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RESEARCH PAPER

Effect of *Psoralea Corylifolia* Extract on Physically Induced Depression in Mice

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ABSTRACT

The mouse forced swimming test (FST) and tail suspension test (TST) are widely used to predict anti-depressant efficacy indicated by immobility time to be reduced by several different classes of anti-depressant drugs. PCE feeding at the dose of 75 mg/kg,150 mg/kg, and 300 mg/kg reduced the immobility duration at 14-days and 21-days, however the decrease was significant in mice treated with PCE for 21-days also, extract had no effect on spontaneous motor activity in mice, indicating that extract had no excitatory or inhibitory action on central nervous system in effective dose range, which eliminated the probability of false-positive results in forced swimming test and tail suspension test. Interestingly, the dose-response effect of PCE on reduction of serum CRF levels was concomitance with that on increase of brain 5-HT contents, as well as on swimming increase, indicating that the serotonergic system and the HPA axis responds with the production of 5-HT and CRF profiles that is characteristic for PCE applied in the mouse FST. Our results demonstrate that the oral administration of PCE possesses an anti-depressant-like activity, as evidenced by behavioural studies. Detailed investigations are needed to fully elucidate the mechanism of action at cellular level for the bioactive constituents present in the extract.

Keywords: *Psoralea corylifolia;* Depression; Tail suspension test; Forced swimming test

1. INTRODUCTION

Psoralea corylifolia has long been used in traditional *Ayurvedic* and Chinese medicine. This plant is pharmacologically studied for its chemoprotective, antioxidant, anti-microbial, and anti-inflammatory properties. The plant of immense biological importance has been exploited since ages against several skin diseases, such as psoriasis, leukoderma, and leprosy[1]. The trade name of *Psoralea corylifolia* is babchi and bakuchi[2]. The plant possesses potent inhibitory activity against 4 species of fungi viz. *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum* and *Microsporum gypseum*[3,4]. The active compound (+) bakuchil 1 exhibited anti-tumoral property *in vitro*[5]. The pure compound 6-(3-methyl but -2-enyl) 6-7 dihydroxy coumestan 1 isolated from chloroform extract of the seed of *Psoralea corylifolia* L. was evaluated for the pesticidal activity against both adults and different instars of *Tribolium casteneum* Hebrst[6]. The chloroform extract of seed was effective against carrageen induced paw edema in rat and mouse ear inflammation[7], anti-helmintic activity using two-enzyme system taking rat brain as a model for *Ascaridia galli*[8]. The aqueous extract of seed furnished one hepatoprotective compound, bakuchiol 1, together with two moderately active compounds, bakuchicin 2 and psoralen 3, on tacrine-induced cytotoxicity in human liver- derived Hep G-2 cells[9]. The fruit extracts exhibited osteoblastic proliferation stimulating activity. Corylin and bavachin compounds from *Psoralea corylifolia* might stimulate bone formation and have potential activity against osteoporosis[10]. These phenolic compounds in *Psoralea corylifolia* were shown to be effective in protecting biological membranes against various oxidative stresses[11]. Bioassay directed purification of the active compounds led to the isolation of the new compound corylifolin 1 and the known compounds led to the isolation of the new compound bakuchiol 2 as DNA polymerase inhibitors[12].

The seed of *Psoralea corylifolia* has significant medicinal properties and is a rich source of isoflavones, daidzein (40, 7-dihydroxyisoflavone) and genistein (40, 5, 7 trihydroxyisoflavone). In view of the action of natural dietary estrogens, they are recognised as potentially health-protective food compounds, which provide health benefits, including the prevention of sex hormone related ailments, cancer and cardiovascular diseases[13]. Isoflavones also exert antioxidant properties thereby provide protective effect against oxidative damage[14,15] and they are used in the treatment of various skin diseases. Traditionally, the plant is used both internally as well as externally. The seed oil is extremely beneficial, externally in numerous skin ailments. Seeds yield essential oil, psoralen, resin, a terpenoid oil, isopsoralen and psoralidin. Seeds also contain a crystalline solid, a furocoumarin, from the pericarp, psoralidin and isopsoralen have been identified. Psoralen are active principle for inducing pigmentation[13,16-17,19].

The depression criteria has gradually developed as documented by both the American Psychiatric Association (Diagnostic and Statistical Manual of Mental Disorders, DSM- IV, 1994) and the World Health Organisation Geneva (International Classification of Diseases, ICD-10, 1993), providing essential guidance for both clinicians and researchers.

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2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Plant Materials and Extraction

The *Psoralea corylifolia* seeds purchased from local market was powdered and soaked in absolute alcohol for 24 h at room temperature and allowed to constant shaking using mechanical shaker. After 24 h, the seeds were filtered through filter paper in order to collect the extract of psoralea. The seeds were again soaked in absolute ethanol for 24 h and the process of soaking and filtration was repeated till the colour of the seed is fainted. The filtrate collected in a flask was concentrated in the rotary flash evaporator. Sufficient extracts were prepared by this method for chemical and biochemical evaluation.

2.2 Methods

2.2.1 Experimental Animals

The animal experiments, male Balb/c mice weighing about 20 g - 25 g were used. These mice had free access to laboratory feed and water under standard laboratory conditions. The animals used in the present study were maintained in accordance with the guidelines of National Institute of Nutrition, India and approved by Institutional Animal Ethics Committee (IAEC). Experiments was carried out between 1 pm - 3 pm For the behavioral test, different doses of the extract were separately suspended in a vehicle comprising 1% (w/v) tween 20 in distilled water and a standard drug (amitriptyline and fluoxetine) were given by gastric gavage once a day over a period of 1 day, 3 days, 7 days, 14 days, and 21 days. Behavioral test was conducted 1 h after the last treatment/administration.

2.2.2 Forced Swimming Test

48 mice were randomly divided into 6 groups comprising of 8 mice in each group (Table 1.) and treated as follows: Group 1 served as normal control and group 2 received tween-80 suspensions and served as experimental control (FST group). Group 3-5 were orally administered with various doses of PCE extract (75 mg, 150 mg, and 300 mg extract/kg of body weight) and group 6 and 7 received standard anti-depressant drug-amitriptyline and fluoxetine (10 mg/kg body weight).

PCE extract was suspended in a vehicle comprising 1 per cent (w/v) tween 20 in distilled water (75 mg, 150 mg, and 300 mg extract/kg of body weight).

The FST conducted in mice was same as that described by Bhattacharya and Satyan[20]. All the groups of mice were subjected to swimming test except group 1 in a cylindrical glass aquarium (20 cm x 14 cm diameter), containing 25±2 ºC water. Mice were allowed to swim for 6 min and the duration of immobility was measured during the final 4 min interval of the test using a video tracking system. Immobility period was regarded as the time spent by the mouse floating in the water without struggling and making only those movements necessary to keep its head above the water. Following swimming sessions, they were then towel dried. In order to determine the time-dependent effects on immobility time, oral treatments with PCE for 1 day, 3 days, 7 days, 14 days, and 21 consecutive days were investigated. Animals were sacrificed on the last day of the experiment and bled between 1 pm - 3 pm to avoid the variation on the hormonal levels due to circadian rhythms. Blood was collected and plasma was separated in a refrigerated centrifuge at 4 °C.

Table 1. Experiment animal groups

Animal groups	Treatment
Group 1	Normal control
Group 2	Tween-20 suspensions + FST
Group 3	PCE (75mg/kg b wt.) + FST
Group 4	PCE (150mg/kg b wt.) + FST
Group 5	PCE (300mg/kg b wt.) + FST
Group 6	Amitriptyline (10mg/kg b wt.) + FST
Group 7	Fluoxetine (10mg/kg b wt.) + FST

2.2.3 Tail Suspension Test

Forty eight mice were randomly divided into 6 groups consisting of 8 mice in each groups as shown in Table 2 and treated as follow: Group 1 served as normal control and group 2 received tween-20 suspensions (TST group). Group 3-5 were orally administered with various doses of PCE extract suspended in a vehicle comprising 1 per cent (w/v) tween 20 in distilled water (75 mg, 150 mg, and 300 mg extract/kg of body weight). Group 6 and group 7 received standard anti-depressant drug-amitriptyline (10 mg/kg b.wt) and fluoxetine (10 mg/kg b.wt).

Table 2. Experiment animal groups

Animal groups	Treatment
Group 1	Normal control
Group 2	Tween-20 suspensions + TST
Group 3	PCE (75mg/kg b wt.) + TST
Group 4	PCE (150mg/kg b wt.) + TST
Group 5	PCE (300mg/kg b wt.) + TST
Group 6	Amitriptyline (10mg/kg b wt.) + TST
Group 7	Fluoxetine (10mg/kg b wt.) + TST

The procedure was employed as that described by Steru[21], *et al.* with slight modifications. Briefly, a box with one side 35 cm was used for the tail suspension test. The front surface of the apparatus was open and each mouse was suspended by fixing the tail in the centre of the upper surface using a tail hanger and non-irritant adhesive tape with the head 5 cm to the bottom. Testing was carried out in a darkened room with minimal background noise for duration of 6 min. The total duration of immobility (total immobility time) was observed and measured during the final 4 min interval of the test period. All test sessions were recorded by a video camera positioned directly above the box. Mice were considered immobile only when they hung passively and completely motionless.

2.2.4 Open Field Test

Spontaneous motor activity was evaluated in open field test as per the method of Bhattacharya & Satyan[20]. The open field apparatus is made up of black plexi glass and consisted of a square 56 cm x 56 cm. The entire apparatus was divided the floor into 16 square of identical dimension. The entire room, except the open field was kept dark during the experiment. One hour after the treatment of vehicle/standard/extract, each animal was placed at one corner of the apparatus and the behavioural aspects were noted in the next 5 min.

Open-field test shows the total distance travelled on the whole of the open-field arena by the mice. Though this

parameter does not reflect changes in emotional behavior, it is important for evaluating the total locomotor activity of the animals during the 5-min trial. The two major behavioral variables evaluated in the open field test were the time spent in the zone of the field and the number of line crossings across the entire zone.

The open-field apparatus was a square, which was demarcated into 16 equal areas. The score locomotion (number of line crossings within 5 min) and rearing frequencies (number of times an animal stood on its hind legs) were recorded. This experiment, the animals received the same drugs and doses as those used when measuring immobility.

2.3 Statistical Analysis

Data are shown as mean ± standard deviation. Comparison between groups was analyzed by ANOVA. The p values less than 0.05 were considered as significantly different.

3. RESULTS AND DISCUSSION

Anti-depressant drugs have little or no effect in healthy individuals. The number of validated animal models for affective disorders is large and still growing. In addition, several minor variations have been applied to each model. A summary of the models can be found in several reviews[4,22-24]. The mouse forced swimming test and tail suspension test are widely used to predict anti-depressant efficacy indicated by immobility time to be reduced by several different classes of anti-depressant drugs[21,25]. The present study investigated the possible time dependent effects on immobility time.

3.1 Effect of PCE, Amitriptyline and Fluoxetine Pre-treatment on Body Weight in Mice (FST and TST Groups)

The effect of extract on the body weight change is presented in Tables 3 and 4. Data shows that there is no difference in body weight gain among all the groups subjected to 1-day, 3-days and 7-days treatment, however there was a slight increase in weight in all groups at 14 days and 21 days of oral administration. The weight gain of mice may be the normal weight gain of rats. It is confirmed that, administration of PCE did not have any effect on the weight of animals.

3.2 Effect of PCE, Amitriptyline and Fluoxetine Pre-treatment on Immobility Time in the Mice (FST and TST Groups)

In FST, mice are forced to swim in a restricted space from which they cannot escape and are induced to a characteristic behavior of immobility. This behavior, reflecting a state of despair is reduced by several agents which are therapeutically effective in human depression. The TST also induces a state of despair in animals like that in FST. This immobility, referred

Table 3. Effect of PCE, amitriptyline and fluoxetine pre-treatment on body weight in mice (FST groups)

Body weight (g) during different treatment period (day(s))		Groups						
		Group 1 (Control)	Group 2 (Stress control)	Group 3 (75 mg/kg b.wt.)	Group 4 (150 mg/kgb. wt.)	Group 5 (300 mg/kg b.wt.)	Group 6 (Amitriptyline 10 mg/kg b.wt)	Group 7 (Fluoxetine 10 mg/ kg b.wt)
1		27.8±2.7	26.6±3.5	29.2±3.1	30.5±2.6	28.5.5±2.6	29.4±3.4	28.3±3.4
3		28.4±3.2	31.8±2.7	28.6±3.5	26.2±3.1	30.5±3.6	27.9±2.6	26.1±2.6
7		30.6±2.8	28.4±3.2	28.4±3.2	27.4±2.4	29.4±2.8	30.2±2.6	27.5±2.6
14	Initial	27.6±3.2	27.9±2.9	27.6±2.9	26.9±2.7	27.7±2.8	29.1±2.9	26.8±3.2
	Final	31.5±2.9	30.4±3.1	30.1±3.0	29.5±2.6	31.3±2.3	31.7±3.1	29.7±2.6
21	Initial	28.4±2.2	28.9±2.5	27.3±3.4	26.2±3.1	29.5±3.2	29.9±2.6	28.1±3.2
	Final	34.3±2.4	33.9±2.9	32.8±2.9	27.4±2.4	33.8±2.9	32.8±3.3	32.4±2.8

Values are presented as the mean ± SD (n=8). There were no significant differences at $p<0.05$.

Table 4. Effect of PCE, amitriptyline and fluoxetine pre-treatment on body weight in mice (TST groups)

Body weight (g) (day(s))		Groups						
		Group 1 (Control)	Group 2 (Stress control)	Group 3 (75 mg/kg b.wt.)	Group 4 (150 mg/kg b.wt.)	Group 5 (300 mg/kg b.wt.)	Group 6 (Amitriptyline 10 mg/kg b.wt)	Group 7 (Fluoxetine 10 mg/kg b.wt)
1		26.4±2.6	27.8±3.2	29.5±2.9	27.8±2.4	29.8±2.4	26.5±3.1	26.3±3.4
3		27.4±3.1	29.7±2.9	28.4±2.4	28.7±2.8	27.6±3.2	26.8±2.8	26.1±2.6
7		27.5±2.8	27.5±2.7	29.3±3.3	29.4±3.1	28.4±2.3	28.7±2.7	27.4±2.3
14	Initial	28.7±2.7	28.5±3.3	28.7±2.4	27.9±2.3	26.5±2.9	26.8±3.2	27.3±3.1
	Final	30.4±3.1	31.7±3.0	31.5±2.6	29.4±2.5	29.7±2.2	29.7±2.6	30.4±2.9
21	Initial	26.4±2.2	26.8±2.9	27.8±3.4	27.4±3.3	30.5±3.1	28.1±3.2	28.2±3.4
	Final	29.3±2.1	29.4±2.5	31.1±2.7	33.4±3.4	34.6±3.1	32.4±2.8	31.4±3.5

Values are presented as the mean ± SD (n=8). There were no significant differences at $p<0.05$.

to as behavioral despair in animals is claimed to reproduce a condition similar to human depression[21,22].

To investigate possible time-dependent effects on immobility time, oral treatments with PCE for 1 day and 3, 7, 14 and 21 consecutive days respectively were investigated under the standardized application schedule preceded by the appropriate vehicle control application.

A reduction in the duration of immobility of animals in the FST reflects their anti-depressant-like performance. PCE administration showed a significant activity to reduce the immobility time at doses of 7 mg/kg, 150 mg/kg, and 300 mg/kg in forced swimming test in dose dependent manner in mice. The effects of PCE, amitriptyline and fluoxetine on immobility in mice FST are presented in Table 5 and TST are presented in table 5.6. respectively. Considering that clinical anti-depressant effects often appear after chronic treatment, PCE was administrated orally for 1 day and consecutively for 3 days, 7 days, 14 days and 21 days respectively for the investigation of the anti-depressant-like property in mice in FST and TST. In these models, PCE there slight decrease in immobility time after 3 days and 7 days treatment and the decrease was non-significant at $p<0.05$. The mice subjected to swimming after PCE pre-treatment for 14 days and 21 days there was a reduction in the duration of immobility compared with stress control and the effect was observed with the classical anti-depressant drug fluoxetine and amitriptyline.

PCE at 300 mg/kg b. wt. exhibited significant decrease in immobility duration after oral treatment for 14-days. After 21-days treatment of PCE, there was a significant treatment effect for dose in immobility time. The maximal effect was observed at 300 mg/kg b.wt. with marked reduction in immobility time was observed in reference with anti-depressants amitriptyline and fluoxetine.

The effect of PCE, amitriptyline and fluoxetine immobility time in the mice TST are presented in Table 6. There was no significant change of immobility time in the mouse subjected to TST and pre-treated with PCE for 1-day and 3-days at the doses from 75and 150 mg/kg .wt. however, there was a slight decrease in immobility in treated groups at 300mg/kg b.wt. PCE produced a decrease in immobility time after 7-day treatment; 300mg/kg b.wt was effective in reducing the time period. After 14-days and 21-days treatment, PCE also significantly exhibited in reducing the duration of immobility at 75, 150 and 300 mg/kg. PCE at 300 mg/kg b.wt. showed maximal effect in TST behavioural in mice. Fluoxetine and amitriptyline resulted in a significant reduction at 10mg/kg b.wt.

FST model is valid for a broad spectrum of anti-depressants mainly including tricyclics and monoamine oxidase inhibitors, which significantly decrease immobility time[4]. When subjected to unavoidable stress mice display of immobility is thought to reflect a state of despair or lowered mood, which reflects depressive illness in humans. It is also assumed that animals have given up the hope of escaping from the restricted area. It has been reported that anti-depressant drugs have the ability to reduce this immobility period in animal model[26,27]. The present results showed that PCE, when administered orally was

Table 5. Effect of PCE, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (FST groups)

Group	Dose mg/kg b.wt	Duration of immobility (s)				
		1 day	3 days	7 days	14 days	21 days
Group 1 (Control)	-	-	-	-	-	-
Group 2 (Stress control)	-	115.2±12.3	105.0±10.3	110.6±10.3	105.1±13.1	108.6±9.9
Group 3	75	105.1±8.6	89.9±6.6^a	92.7±7.6	75.4± 08.1^a	68.2±7.6^a
Group 4	150	99.9±12.6	88.4±8.3^a	78.6±4.3^a	61.7±05.0^a	59.8±6.7^a
Group 5	300	89.5±6.1^a	74.0±5.9^b	66.9±6.7^b	43.8±09.0^b	23.7±5.6^b
Group 6 (Amitriptyline)	10	74.0±5.9^b	64.1±10.5^c	57.5±8.1^c	30.0±12.4^b	15.4±7.9^c
Group 7 (Fluoxetine)	10	81.0±13.6^a	69.7±8.7^b	64.8±5.6^b	37.0±06.6^c	28.4±7.2^b

Values are presented as the mean ± SD (n=8). Values bearing different superscripts in the same column are significantly different ($p<0.05$) (ANOVA).

Table 6. Effects of PCE, amitriptyline and fluoxetine pre-treatment on the duration of immobility in the mice (TST groups)

Group	Dose	Duration of immobility (s)				
	mg/kg b.wt.	1 day	3 days	7 days	14 days	21 days
Group 1 (Control)	-	-	-	-	-	-
Group 2 (Stress control)	-	98.1±8.9	97.4±10.3	102.4± 8.7	99.7±10.1	101.3±12.4
Group 3	75	90.5±8.6	91.4±8.9	87.7± 6.7^a	77.6±8.8^a	71.5±9.2^a
Group 4	150	89.9±12.6	83.2±7.2	80.6± 7.6^a	69.8±7.6^a	62.7±7.9^a
Group 5	300	89.6±6.1	74.5±8.4^a	71.8± 6.7^b	59.4±8.1^b	54.7±9.3^b
Group 6 (Amitriptyline)	10	84.0±5.9	68.7±11.1^a	62.4±10.4^b	52.7±10.4^b	47.4±8.9^b
Group 7 (Fluoxetine)	10	82.8±13.6	73.4±7.6^a	67.5±9.7^b	54.0±6.6^b	49.4±5.9^b

Values are presented as the mean ± SD (n=8). Values bearing different superscripts in the same column are significantly different ($p<0.05$) (ANOVA).

effective in producing significant anti-depressant-like effects in these models. On the immobility behavioral measure, PCE showed clear dose-response pattern among the treatment period in the mouse FST. The positive anti-depressant amitriptyline and fluoxetine was significant effective after 7 days, 14 days and 21 days treatment. The present study showed that administration of PCE for 14 days and 21 days could significantly reduce the immobility time in FST and TST models compared to stress control in a dose-dependent manner.

3.3 Effect of PCE Pre treatment on Locomotor Activity

To detect any association of immobility in the FST and TST with changes in motor activity, the locomotor behaviours of animals treated with PCE were tested in an open field. Open field test was arranged to avoid the effects on locomotor activity caused by central nervous system stimulants. The results showed that all the doses in FST and TST did not significantly change locomotor activity.

Table 7 shows the results obtained with open field test. The treatment of animals with 14 days and 21 days showed no differences compared with control animals in the number of crossing and rearing in the 5 min open field test at the dose. Open-field test shows the total distance travelled in the whole of the open-field arena by the mice. Though this parameter does not reflect changes in emotional behavior, it is important for evaluating the total locomotor activity of the animals during the 5 min trial. The two major behavioral variables evaluated in the open field test were the time spent in the zone of the field and the number of line crossings across the entire zone. Novel object test model investigates the approach avoidance behaviors of mice in response to novel stimuli[28].

In FST and TST, false-positive results can be obtained with certain drugs in particular psychomotor stimulants, which decrease immobility time by stimulating locomotor activity[29]. Changes in the duration of immobility could also result from effects on locomotor activity caused by central nervous system stimulants the mice were tested in the open field test just before FST. The results showed that PCE, at the given dose (300 mg/kg b.wt.) produced an anti-depressant like effect, did not significantly change locomotor behavior. Therefore PCE appears to produce a specific anti-depressant-like behavioral effect and was not associated with the locomotor effects.

The present investigation demonstrated the anti-depressant activity in behavioral despair models of animals viz. forced swimming test and tail suspension test the widely used models to predict anti-depressant efficacy indicated by immobility time. Detailed investigations are needed to fully elucidate the mechanism of action at cellular level for the bioactive constituents present in the extract. Further pre-clinical and clinical studies seem warranted to assess in more detail possible anti-depressant effects of *Psoralea corylifolia*, and their therapeutic role in the treatment of depression.

Table 7. Effect of PCE, amitriptyline, and fluoxetine pre-treatment on locomotor activity (open field test)

Groups	Dose mg/ kg.b.wt	14 days treatment		21 days treatment	
		Crossing (s/5 min)	Rearing (s/5 min)	Crossing (s/5 min)	Rearing (s/5 min)
Group 1 (Control)	-	80.93±13.5	19.75±2.2	75.08±10.3	20.48±2.8
Group 2 (Stress control)	-	81.25±13.5	19.85±3.5	81.25±11.5	19.85±3.5
Group 3	75	82.48±9.3	17.16±5.3	79.58± 10.4	18.41±2.9
Group 4	150	78.27±12.0	17.85±5.8	77.91±12.6	19.11±1.8
Group 5	300	83.14±11.5	18.5±5.5	80.22±13.5	18.25±3.8
Group 6 (Amitriptyline)	10	80.95±14.7	18.65±2.3	78.45±12.2	18.17±2.5
Group 7 (Fluoxetine)	10	78.67±13.5	18.25±3.3	79.25±13.5	17.63±3.5

Values are presented as the mean ± SD (n=8). There were no significant differences at $p<0.05$.

REFERENCES

1. Sah, P.; Agrawal, D. & Garg, S.P. Isolation and identification of furocoumarins from the seeds of psoralea corylifolia L. *Indian J. Pharma Sci.,* 2006, **68**, 768-71. doi: 10.4103/0250-474X.31012
2. Oudhiya, P. Traditional medicinal knowledge about herb Bemchi(Psoralea corylifolia) in chhatisgarh, India. *Pharmacy*, 2001, **61**(7), 312-332.
3. Jiangning, G.; Xinchu, W.; Hou, W.; Qinghua, L.; & Kaishun, B. Antioxidants from a Chinese medicinal herb-Psoralia corylifolia L. Phyto-therapy research. 2004, **16**, 539-544.
4. Shaffery, J.; Hoffmann, R. & Armitage, R. The neurobiology of depression: perspectives from animal and human sleep studies. *Neuroscientist*, 2003, **9**(1), 82-98. doi: 10.1177/1073858402239594
5. Prasad, R.; Anandi, C.; Balasubramanian, S. & Pugalendi, K.V. Antidermatophytic activity of extracts from Psoralea corylifolia (fabaceae) correlated with the presence of a flavonoid compound. Journal of ethanopharmacology. 2004, 91, 21-24.
6. Ryu, S.V.; Choi, S.U.; Lee, C.O. & Zee, O.P. Antitumor activity of psoralea corylifolia. *Archives of Pharmacal Research,* 2008, **15**, 356-359. doi: 10.1007/BF02974112
7. Khatune, N.A.; Islam, M.E.; Rahman, M.A.A.; Baki, M.A.; Gadik, G. & Haque, M.E. Pesticidal activity of a novel coumestan derivative isolated from psoralea corylifolia L. Against Tribolium casteneum Herbst. Adults and Larvae (coleptera : Tenebrionidae). *Pakistan J. Agronomy*, 2002, (4), 112-115.
8. Forestieri, A.M.; Monfortre, M.T.; Ragusa, S.; Trovato, A. & Lauk, L. Antiinflammatory analgesic and antipyretic activity in rodents of plant extract used

in African medicine. *Phytother Res.,* 1996, **10**(2), 100-103.
doi: 10.1002/(SICI)1099-1573(199603)10:2<100::AID-PTR724>3.0.CO;2-I

9. Shilaskar, D.V. & Parasar, G.C. Studies on effect of *Psoralea corylifolia* and piper bettle on cholinesterase and succinil dehydrogenase. Enzymes as possible targets of their anthelmintic action. *Planta Med.* 2001, **62**(7), 557-62.
10. Cho, H.; Jun, J.Y.; Song, E.K.; Kang, K.H.; Baek, H.Y.; Kd, Y.S. & Kim, Y.C. Bakuchiol : A hepatoprotective compound of *Psoralea corylifolia* on tacrine – induced cytotoxicity in Hep G2 cells. *Planta Med.,* 2001, **67**, 784 -749.
doi: 10.1055/s-2001-18347
11. Wand, D.; Famei, H. & Jiang, Z. Osteoblastic proliferation stimulatin activity of *Psoralea corylifolia* extracts and two of its flavonoids. *International Immunopharmacology*, 2001, **1**, 1849 -1855.
12. Sun, N.J.; Woo, S.H.; Cassady, J.M. & Snapka, R.M. DNA polymerase and topoisomerase II inhibitors from *Psoralea corylifolia*. *Nat. Prod.,* 1998, **61**,362-366.
doi: 10.1021/np970488q
13. Shinde, A.N.; Malpathak, N. & Fulzele, D.P. Induced high frequency shoot regeneration and inhanced isoflevonces productin in *Psoralia corylifolia*. *Rec. Nat. Prod.,* 2009, **3**,38-45.
14. Akitha Devi, M.K.; Gondi, M.; Sakthivelu, G.; Giridhar, P.; Rajasekaran, T. & Ravishankar, G.A. Functional attributes of soybean seeds and products, with reference to isoflavone content and antioxidant activity. *Food Chemistry*, 2009, **114**, 771–776.
doi: 10.1016/j.foodchem.2008.10.011
15. Slavin, M.; Cheng, Z.; Luther, M.; Kenworthy, W. & Yu, L. Antioxidant properties and phenolic, isoflavone, tocopherol and carotenoid composition of Maryland-grown soybean lines with altered fatty acid profiles. *Food Chemistry*, 2009, **11**, 420-427.
16. Zhao, L.H.; Wu, M.H. & Xiang, B.R. Analysis of *Psoralea corylifolia* L. fruits in different regions. *Chem. Pharm. Bull., (Tokyo)*, 2005.
17. Xu, Q.; Pan, Y.; Li, Y.; Mo, S.; Jiang, F.; Qiao, C.; Xu, H.; Lu, X.; Kong, L. & Kung, H. Antidepressant-like effects of psoralen isolated from the seeds of *Psoralea corylifolia* in the mouse forced swimming test. *Biol. Pharm. Bull.*, 1995, **31**, 1109-1114.
doi: 10.1248/bpb.31.1109
18. Yin, S.; Fan, C.Q.; Wang, Y.; Dong, L. & Yue, J.M. Antibacterial prenylflavone derivatives from *Psoralea corylifolia*, and their structure-activity relationship study. *Bioorg. Med. Chem*., 2004.
19. Rajput, S.J.; Vijaya, Z. & Pallavi, R. Studies on extraction, isolation and estimation of *Psoralea corylifolia*. *Pharmaco. Magazine*., 2008, **4**, 13.
20. Bhattacharya, S.K. & Satyan, K.S. Experimental methods for evaluation of psychotropic agents in rodents. *Ind. J. Exp. Biol.,* 1997, **35**, 565-75.
21. Steru, L.; Chermat, R.; Thierry, B. & Simon, P. The tail suspension test: a new method for screening antidepressants in mice. *Psychopharmacology*, 1985, **85**, 367-370.
doi: 10.1007/BF00428203
22. Willner, P. Validity, reliability and utility of the chronic mild stress model of depression: a 10-year review and evaluation. *Psychopharmacology (Berl).,* 1997, **134**(4), 319-29.
doi: 10.1007/s002130050456
23. Cryan, J.F.; Markou, A. & Lucki, I. Assessing antidepressant activity in rodents: recent developments and future needs. *Trends Pharmacol Sci*., 2002, **23**, 238-245.
doi: 10.1016/S0165-6147(02)02017-5
24. Nestler, E.J.; Barrot, M.; Dileone, R.J.; Eisch, A.J.; Gold, S.J. & Monteggia, L.M. Neurobiology of depression. *Neuron.,* 2002, **3**(4), 13-25.
doi: 10.1016/S0896-6273(02)00653-0
25. Porsolt, R.D.; Le Pichon, M. & Jalfre, M. Depression: a new animal model sensitive to antidepressant treatments. *Nature*., 1977, **266**, 730-732.
doi: 10.1038/266730a0
26. Lucki, I. The forced swimming test as a model for core and component behavioral effects of antidepressant drugs. *Behavioural Pharmacol*, 1997, **8**, 523-532.
doi: 10.1097/00008877-199711000-00010
27. Dhingra, D. & Sharma, A. Evaluation of antidepressant-like activity of glycyrrhizin in mice. *Ind. J. Pharmacol*, 2005, **37**, 390-394.
doi: 10.4103/0253-7613.19077
28. Powell, S.B.; Geyer, M.A.; Gallagher, D. & Paulus, M.P. The balance between approach and avoidance behaviors in a novel object exploration paradigm in mice. *Behavioural Brain Res.*, 2004, **152**, 341-9.
doi: 10.1016/j.bbr.2003.10.020
29. Bourin, M.; Fiocco, A.J. & Clenet, F. How valuable are animal models in defining antidepressant activity? *Human Psychopharmacol*, 2001, **16**, 9–21.
doi: 10.1002/hup.178

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