Acute Effect of Ethanolic Extract of Moringa oleifera on Haloperidol Induced Catalepsy in Mice Models

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Parkinson’s disease is a major neurodegenerative disorder caused due to deficiency of dopamine in the basal ganglia of the brain. The exact etiology of Parkinson’s disease still remains unclear. This CNS disorder may be caused due to oxidative stress, toxin induced free radicals, or drugs that destroys dopamine producing neuron in Substantia nigra. Catalepsy is a symptom of extrapyramidal disorders like Parkinson’s disease in animals. Neuroleptic induced catalepsy is an effective animal model for screening the antiparkinsonian activity of a chemical. The results indicate that administration of haloperidol (1mg/ kg, i.p) significantly induced catalepsy in Swiss albino mice, which was significantly reversed by the ethanolic extract of Moringa oleifera (200mg/ kg i.p). The anticataleptic activity of Moringa oleifera can be due to its antioxidant potential or due to its effect on brain monoamines.

Key words: Parkinson’s disease, Catalepsy, Haloperidol, Moringa oleifera, Anticataleptic.

INTRODUCTION

Parkinson’s disease is a chronic progressive neurodegenerative disorder of the substantia nigra, a nucleus of basal ganglia [1]. Parkinson’s disease occurs when nerve cells or neuron in an area of the brain known as the Substantia nigra degenerate[2]. Dopamine is a chemical messenger responsible for transmitting signals between the Substantia nigra and the next “relay station” of the brain, the corpus striatum to produce smooth, purposeful movement [3]. The loss of dopaminergic neurons in the pars compacta region of the substantia nigra is the cause for the progressive movement disorder[4]. Parkinson’s disease has unknown etiology, with uncertainty about the role of environmental toxins, genetic factors and medications [5]. The drug that blocks the action of dopamine may result in parkinsonism[6]. The neuroleptic drug like haloperidol is one of the major cause for drug induced parkinsonism worldwide [5][7]. The incidence of drug induced parkinsonism progresses with age[7]. The treatment for parkinsonism requires a continuing regimen on replacing dopamine with L-Dopa or the drugs like pramipexole which mimics the action of dopamine in CNS. The commonly prescribed drugs in drug induced Parkinsonism, are centrally acting anticholinergics like benzhexol or butabemut to counter the excessive over activity of acetylcholine in substantia nigra pars compacta[8][9]. Though the treatments now available for parkinsonism subsides the symptoms, it will not give complete cure for the disease and is often associated with frequent side effects[10][11]. In this context the use of many indigenous medicinal plants and their phytoconstituents in the treatment of Parkinsonism with minimal side effect profile arises. Moringa oleifera commonly known as drumstick tree is most widely cultivated species of Moringaceae family in India. It’s a perennial soft wooded tree; all parts of the tree are edible. Every part of the tree is useful for humans, so it is known as the miracle tree. Its leaves and fruits are used by human as food. Leaves are rich in Vitamin C, Calcium, Vitamin A, Potassium, Protein, and Iron. Traditionally the leaves are used for the treatment of variety of disorder [11][12]. Leaves are known to have Hepatoprotective [13], antimicrobial [14], antihyperlipidemic [15], anti-inflammatory [11], Anti hyperglycemic[16], antioxidant properties [17][18][19], anti convulsant [20]. It also has proved to increase brain monoamine levels [21]. This study is to evaluate the effect of ethanolic extract of Moringa oleifera (MOEE) in the treatment of Haloperidol induced catalepsy, which is an established model for screening antiparkinsonian drugs.

MATERIALS AND METHODS

Animals:
Adult Swiss albino mice of either sex weighing 20-25 g were used in this study after obtaining Institutional Animal Ethical Committee Clearance (IAEC), Yenepoya University. The mice were maintained under standard conditions in the Animal House (CPCSEA approved, Reg No: 347) under Dept of Pharmacology, Yenepoya University, Mangalore. The mice were kept in polypropylene cages (U.N.Shah manufacturers, Mumbai) under standard housing conditions and maintained on standard pellet diet (Amrut Lab Animal Feed, Sangli, Maharashtra), and water ad libitum. The mice were maintained on a 12:12 hour light-dark cycle.

Drugs and Chemicals
Haloperidol (Serenace, R.P.G Life Science Ltd, Ankleshwar.) was obtained from a pharmacy in Mangalore. It was administered at a dose of (1 mg/ kg i.p) [10]. The Standard drug Scopolamine (Buscopan, Cadilla Health Care Ltd, Goa.) was also obtained from a pharmacy in Mangalore. It was administered at a dose of (1 mg/ kg i.p) [10].

Plant Materials
Leaves of Moringa oleifera were used in the study. The leaves were collected from Thiruvalla, Kerala. The leaves were authenticated by Dr. Noeline J.Pinto, Head of Botany department, S.L.Agnes College, Mangalore, Karnataka, India. They were shade dried, and then grinded into coarse powder.

Preparation of the Extracts
Moringa oleifera ethanolic extract (MOEE)
A weighed quantity (500 gm) of the coarse powder was taken and extracted with ethanol (90 %) in a Soxhlet apparatus. The extract was concentrated on a water bath at a temperature not exceeding 60ºc. The percentage yield of the extract was 10%. The ethanol...
extract was suspended in distilled water. MOEE was administered at a dose of 200 mg/kg/day intraperitoneally (i.p).

**A assessment of Catalepsy:**
It was done at the Ethno pharmacology lab, Department of Pharmacology, Yenepoya University. Catalepsy was induced by intraperitoneal administration of haloperidol (1mg/kg). In order to measure cataleptic symptoms such as akinesia and rigidity, Bar test was used. Catalepsy was evaluated by placing both forepaws of the mouse over a horizontal bar (diameter: 1 cm), elevated 4 cm from floor. The end point of catalepsy was considered to occur when the animal moved its head in an exploratory manner or when both the front paws were removed from the bar.[22]

**Experimental Design**
48 animals were used in this study. The animals were divided into four groups. Each group consisting of 6 males and 6 females (n=12).

- **Group I:** Normal Saline (NS) i.p
- **Group II:** Haloperidol [H] i.p
- **Group III:** MOEE i.p +H i.p (1 hour after MOEE administration).
- **Group IV:** Scopolamine (S) i.p + H i.p (1 hour after Scopolamine administration)

The test drug Moringa oleifera was administered i.p. After one hour, haloperidol was given i.p to induce catalepsy. After half an hour of the administration of Haloperidol the animals were taken to measure the degree of catalepsy. Same pattern was followed for Scopolamine. Once the experiments were over, the animals were rehabilitated.

**Statistical Analysis**
Results were expressed as Mean ± S.D. One-way analysis of variance (ANOVA) was carried out and the statistical comparisons among the groups were performed with Tukey Kramer test using a statistical package program. p<0.05 was taken as significant.

**RESULTS**
As seen in table-1, there was a considerable decrease in cataleptic activity in MOEE treated groups. The anticafeptatic activity of MOEE is equal to that of Scopolamine treated groups.

**Table 1: Effect of MOEE on haloperidol induced catalepsy**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Drugs</th>
<th>Withdrawal of both paws in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>NS</td>
<td>0.47 ± 0.015</td>
</tr>
<tr>
<td>II</td>
<td>H</td>
<td>3.45 ± 1.76</td>
</tr>
<tr>
<td>III</td>
<td>MOEE + H</td>
<td>0.53 ± 0.12</td>
</tr>
<tr>
<td>IV</td>
<td>SH</td>
<td>1.42 ± 0.05</td>
</tr>
</tbody>
</table>

One Way ANOVA, followed by Tukey Kramer multiple comparison test, n = 12

This test is widely used to evaluate the effect of drugs on extra pyramidal system.

Typical neuroleptic induced catalepsy has been linked to a blockade of postsynaptic striatal dopamine D1 and D2 receptors.[26] The generation of free radicals and increased lipid peroxidation due to the increase in turnover of the monoamine may lead to haloperidol induced extra pyramidal disorder.[27] Deficiency in oxidative defense mechanisms in the brain causes a greater risk of cellular damage by free radicals.[28] The dysfunction of other neurotransmitters like acetylcholine, GABA and serotonin, have also been implicated in neuroleptic induced catalepsy.[24,27,28]

In conclusion, Moringa oleifera was found to be effective in reducing cataleptic scores in mice model of haloperidol induced catalepsy. Anticataleptic action of MO might be due to the free radical scavenging property. The effect of Moringa oleifera on the neurotransmitters like acetylcholine, dopamine, serotonin, GABA cannot be ruled out. However, further studies are required to confirm the exact mechanism of action of this plant.

**REFERENCES**
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