL EDTA (0.018%) and 1.0 ml of DMSO (0.85%) (in 0.1M phosphate buffer, pH 7.4) were added to the test tubes. The test tubes were firmly closed after the addition of 0.5 ml of 0.22% ascorbic acid and incubated on a water bath at 85 ºC for 15 min. After incubation, ice-cold trichloroacetic acid (17.5%) was added to each test tube followed by 3.0 ml of Nash reagent (7.5 g of ammonium acetate, 300 µl glacial acetic acid and 200 µl acetyl acetone were mixed and made up to 100 ml with distilled water). After 15 min incubation at room temperature, absorbance of the reaction mixture was measured. Percentage hydroxyl radical scavenging activity was calculated using equation 1.

Animal Experimental Design

Antidepressant activity of the '*Mentha arvensis*' plant extracts was evaluated in swiss albino mice of either sex using locomotor test, forced swim test and tail suspension tests. Plant extracts and fluoxetine were formulated in a 0.25% Na-CMC. All the groups of animals were divided into different 8 groups of 6 each and treated orally (once in a day) with 0.25% Na-CMC or Fluoxetine 10 mg/kg or test extracts (MA-AQ or MA-ME) at 125, 250 and 500 mg/kg. All the assessments were performed on acute (single dose) and after 7th dose of vehicle or fluoxetine or plant extracts administration.

Table 1: The protocol for the vehicle, standard drug and plant extracts administration to the mice

Groups	Treatment	Dose	No. of Animals
I	Control	0.25% Na-CMC	06
II	Fluoxetine	10 mg/kg; *p.o.*	06
III	MA-AQ	125 mg/kg; *p.o.*	06
IV	MA-AQ	250 mg/kg; *p.o.*	06
V	MA-AQ	500 mg/kg; *p.o.*	06
VI	MA-ME	125 mg/kg; *p.o.*	06
VII	MA-ME	250 mg/kg; *p.o.*	06
VIII	MA-ME	500 mg/kg; *p.o.*	06

Locomotor activity

Locomotor activity in mice was measured according to the slightly modified methods of Rajkumar V et al (13) and Dhir A et al (12). Actophotometer instrument was used to calculate locomotion of the animals. Locomotion was expressed in terms of total photobeam counts per 10 min per animal. Before performing the test, all the animals were acclimatized for 2 min to the observation chamber. An array of 16 infrared emitter and detector pairs measured animal activity along a single axis of motion, the digital data being displayed on the front panel meters as ambulatory movements. Between testing, the activity cages and floor surfaces were completely cleaned with 70% ethanol.

Forced swim test

The Forced swim test is a validated neurobiological model of depression (14). Test was carried out with slightly modified methods of Zhou D et al (15) and Bhurat M et al (16). Mice were forced to swim individually in a glass jar (dimension: 25 × 12 × 25 cm^3) filled with water to a height of 15 cm at 30°C. After an initial 2 min period of vigorous activity, each animal assumed a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head above water. During the next 4 minutes of a total 6-minute test, the total time of immobility was recorded. Immobile time was defined as the time spent by the mouse to float in the water without struggling. After the test, all the mice dried with clean towel and finally returned to their cage.

Tail suspension test

Tail suspension test was performed according to the previously reported method of Rajkumar V et al (13) and Zhou D et al (15) with minor modifications. Mice were suspended on the edge of a lever 58 cm above the table top by using adhesive tape placed 1 cm from the tip of

the tail. Mice suspended by the tail showed initial struggling, followed by periods of immobility that increase in duration across the 6 min test. Immobility was measured during a six-minute period, with the first two minutes eliminated. Immobility was defined as the absence of any limb or body movements, except for those caused by respiration or when they hung passively and completely motionless. The duration of immobility was recorded during the total 6-min test.

Statistical analysis

In-vitro data is expressed as mean±SD of triplicate determinations. Linear regression analysis was used to calculated IC_{50} value. *In-vivo* experimental data is expressed as mean±SEM and was analyzed using software GraphPad Prism 4. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference for *in-vivo* tests. A value of $p<0.05$ was considered as significant.

RESULTS AND DISCUSSION

Natural antioxidants have recently been in great demand, notably in the food business, due to various advantages over synthetic antioxidants (17). Plants high in secondary metabolites such as phenolic and polyphenolic chemicals have been scientifically proven to have antioxidant capabilities and can protect against oxidative stress (18-20). Furthermore, because of their radical scavenging characteristics, these chemicals can alter a wide spectrum of cell biological activities. The intake of antioxidants such as polyphenols has been effective in the prevention of variety of illnesses (21). Flavonoids are the class of compounds that have been proven for potent antioxidant activity based on phenolics hydroxyl group. A substantial positive association between flavonoids and antioxidant activity has also been demonstrated by several scientific research. Therefore, we calculated the amount of total phenolic, flavonoid, and flavonols in plant extracts in this study (MA-AQ and MA-ME). The present data suggest that, total phenolic contents of the MA-AQ and MA-ME was found to be 71.8±1.8 and 51.9±0.7 mg of gallic acid equivalent per gm of extract respectively. Flavonols content were found to be absent in MA-AQ. However, MA-ME showed flavonol content, 36.1±1.0 mg of rutin equivalent per gram of extract. The Total flavonoid content was found to be 20.6±2.6 and 91.3±5.3 mg of rutin equivalent per gm of extract for MA-AQ and MA-ME respectively. The content of total phenols and flavonoids in MA-ME and MA-AQ indicates the presence of anti-oxidative components.

Table.2: Quantitative analysis of antioxidative components of MA-AQ and MA-ME

Extracts	Total phenols[a]	Total flavonoids[b]	Total flavonols[c]
MA-AQ	71.8± 1.8	20.6±2.6	Ab
MA-ME	51.9±0.7	91.3±5.3	36.1 ±1.0

Each value is expressed as mean±SD (n=3); 'Ab' indicates absent

[a] Total phenols expressed as gallic acid equivalents per gm of extract; [b] Total flavanoids expressed as rutin equivalents per gm of extract; [c] Total flavanols expressed as rutin equivalents gram of extract.

The significant quantity of anti-oxidative components in the MA-ME and MA-AQ encouraged us to carry out further studies. Therefore, we evaluated anti-oxidant activities of these plant extracts using different assay methods. DPPH radical scavenging assay is a widely used method to evaluate the antioxidant property of various compounds. The rate of reduction in absorbance of the DPPH attributed due to hydrogen donation capability of antioxidants. The antioxidant activity for MA-ME and MA-AQ by DPPH radical scavenging assay method is shown in Figure 1. In accordance to the DPPH assay results, MA-ME extract was found to be a good scavenger of free radicals. MA-ME and MA-AQ showed considerable antioxidant activity in a concentration dependent manner, with IC_{50} 362.24 µg/ml (R^2 =0.948) and 335.66 µg/ml (R^2 =0.959) respectively. Both the extracts were shown to be effective DPPH free radicals scavenger.

Nitric oxide (NO) and reactive nitrogen species (RNS) are free radicals that are derived from the interaction of NO with oxygen or reactive oxygen species. Excessive NO production has negative consequences for the human body, including neurological disorders, inflammation, cancer, and other pathological issues (21). Figure 2 illustrates the Nitric oxide radical inhibition estimated by the use of Griess Illosvory reaction. MA-ME and MA-AQ showed substantial nitric oxide scavenging activity in a concentration-dependent manner, with IC_{50} 1478.6 µg/ml (R^2 =0.9933) and 562.5 µg/ml (R^2 =0.937) respectively.

Hydroxyl radical are extremely reactive and capable of damaging almost every molecule found in living cells (22-25). Hence it is necessary to prevent the imbalance of the radicals in the body. The antioxidant compounds act by various mechanisms; either by prevention of chain initiation, binding of transition metal on catalysts, decomposition of peroxides, prevention of continued hydrogen abstraction, reductive capacity and radical scavenging (26). The antioxidant activity of MA-ME and MA-AQ evaluated by Hydroxyl Radical scavenging assay method is shown in Figure 3. Data represents, MA-ME and MA-AQ demonstrated substantial hydroxyl radical scavenging activity in a concentration-dependent manner with IC_{50} 489.5 µg/ml (R^2 =0.9155) and 138.1 µg/ml (R^2 =0.9453) respectively.

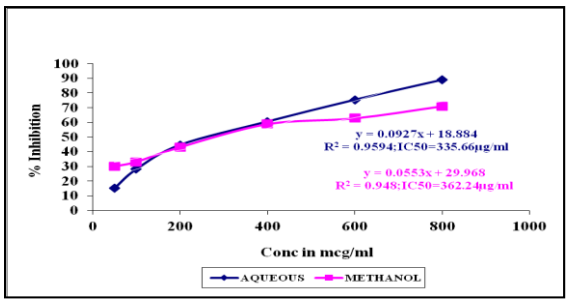

Figure 1: Antioxidant activity of MA-AQ and MA-ME by DPPH radical scavenging activity

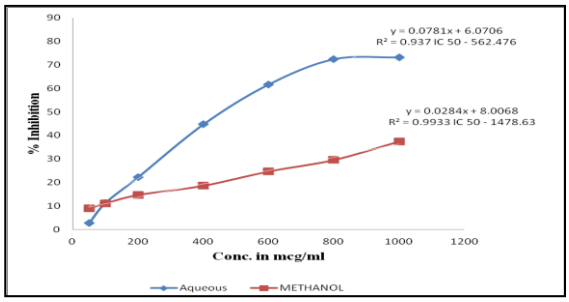

Figure 2: Antioxidant activity of MA-AQ and MA-ME by nitric oxide scavenging assay method

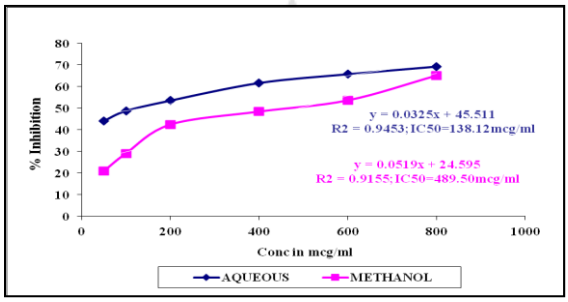

Figure 3: Antioxidant activity of MA-AQ and MA-ME by hydroxyl radical scavenging assay method

Depression has been associated to abnormalities in neurotransmission including 5-HT, norepinephrine, and dopamine activity in the brain (27, 28). Both the FST and TST models of depression are frequently used to test novel antidepressant compounds because they are very sensitive and specific to all major antidepressant drug classes, including tricyclics, serotonin reuptake inhibitors, MAO inhibitors, and atypicals.

The forced swimming-induced immobility in rats was suggested to be a condition akin to human depression, which might be treated with antidepressants. The monoamine hypothesis of depression is based on a lack of one or more monoamines, which is frequently used to explain the pathophysiology of mental depression. This hypothesis initially based on noradrenaline and serotonine deficiency, is recently extended to dopamine (12). The results

of this investigation showed that, acute MA-AQ and MA-ME treatment reduced immobility time in the FST considerably ($p<0.001$) when compared to control mice. Furthermore, MA-AQ and MA-ME treatment for 7 days showed promising ($p<0.001$) dose-dependent antidepressant effect at the dosage levels tested (125, 250, and 500 mg/kg). The effect of MA-ME at 500 mg/kg (7 days treatment) was found to comparable to that of the fluoxetine at 10 mg/kg, an SSRI type antidepressant drug (Figure 4 and 7). These findings imply that the MA-ME and MA-AQ significantly reduced immobility time through promoting swimming rather than climbing activity, validating their antidepressant effects.

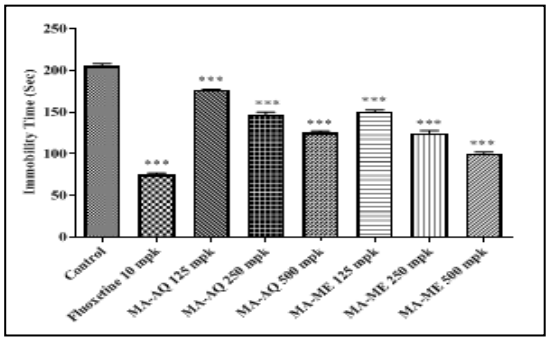

Figure 4. Effect of acute treatment of MA-AQ and MA-MA on immobility time in the FST

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

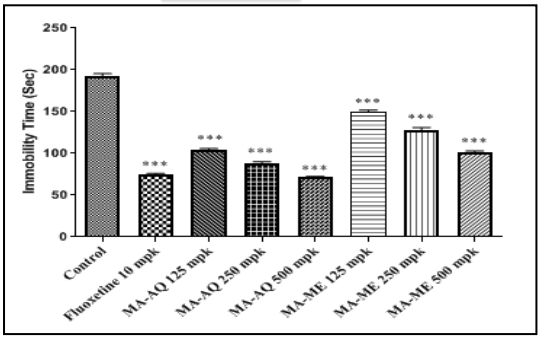

Figure 5. Effect of acute treatment of MA-AQ and MA-ME on immobility time in the TST

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

When compared to the forced swim test, the tail suspension test is thought to have a higher pharmacological sensitivity. At 125, 250, and 500 mg/kg treatment levels, MA-AQ and MA-ME produced a substantial ($p<0.001$) decrease in immobility time when compared to control animals. The efficacy of the MA-AQ and MA-ME was boosted in the 7 days dose regimen. The maximum effect of MA-AQ and MA-Me was shown at 500 mg/kg. Both MA-ME and

MA-AQ decreased immobility time with increasing swimming behavior in FST also decrease in immobility time in TST (Figure 5 and 8). The increase in swimming behaviour showed that 5 HT receptors may play a role in antidepressant mechanism of action. As a result, MA extracts show antidepressant effect, suggesting that serotonergic mechanisms are involved.

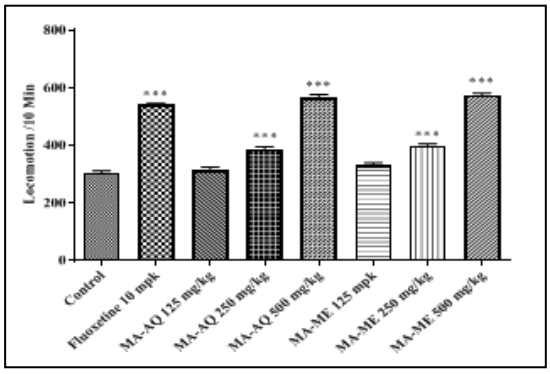

Figure 6: Effect of acute treatment of MA-AQ and MA-ME on locomotor activity

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

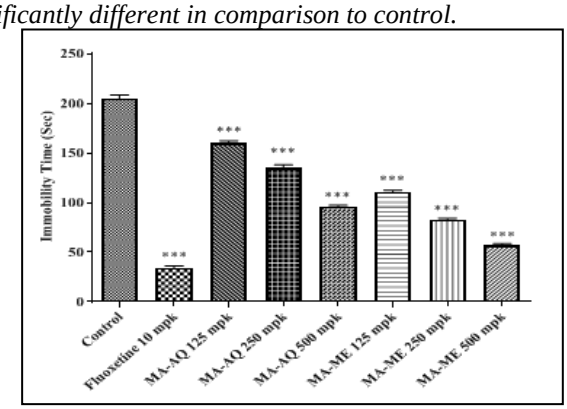

Figure 7: Effect of 7 days treatment of MA-AQ and MA-ME on immobility time in the FST

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

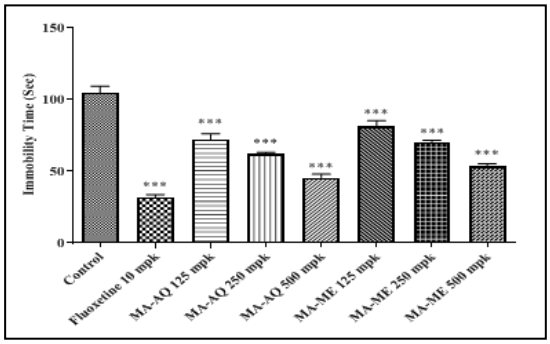

Figure 8: Effect of 7 days treatment of MA-AQ and MA-ME on immobility time in the TST

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

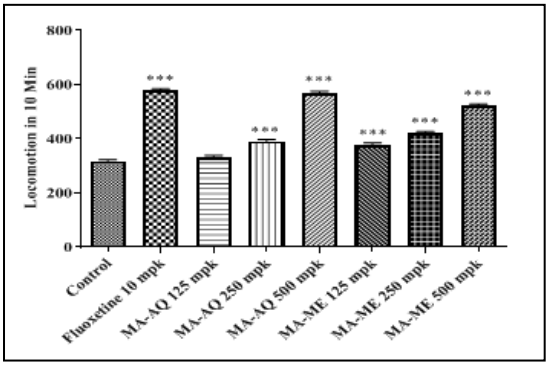

Figure 9: Effect of 7 days treatment of MA-ME on locomotor activity by actophotometer

*Values in the results are represented as mean±SEM. A one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison t-test was used to calculate statistical difference. *p<0.05, **p<0.01, ***p<0.001 considered significantly different in comparison to control.*

In addition to FST and TST, locomotor activity was done to ensure the antidepressant activity of MA-AQ and MA-ME. The locomotor activity is a measure of the level of excitability of the CNS; increased activity results from excitation of the central nervous system. It indicates attentiveness and the decline indicates sedative action (29). Here, study results explored substantial ($p<0.01$) increase in locomotion by the MA-AQ and MA-ME at a single dose treatment of the mid dose (250 mg/kg) and high dose (500mg/kg). Low dose of MA-AQ and MA-ME showed marginal increase in the locomotion after single dose treatment, however results were found non-significant ($p>0.05$). Furthermore, 7 days treatment of MA-AQ and MA-ME resulted in considerable ($p<0.001$) increase in locomotion at all the treated dose levels expect MA-AQ at 125 mg/kg. The antidepressant effect of MA-ME was found to be slightly greater than MA-AQ, after 7 days treatment (Figure 6 and 9). Fluoxetine, a standard antidepressant drug demonstrated prominent ($p<0.001$) decrease in immobilization in FST and TST at single and 7 days treatment regimen. It also exhibited considerable increase in locomotion in actophotometer test in both drug treatment regimens. Overall, study outcomes of FST, TST and locomotion test suggests the prominent anti-depressant activity of MA-AQ and MA-ME. Antioxidant activity has been linked to a variety of pharmacological actions, including antidepressant activity, according to the literature (30, 31). Therefore, it can be suggested that the antidepressant activity of the plant extracts could be due the presence of anti-oxidative components and its free radical scavenging potential.

CONCLUSION

Based on the findings of this study, it can be stated that the aqueous and methanolic extracts of *'Mentha Arvensis*' (MA-AQ & MA-ME) possesses significant antidepressant effect, which may be related to the presence of anti-oxidative components such as total phenols and flavonoids. MA-AQ and MA-ME have anti-oxidant capabilities, which contribute to their antidepressant impact. However, further studies are required to explore the exact mechanism of action.

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Conflict of Interest statement

Authors declared no conflict of interest.

REFERENCES

1. Moorkoth S, Prathyusha NS, Manandhar S, Xue Y, Sankhe R, Pai KSR, Kumar N. Antidepressant-like efect of dehydrozingerone from Zingiber ofcinale by elevating monoamines in brain: in silico and in vivo studies. Pharmacol Rep. 2021;73:1273–1286.
2. Singh G, Garabadu D, Muruganandam A, Joshi V, Krishnamurthy S. Antidepressant activity of Asperagus racemosus in rodent models. Pharmacol Biochem. Behav. 2009;91:283-290.
3. Bilici M, Efe H, Koroglu M, Uydu H, Bekaroglu M, Deger O. Antioxidative enzyme activities and lipid peroxidation in major depression: alterations by antidepressant treatments. J Affect Disord. 2001;64:43–51.
4. Abdalla D, Bechara E. The effect of chlorpromazine and Li2CO3 on the superoxide dismutase and glutathione peroxidase activities of rat brain, liver and erythrocytes. Biochem Mol Biol Int. 1994;34:1085–1090.
5. Katrenčíková B, Vaváková M, Paduchová Z, Nagyová Z, Garaiova I, Muchová J, Ďuračková Z, Trebatická, J. Oxidative Stress Markers and Antioxidant Enzymes in Children and Adolescents with Depressive Disorder and Impact of Omega-3 Fatty Acids in Randomised Clinical Trial. Antioxidants (Basel). 2021;10(8):1256.
6. Hsu LC, Ko YJ, Cheng HY, Chang CW, Lin YC, Cheng YH, Hsieh MT, and Peng WH. Antidepressant-Like Activity of the Ethanolic Extract from Uncaria lanosa Wallich var. appendiculata Ridsd in the Forced Swimming Test and in the Tail Suspension Test in Mice. Evid-based Complement Altern. Volume 2012; Article ID 497302: 12 pages.
7. Khanzode S, Dakhale G, Khanzode S, Saoji A, Palasodkar R. Oxidative damage and major depression: the potential antioxidant action of selective serotonin re-uptake inhibitors. Redox Rep. 2003;8:365–370.
8. Kirtikar K and Basu B. Indian Medicinal Plants. Mentha arvesis In Blatter E Caius J, Mhasekar K, Editors 2nd ed. Vol 3. LMB Publishers: Allahabad India: 1980.
9. Tunalier, Z, Koşar M, Küpeli E, Caliş I, Başer K. Antioxidant, anti-inflammatory, anti-nociceptive activities and composition of Lythrum salicaria L. extracts. J Ethnopharmacol. 2007;110(3):539–547.
10. Nagmoti D, Khatri D, Juvekar P, Juvekar A. Antioxidant activity and free radical-scavenging potential of Pithecellobium dulce Benth seed extracts. Free radic antioxid. 2012;2(2):37-43.
11. Klein S, Cohen G, Cederbaum A. Production of formaldehyde during metabolism of dimethyl sulphoxide by hydroxyl radical generating system. Biochemistry 1981;20:6006-6012.
12. Dhir A, Kulkarni S. Involvement of nitric oxide (NO) signaling pathway in the antidepressant action of bupropion, a dopamine reuptake inhibitor. Eur J Pharmacol. 2007; 568:177-185.

13. Rajkumar V, Guha G, Kumar A, Mathew L. Evaluation of Antioxidant Activities of Bergenia ciliata Rhizome. Rec. Nat. Prod. 2010;4:1:38-48.
14. Kulkarni S. Handbook of Experimental Pharmacology. 3rd ed. Delhi: Vallabh Prakashan: 2005.
15. Zhou D, Jin H, Lin HB, Yang XM, Cheng YF, Deng FJ, Xu JP. Antidepressant effect of the extracts from Fructus akebiae. Pharmacol Biochem Behav. 2010;94:488-495.
16. Bhurat M. Effect of remusatia vivipara (ROXB) schott tubers on animal models of depression. Int J Curr Pharm Res. 2011;3(1):90-92.
17. Patel D, Kumar R, Prasad S, Hemalatha S. Pedalium murex Linn (Pedaliaceae) fruits: a comparative antioxidant activity of its different fractions. Asian Pac J Trop Biomed. 2011;1(5):395-400.
18. Socha R, Juszczak L, Pietrzy S, Fortuna T. Antioxidant activity and phenolic composition of herb honeys. Food Chem. 2009;113(2):568-574.
19. Zhang Y, Wang Z. Phenolic composition and antioxidant activities of two Phlomis species: a correlation study. C R Biol. 2009;332(9):816-826.
20. Matkowski A, Piotrowska M. Antioxidant and free radical scavenging activities of some medicinal Plants from the Lamiaceae. Fitoterapia 2006;77(5):346-353.
21. Kumaran A, Karunakaran R. In vitro antioxidant activities of methanol extracts of five Phyllanthus species from India. LWT. Food Sci Technol. 2007;40(2):344-352.
22. Singha R, Singh S, Kumar S, Arora S. Evaluation of antioxidant potential of ethyl acetate extract/fractions of Acacia auriculiformis. Food Sci Technol. 2007;45(7):1216-1223.
23. Kumar B, Lakshman K, Jayaveera K, Shekar D, Kumar A, Manoj B. Antioxidant and antipyretic properties of methanolic extract of Amaranthus spinosus leaves. Asian Pac j trop med. 2010;3(9):702-706.
24. Rai B, Kaur J, Catalina M. Anti–oxidation actions of curcumin in two forms of bed rest: oxidative stress serum and salivary markers. Asian Pac j trop med. 2010; 3(8):651-654.
25. Prabhu K, Reddy G, Rao A. Can antioxidants predispose to cancer recurrence? Asian Pac j trop med. 2010;3(6):494-495.
26. Koncić M, Kremer D, Gruz J, Strnad M, Bisevac G, Kosalec I, Samec D, Zegarac JP, Karlovic K. Antioxidant and antimicrobial properties of Moltkia petraea (Tratt.) Griseb. Flower, leaf and stem infusions. Food Chem Toxicol. 2010;48(6):1537-1542.
27. Maes M, Meltzer HY. The serotonin hypothesis of major depression. In: Bloom FE, et al. editor. Psychopharmacology: the third generation of progress. Raven Press: New York: 1995: 993–1044.
28. Posener JA, Schildkraut JJ, Williams GH, Gleason RE, Salomon MS, Mecheri G, Schatzberg AF. Acute and delayed effects of corticotrophin-releasing hormone on dopamine activity in man. Biol Psychiatry. 1994;36(9):616–621.
29. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: a new method for screening antidepressants in mice. Psychopharmacology (Berl). 1985;85(3):367–370.
30. Scapagnini G, Davinelli S, Drago F, Lorenzo AD, Oriani G. Antioxidants as antidepressants: fact or fiction? CNS Drugs. 2012 Jun 1;26(6):477-490.
31. Tosaka M, Hashiba Y, Saito N, Imai H, Shimizu T, Sasaki T. Contractile responses to reactive oxygen species in the canine basilar artery *in vitro*: Selective inhibitory effect of MCI-186, a new hydroxyl radical scavenger. Acta Neurochir (Wien) 2002;144(12):1305–1310.