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Original Research Article

Assessment of *Morus alba* (mulberry) leaves extract for anti-psychotic effect in rats

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ABSTRACT

Background: *Morus alba* commonly known as white mulberry has been widely cultivated to feed silkworms. This widely grown plant has been in use by tribals of this country for ailments such as asthma, cough, bronchitis, edema, insomnia, wound healing, diabetes, influenza, eye infections and nose bleeds. Various parts of morus alba linn are used as an cardioprotective, hepatoprotective anti-inflammatory, hypoglycemic, free radical scavenging activity and neuro-protective agent. In this study, anti-psychotic property of *M. alba* leaves extract (MAE) was evaluated by Haloperidol induced catalepsy model in rats.
Methods: In this study Haloperidol induced catalepsy model was used to evaluate antipsychotic effects in rats. Haloperidol (1 mg/kg) was injected intraperitoneally to rats (n=6) pretreated with vehicle (0.5 mg/kg, i.p.) or MAE (100, 200 and 400 mg/kg, i.p).
Results: In control treated animals, haloperidol produced the maximum catalepsy at 90 min 212.66 ±10.23. In animals treated with MAE at dose of 100 mg/kg, 200 mg/kg and 400 mg/kg significantly potentiated haloperidol induced catalepsy at each time interval, in a dose dependent manner. At dose 100, 200 and 400 mg/kg, animals treated with MAE showed maximum cataleptic score of 228.33±12.29, 265.66±7.33 and 274.16±8.86 respectively at 120 min ($p<0.001$).
Conclusions: Results indicate that the MAE have anti-psychotic effects in haloperidol induced catalepsy model in rats.

Keywords: *Morus alba* leaves extract, Haloperidol induced catalepsy, Anti-psychotic property

INTRODUCTION

Medicinal plants are the major components of all indigenous or alternative systems of medicine. Medicinal plants are sources and can be a good start for the discovery of new chemical compound which leads to new drug.[1] India is one of the nations blessed with rich heritage of traditional medicinal system and rich biodiversity to complement the herbal needs of the treatment administered by these traditional medicinal systems.[2]

Psychosis is a symptom of mental illnesses characterized by a distorted or non-existent sense of reality. Psychotic disorders have different etiologies, each of which demands a unique treatment approach. Schizophrenia has a worldwide prevalence of 1% and is considered the prototypic disorder for understanding the phenomenology of psychosis and the impact of antipsychotic treatment, but patients with schizophrenia exhibit features that extend beyond those seen in other psychotic illnesses. Hallucinations, delusions, disorganized speech, and disorganized or agitated behavior comprise the types of psychotic symptoms found individually, or rarely

together, in all psychotic disorders, and are typically responsive to pharmacotherapy.[3]

Morus alba Linn., commonly known as white mulberry belongs to family Moraceae. *M. alba* is a moderately sized tree, three to six meters high. White mulberry is cultivated throughout the world, wherever silkworms are raised. The leaves of white mulberry are the main food source for the silkworms.[1] This widely grown plant has been in use by tribals of this country for ailments such as asthma, cough, bronchitis, edema, insomnia, wound healing, diabetes, influenza, eye infections and nosebleeds.[4] *M. alba* leaves contain rutin, quercetin and apigenin as bioactive constituents.[5] The one of major constituent of Morus alba is 1-deoxynojirimycin.[6] *M. alba* leaf extract has been found to produce nitric acid, prostaglandin E2 and cytokines in macrophages.[7] Many biochemical compounds such as Moranoline, Albafuran, Albanol, Morusin, Kuwanol, Calystegin and Hydroxymoricin are isolated from mulberry plants which play an important role in pharmaceutical industry.[8] The other uses of *M. alba* are as a hypoglycemic, cardioprotective, and neuroprotective agent The mulberry fruit has been used as a medicinal agent to nourish the blood and for the treatment of weakness, fatigue, anemia, and premature graying of hair. In addition, some phenolic compounds from *M. alba* have been reported to have antioxidant properties.[9,10] The crude hydroalcoholic extract of *M. alba* L. leaves was evaluated for hepatoprotection against hepatotoxicity induced by carbon tetrachloride.[11]Anti-inflammatory activity is documented for mulberroside A and oxyresveratrol from the root bark of white mulberry in reducing carrageenin-induced paw edema in rats.[12] *M. alba* leaves extract showed anticonvulsant effects in MES induced convulsions and in PTZ induced convulsions.[13] A piperidine alkaloid and some glycoproteins were isolated from the bark and leaves, which had antidiabetic effects.[14]

Taking this into consideration the reported psychopharmacological effects of morus alba leaves in various animal models, ignited a spirit to evaluate anti-psychotic effects of *M. alba* leaves extract by haloperidol induced catalepsy model in rats.

METHODS

Animals

This study was executed in the Department of Pharmacology, Narayana Medical College. The animals (Wister strain albino rats) weighing 150-250 gms were obtained from central animal house of Narayana Medical College, Nellore for all the animal experiments. They were housed in standard polypropylene cages. Colony breeds Albino rats of either sex weighing between 150-250 gms were included in this study. The animals were excluded if the weight of rats was below 150 gms and if they had any visible diseases. The animals were maintained under standard laboratory conditions (light period of 12 hrs/day and temperature 250C±10C) with free access to food and water ad libitum. The animal experiments were approved by the IAEC (Institutional Animal Ethics Committee) with protocol number – 27/2013/NMC, dated 20/12/2013.

Plant material

The mulberry leaves were collected from Udayagiri, Nellore district, Andhra Pradesh and the leaves were identified by Botanist Mr. K. Vishnu vardhan, junior lecturer in botany, Govt. junior college, venkatagiri, Nellore district with plant identification number 12/2013/GJCV, dated 15/12/2013. The leaves were washed thoroughly under running tap water, shade dried for 5 days and ground to a fine powder in an electric mixer. The powder plant material was extracted twice with 90% ethanol at room temperature. Extracts were filtered with whatman filter paper No.1. The filtrate was evaporated until dry, using a soxhlet evaporator, to obtain the extract. Before use, the extract was dissolved in distilled water for administration intraperitoneally (i.p).[15]

Albino rats of male sex weighing from 150-250 gms were used in this study. These were acclimatized to their environment for one week prior to experimentation. The animals were randomly distributed into four different groups. Each experimental group consisted of 6 animals. Each group was caged separately after recording its body weight and the animals were marked with marker for identification.

In this study Haloperidol induced catalepsy model was used to evaluate anti-psychotic effects in rats.

Principle[16]

Anti-psychotic drugs are well known for their extra pyramidal side effects. Present experiment demonstrates extra pyramidal side effects like tardive dyskinesia animal followed by the butyrophenones (Haloperidol) treatment. Phenothiazine neuroleptics act through the blockade of D2 receptors in temporal, limbic system and mesocortical areas. In the experiment, extra pyramidal side effects are identified by catalepsy. It is an extreme tonus, muscular rigidity which is characterized by a tendency to remain in a fixed position for long period, hence unable to correct an externally imposed, unusual posture over a period of time.

Procedure[17]

Haloperidol (1 mg/kg) was injected intraperitoneally to rats (n=6) pretreated with vehicle (0.5 mg/kg, i.p.) or MAE (100, 200 and 400 mg/kg, i.p). The vehicle or MAE was administered 30 min prior to the administration of haloperidol. The duration of catalepsy was measured at 30, 60, 90 and 120 min, using bar test. Both the forepaws of rats were placed on a horizontal bar raised 3 cm from

the table, and the time required to remove the forepaws from the bar was recorded as the duration of catalepsy.

Statistical analysis

The data were entered into excel spreadsheet 2007. Statistical analysis was performed using Sigma Graph pad prism version-6 USA. Data was described as mean ± standard deviation. One way ANOVA followed by Post hoc Tukey's multiple Comparison tests was used for analysis of data among all groups. All the results of test drug (*M. alba*) were compared with control & standard.

RESULTS

In control treated animals, haloperidol produced the maximum catalepsy at 90 min 212.66±10.23. In animals pretreated with MAE at dose of 100 mg/kg, 200 mg/kg and 400 mg/kg significantly potentiated haloperidol induced catalepsy at each time interval, in a dose dependent manner. At dose 100, 200 and 400 mg/kg, animals pretreated with MAE showed maximum cataleptic score of 228.33±12.29, 265.66±7.33 and 274.16±8.86 respectively at 120 min ($p<0.001$) (Table 1).

Table 1: Effect of MAE on haloperidol induced catalepsy.

S. No	Group and Dose (I.P)	Duration of Catalepsy in Mean ± S.D (sec)			
		30 min	60 min	90 min	120 min
1	Group-I : Control Saline : 0.5 ml/kg + Haloperidol 1 mg/kg	108.33 ± 7.73	151.33 ± 5.88	212.66 ± 10.23	191.33 ± 10.32
2	Group-II MAE : 100 mg/kg + Haloperidol 1 mg/kg	120 ±9.71	167.33 ± 7.33*	223.83 ± 10.36*	228.33 ± 12.29***
3	Group-III MAE : 200 mg/kg + Haloperidol 1 mg/kg	170.16 ±9.80***	207.5±10.03***	250 ± 9.71***	265.66 ± 7.33***
4	Group-IV MAE : 400mg/kg + Haloperidol 1 mg/kg	212 ± 12.64***	237 ± 8.83***	264.66 ±8.81***	274.16 ± 8.86***

*p<0.05, **p<0.01, *** p<0.001 compared to control group. ANOVA followed by Tukeys multiple comparison tests was used for analysis of data between the groups.

DISCUSSION

In this study to evaluate the effect of *M. alba* leaves extract on Haloperidol induced catalepsy in rats, the method described by Adhikrao et al was followed.[17] Catalepsy means failure to correct an externally imposed posture. In this study the cataleptic score by bar test was used as the index of antipsychotic effect.

Haloperidol, an anti-psychotic used in humans, is well known to cause extrapyramidal symptoms, due to blockade of dopamine D2 receptors in the striatum.

In haloperidol induced catalepsy test, *M. alba* leaves extract in dosage of 200, 400 mg/kg body weight showed significant potentiation of haloperidol induced catalepsy and exhibited maximum catalepsy score at 120 minutes.

The potentiation of haloperidol induced catalepsy is depend on multiple mechanisms. Postsynaptic striatal dopamine D1 and D2 receptors are blocked in case of a typical neuroleptic induced catalepsy.[18]

This study results were in accordance to Adhikrao et al.[17] They showed that *M. alba* demonstrated a significant anti-psychotic activity tested by haloperidol and metoclopramide induced catalepsy and Amphetamine-induced stereotyped behavior models. They mentioned that the striatum and nucleus accumbens have been implicated as the major brain structures involved in anti-psychotic induced catalepsy, which appears due to the blockade of dopamine neurotransmission. Thus, the results suggest that MAE shows antidopaminergic activity.

Girish et al reported that aqueous leaves extract of morus alba in doses of 25, 50, 100 mg/kg showed significant anti-psychotic activity when compared with vehicle tested by lithium sulphate induced head twitches, lithium sulphate induced stereotypy, 5-Hydroxytryptophan potentiating models.[19]

The results shows that the highest dose extract (100 mg/kg) was comparable to clozapine in lowering psychotic behavior by significantly inhibiting serotonin activity, however in our study a dose of 400mg/kg showed highly significant result in haloperidol induced catalepsy suggesting that *M. alba* may have different mechanism of action for its anti-psychotic activity. So, further investigation on the mechanism of action of the plant extract, as well as the active substance responsible for its biological actions is necessary.

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