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Antidepressant Effect of Petroleum Ether Extract of Malkangni (Celastrus Paniculatus) in Rats and Mice

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Abstract
The present study was designed to evaluate the antidepressant effect of petroleum ether extract of seeds of Malkangni (Celastrus paniculatus) in rats and mice. The petroleum ether extract was found to reduce the immobility period in forced swimming test and tail suspension test and reverse the reserpine induced extension of immobility in mice. Similar to Imipramine (IMI), the test drug extract reversed the degree of ptosis and catalepsy induced by reserpine in rats. The effects exhibited were dose dependent. These results suggest that the drug possesses antidepressant activity, the mechanism of action and the ingredients responsible for the action, however, remains to be elucidated.

1. Introduction

Celastrus paniculatus (CP) wild (Celastraceae) is a large woody, climbing shrub, upto 10 meters in height, distributed almost all over India. The seeds, which are ellipsoid or ovoid in shape and yellowish or reddish brown in colour, constitute the drug used in traditional systems of medicine. The drug is considered as a nerve stimulant and has been employed for treating disorders like cognitive disorders, rheumatism, paralysis, hysteria etc. in Ayurvedic and Unani systems of medicine[1,2]. Phytochemical analysis of the drug showed presence of steroids, terpenoids and alkaloids[3]. Several sesqueterpene polyalcohalswere also reported, malkanguniol being the major one[4]. Paraffinic hydrocarbons, Beta-sitosterol, Beta-amyrin pentacyclic triterpene diol paniculatadiol were isolated from the seed oil [5]. Besides fatty acids like oleic, linoleic, linilenic, palmitic, stearic, lignoceric acid, acetic acid and volatile acids are present in the seeds [6]. Pharmacological study of oil of seeds revealed that the drug enhanceslearning process in albino rats [7]. The oil extracted from the seeds is known to have effects on CNS [8]. In an investigation in open field behavior test, petroleum ether extract of the drug behaved like tricycle antidepressant Imipramine[9]. So we became interested in studying the effect of petroleum ether extract of this drug on other animal models of depression.

2. Materials and Methods

2.1. Animals

Male Swiss albino mice (22-28 gms) and male Wistar rats (150-180 gms) used in the

House Facility, Jamia Hamdard, New Delhi and housed under standard laboratory conditions. The experiments were conducted between 09.00 hrs and 17 hrs after overnight fasting with ad libitum access to water, in accordance with the guidelines for the care and use of laboratory animals, laid down by the committee for the purpose of control and Supervision of Experiments on animals, laid down by the committee for the purpose of control and Supervision of Experiments on animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India, January 2000.

2.2. Preparation of the Extract

The drug was purchased from local market of New Delhi and authenticated in the Department of Phytochemistry and Pharmacognosy, Faculty of Pharmacy, Jamia Hamdard. A voucher specimen has been retained and deposited in the museum, Department of Ilmul Advia, Faculty of Unani Medicine, Jamia Hamdard. The seeds were crushed and extracted with petroleum ether in Soxhlet apparatus for 24 hours and the solvent was recovered under reduced pressure. The yield was approximately 30% (w/w of the dried starting material). The extract was suspended in water using CMC (0.25%) for experiments.

2.3. Drugs

Reserpine (S.D fine chemicals) was suspended in 5% ascorbic acid and injected intraperitoneally (i.p) in the dose vol. of 1ml/kg. Imipramine (Ranbaxy) was suspended in water using CMC and given per orally(p.o) in the volume of 1 ml/ 100gms. The water emulsion of the test drug extract was given per p.o in the dose vol. of 1ml/100gm.

2.4. Statistical Analysis

The data obtained were evaluated by one way analysis of variance (ANOVA) followed by Dunnetts ''t'' test and expressed as Mean ±S.E.M. The results were considered significant when $P<0.05$.

2.5. Experiments

2.5.1. Effect on Forced Swimming Induced Behavioral Despair in Mice

The method developed by Porsolt et al was used [10], which is based on the observation that mice exposed to a situation of forced swimming become passive and immobile after a period of vigorous activity and only produce movements sufficient to keep their heads above the water. Antidepressant drugs reduce duration of passive period. In the present study, four groups of 6 mice each were used. Group I received distilled water and served as control. Group II, the standard group received Imipramine (IMI) 20 mg/Kg P.o, whereas Group III and Group IV was administered with the test drug extract in the doses of 200mg and 400 mg/kg respectively. One hour after the treatment, each animal was placed individually in a polythene cage (45x25x15 cm) with water (15 cm high) at 20± 2°C. The time of immobility of each animal was noted in a test session of 10 minutes and the mean result obtained with each group was compared with the control group.

2.5.2. Reversal of Reserpine Induced Behavioral Changes

Reserpine administration in rats has been found to produce symptoms such as ptosis and catalepsy, which are characteristic of human depression [11,12]. In the present study four groups of 6 rats each, were used in the experiment and treated with vehicle / standard drug/ test drug extract as mentioned in the experiment 2.5.1 above. After 60 minutes, all the animals were injected with reserpine 16 mg/kg i.p and the duration of catalepsy was noted at 120, 240 and 360 minutes after the drug administration.

The degree of ptosis was noted as the fraction of eyelid closure from the normal aperture. The ptotic rating was given as follows:

4 for complete ptosis, 3 for ¾th, 2 for ½, 1 for ¼th.

The degree of ptosis was measured at 60, 120, 240 and 360 minutes after the injection of reserpine. The score of each group was averaged and the degrees of ptosis was compared in the control and treated groups of rats.

2.5.3. Reversal of Reserpine Induced Extension of Immobility in Mice

This test is based on the fact that reserpine causes depletion of catecholamines, thus enhancing the immobility period (despair behavior) in swimming test [13]. The maximum immobility is obtained after 4 hours of administration. This despair behavior is sensitive to reversal by classical antidepressants like Imipramine [14].

Four groups of 6 animals each were injected with reserpine 2 mg/kg intraperitoneally. After three hours, the animals were administered with distilled water/ standard/ test drug extract like in the previous experiments. One hour after treatment, the mice were forced to swim in a polythene cage (45x25x15 cm) with water (15cm high) and the duration of immobility was noted in a 6 minutes test session. The mean result obtained with each group was compared with the control.

2.5.4. Trial Suspension Test (TST)

The method described b stern etal was used in our study[15]. The animals were hung by the trial on a plastic string 75 cm above the surface with the help of adhesive tape. The duration of immobility was recorded during the last 6 minutes of the observation period. Mice were considered to be immobile only when they hung passively and were completely motionless.

3. Results

3.1. Effect of the Test Drug Extract on Forced Swimming Despair

The result of the test is shown in table 1. In the animal groups treated with the test drug extract at doses of 200mg/kg

and 400 mg/kg (CP 200 & 400), the immobility time was significantly reduced comparable to IMI 20mg/kg, the standard drug.

3.2. Reversal of Reserpine Induced Behavioral Effects

The duration of catalepsy was significantly reduced both at 240 and 360 minutes in the test drug extract treated (CP 200 & 400 mg/kg) animals in comparison to the control animals. The effect was dose dependent (table 2). The degree of ptosis induced by reserpine was also significantly antagonized by the extract (CP 200 and 400mg/kg) both at 120 and 240 minutes (Table 3).

3.3. Reversal of Reserpine Induced Extension of Immobility

The duration of immobility was significantly reduced in CP 200 and CP 400 mg/kg treated animals in a dose dependent manner (Table 4).

3.4. Effect of Test Drug on Trial Suspension Test

The result of the test is shown in Table 5. The immobility time was significantly reduced by the test drug (CP 200 and 400 mg/kg) and Imipramine (IMI 20 mg/kg).

Table 1. *Effect of CP 200 and 400 mg/kg on forced swimming induced despair in mice.*

Treatment (mg/kg)	Duration of immobility in seconds (Mean ±S.E.M)
Control	271.25 ± 9.23
CP 200	210 ± 4.86*
CP 400	182.5 ± 7.29*
IMI 20	166.12 ± 8.54 *

n=6, * =P<0.05

Table 2. *Effect of CP 200 and 400 mg/kg on duration of catalepsy induced by reserpine in rats.*

Treatment (mg/kg)	Duration of catalepsy in seconds (Mean ± S.E.M)			
	Basal	120 min.	240 min.	360 min
Control	0	0	335± 12.25	810±27.31
CP 200	0	0	271±20.15*	710 ± 23.75*
CP 400	0	0	238 ± 18.37*	665 ± 18.8*
IMI 20	0	0	219 ± 21.12*	592 ±21.87 *

n=6,*= p<0.05

Table 3. *Effect of CP 200 and 400 mg/kg on degree of ptosis induced by reserpine in rats*

Treatment (mg/kg)	Degree of ptosis (Mean ± S.E.M)			
	Basal	60	120	240
Control	0	0	3 ± 0.36	3.83 ± 0.16
CP 200	0	0	1.66 ± 0.33*	2 ± 0.36*
CP 400	0	0	1.53 ±0.21 *	1.06±0.42*
IMI 20	0	0	1.16± 0.47 *	1.35±0.33*

n=6, *= P< 0.05

Table 4. *Effect of CP 200 and 400 mg/kg on reserpine induced immobility in mice*

Treatment (mg/kg)	Duration of immobility in seconds (Mean ± S.E.M)
Control	195.62 ± 7.09
CP 200	156.25 ± 44 *
CP 400	139.25 ± 573 *
IMI 20	113.37 ± 4.56*

n=6, *=P <0.05

Table 5. *Effect of CP 200mg and 400 mg/kg on TST in mice*

Treatment Drug (mg/kg)	Duration of immobility in seconds (Mean ± S.E.M)
Control	233.16 ± 1.33
CP 200	171.50 ± 0.87*
CP 400	161.33 ± 03.55**
IMI 2.0	153.32 ± 12.36**

n= 6, * = P<0.05

4. Discussion

Mood disorders are one of the most common mental illnesses with a lifetime risk of 10% in general population. Prevalence of depression alone in general population is estimated to be around 5% with suicide being one of the most common outcomes. Although a number of synthetic drugs are being used as the standard treatment, they have adverse effect that can compromise the therapeutic treatment. Several drug interactions can also occur, leading to patient's noncompliance to medication .These conditions create an opportunity for alternative treatment of depression by use of medicinal plants or plants based antidepressant formulations. Unani and Ayurveda mentions a number of single and compound drug formulations of plant origin that are used in the treatment of psychiatric disorders and are claimed to have a better side effect profile than conventional drugs. Celastrus paniculatus is one such plant origin drug used to counter tension states in over wrought neurotics in traditional systems of medicine. The study of its pharmacological actions revealed that the drug possess sedative and tranquilizing activity [16,17,18]. In our previous study, petroleum ether extract of the drug behaved like Imipramine in open field test 9. The present results also tend to confirm these observations. Thus, similar to the effect of IMI, the test drug extract shortened the immobility period in both forced swimming induced behavior despair test & tail suspension test. Forced swimming is thought to cause a state of despair in animals, which may be a component of human depression [19,20]. Reduction of immobility in forced swimming induced despair test is characteristic of antidepressant agents 10. Furthermore, the extract also reverted reserpine induced extension of immobility as well as reserpine induced ptosis and catalepsy in a dose dependent manner.It proves the antidepressant property of the drug.

Reserpine is known to deplete both the catecholamines and serotonin and enhance immobility, thus leading to behavioral despair [21]. Through the same mechanism, it leads to catalepsy

and ptosis. These effects are sensitive to reversal by typicalantidepressants like Imipramine, although this method is known to be not very effective in demonstrating the antidepressant properties of atypical antidepressants such as Mianserin. The immobility in forced swimming test (TST) and FST (forced swimming test is thought to reflect either a failure of persistence in escape directed behavior (behavioral despair) or the development of passive behavior that disengages animal from active forms of coping with stressful stimuli [22]. It has been argued that the TST is less stressful than the FST and has greater pharmacological sensitivity. Remarkably TST detects the anti-immobility effects of wide array of antidepressants including tricyclic, antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), monoamineoxidase inhibitors (MAOI) and even a typical antidepressants. It has been established that the shortening of immobility time in the FST and TST depends mainly on the enhancement of central 5- HT and catecholamine neurotransmission [13]. This clearly shows that Celastrus paniculatus possesses antidepressant activity and could involve one of the mechanisms of the established agents as described above. However further work needs to be done to ascertain this.

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