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# Evaluation of antidepressant-like activity of aqueous and ethanolic extracts of *Terminalia bellirica* Roxb. fruits in mice

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The present study was undertaken to investigate the effect of aqueous and ethanolic extracts of *T. bellirica* on depression in mice using forced swim test (FST) and tail suspension test (TST). The extracts were administered orally for 10 successive days in separate groups of Swiss young male albino mice. Aqueous extract (50, 100 and 200 mg/kg) in a dose-dependent manner and ethanolic extract (100 mg/kg) significantly reduced the immobility time of mice in both FST and TST. The extracts were without any significant effect on locomotor activity of mice. The efficacies of aqueous extract (200 mg/kg) and ethanolic extract (100 mg/kg) were found to be similar to that of imipramine (15 mg/kg, po) and fluoxetine (20 mg/kg, po) administered for 10 successive days. Both extracts reversed reserpine-induced extension of immobility period of mice in FST and TST. Prazosin (62.5 μg/kg, ip; an $\alpha_1$-adrenoceptor antagonist), sulpiride (50 mg/kg, ip; a selective $D_2$ receptor antagonist) and p-chlorophenylalanine (100 mg/kg, ip; an inhibitor of serotonin synthesis) significantly attenuated the aqueous and ethanolic extract-induced antidepressant-like effect in TST. Thus, both the aqueous and ethanolic extracts of *T. bellirica* elicited a significant antidepressant-like effect in mice by interaction with adrenergic, dopaminergic and serotonergic systems.

**Keywords**: Antidepressant, Forced swim test, Reserpine, Tail suspension test, *Terminalia bellirica*

*Terminalia bellirica* Roxb. (Family: Combretaceae) also known as Bahera in Hindi, is one of the important constituents of Indian preparation Triphala (the other two constituents being *Terminalia chebula* and *Emblica officinalis*). Fruits of *Terminalia bellirica* (TB) contain about 17% tannin and β-sitosterol, gallic acid, ellagic acid, ethyl gallate, galloyl glucose and chebulagic acid[1]. The fruits are useful in cough, hoarseness, eye disease, scorpion sting etc. when given along with salt and long pepper[2]. The fruit is bitter, astringent, laxative, antipyretic, analgesic and brain tonic. It is chiefly used in piles, dropsy, diarrhea and leprosy[3]. It cures tuberculosis, nose, throat, heart diseases and impurity of blood and fat[4]. The fruits exhibited bronchodilatory, antispasmodic, antiasthmatic[5], hepatoprotective[6] and spermicidal activities[7]. Alcoholic extract of the fruits showed antistress and endurance promoting properties in hypoxia test in mice and swimming performance test in rats[8]. Ethanolic extract of fruits possessed hypoglycemic activity in alloxan-induced diabetes in rats[9] and amoebicidal activity *in vitro*[10]. Aqueous, hexane and alcoholic extracts of the fruits showed significant antimicrobial activity[11]. Alcoholic and aqueous extract of fruits possessed antifungal activity against the pathogenic yeast, *Candida albicans* and dermatophytes[12]. Aqueous extract of the fruits showed negative chronotropic, negative inotropic, hypotensive[13], hypolipidemic[14] and antioxidant activities[15].

In light of above information, the present study has been undertaken (i) to study the effect of the aqueous and ethanolic extracts of fruits of TB on depression in mice employing forced swim test and tail suspension test and (ii) to explore the possible underlying mechanisms of antidepressant-like activity of the extracts. Standard antidepressant drugs like fluoxetine, a selective serotonin reuptake inhibitor, and imipramine, a tricyclic antidepressant were employed to standardize the animal models of depression and to compare the antidepressant efficacy of the extracts. (±) Sulpiride (a $D_2$ - receptor antagonist), prazosin (a $\alpha_1$-adrenoceptor antagonist), p-chlorophenylalanine (a serotonin synthesis inhibitor) and reserpine were used to evaluate the probable mechanisms of antidepressant-like effect of TB extracts in mice.

## Materials and Methods

*Animals* — Swiss male albino mice (3 months old and

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weighing around 20-30 g) were procured from Disease Free Small Animal House, CCS Haryana Agricultural University, Hisar (Haryana, India). There is no significant effect of sex variation of mice in the induction of depression models[16]. Animals had free access to food and water, and were maintained under standard laboratory conditions with alternating light and dark cycles of 12 hr each. The food was withdrawn 1hr before and 2hr after administration of drugs to mice. The animals were acclimatized for at least 5 days before behavioral experiments. Experiments were carried out between 1000 to 1700 hrs. The experimental protocol was approved by the Institutional Animals Ethics Committee (IAEC) and care of laboratory animals was taken as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Govt. of India (Registration Number- 0436).

*Drugs and chemicals* — The dried fruits of *Terminalia bellirica* Roxb. were purchased from commercial source. The crude drug was authenticated by Raw Materials, Herbarium and Museum, NISCAIR, New Delhi (voucher specimen number 584/64). The dried fruits were crushed to make coarse powder.

Fluoxetine hydrochloride (FLUDAC®, Cadila Pharmaceuticals, Ahmedabad, India), reserpine (Otto Kemi, Mumbai, India), acetic acid glacial (Central Drug House (P) Ltd., New Delhi, India), sodium hydroxide pellets (Hi-Media, Mumbai, India), Tween 80 (Loba Chemie, Mumbai, India), carboxy methyl cellulose (Hi-Media, Mumbai, India), (±) sulpiride, prazosin hydrochloride, DL-p-chlorophenylalanine, imipramine hydrochloride (Sigma-Aldrich, St. Louis, USA) were used in the present study.

**Preparation of extracts of fruits of *T. bellirica***

*Ethanolic extract* — Coarse powder (1 kg) of fruits of *T. bellirica* was imbibed in ethanol (95%) and kept for 24 hr. Then, this moistened drug was extracted with ethanol (95%) at 70°C using Soxhlet Apparatus for 48 hr. The extract was collected and ethanol was distilled off. The extract was evaporated to dryness in vacuum and stored in a refrigerator. The yield of extract was 26.05%.

*Aqueous extract* — Coarse powder (450 g) of fruits was extracted with distilled water by double maceration for 48 hr. The extract was filtered through muslin cloth. The filtrate was evaporated to dryness in vacuum and kept in a refrigerator. The yield of extract was 26.63%.

*Vehicle* — The aqueous extract of TB was dissolved in 0.25% w/v carboxymethylcellulose. The ethanolic extract was emulsified in 10% v/v Tween 80. Fluoxetine, imipramine and prazosin were dissolved separately in normal saline (0.9% sodium chloride). Sulpiride was dissolved in normal saline followed by addition of one drop of glacial acetic acid. p-Chlorophenylalanine (p-CPA) was dissolved in minimum quantity of 0.1 *N* sodium hydroxide and *p*H was adjusted to 7 with 0.1 *N* hydrochloric acid. Reserpine (2 mg) was dissolved in a drop of acetic acid glacial. The volume was made up with distilled water, giving a solution with *p*H 3.3. The *p*H was adjusted with 5 drops of 1 *N* sodium hydroxide, giving a solution with *p*H 5.4. The volume for oral administration and intraperitoneal injection was 1 ml/100 g of mouse.

**Tests for evaluating antidepressant activity**

*Forced swim test (FST)* — Forced swim test was proposed as a model to test for antidepressant activity by Porsolt *et al*[17]. The procedure was same as followed earlier[18,19]. Mice were forced to swim individually in a glass jar (25 × 12 × 25 $cm^3$) containing fresh water of 15 cm height and maintained at 25°C (± 3°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. The total duration of immobility was recorded during the next 4 min of a total 6 min test. The changes in immobility periods were studied after administering drugs in separate groups of animals. Each animal was used only once.

*Tail suspension test (TST)* — The total duration of immobility induced by tail suspension was measured according to the method described earlier[18-20] as a means of evaluating potential antidepressants. Mice were suspended on the edge of a table 50 cm above the floor by the adhesive tape placed approximately 1 cm from the tip of the tail. Immobility time was recorded during a 6 min period[21]. Animal was considered to be immobile when it did not show any movement of body and hanged passively.

*Drug protocol* —Animals were divided into 39 groups and each group comprised a minimum of 5 animals each (Table 1)

Table 1— Drug protocol

| Group No. | Treatment |
|---|---|
| | Forced swim test (FST) |
| I | Control group (vehicle for aqueous extract): 0.25% w/v carboxy methyl cellulose (CMC) was administrated orally for 10 successive days. At 90 min after administration on $10^{th}$ day, immobility period was recorded. |
| II | Control group (vehicle for ethanolic extract): 10% v/v Tween 80 was administrated orally for 10 successive days. At 90 min after administration on $10^{th}$ day, immobility period was recorded. |
| III and IV | Fluoxetine (20 mg/kg) and imipramine (15 mg/kg) respectively were administrated orally for 10 successive days. At 90 min after administration on $10^{th}$ day, immobility period was recorded. |
| V, VI and VII | Aqueous extract of TB (50, 100 and 200 mg/kg, respectively) was administered orally for 10 successive days. At 90 min after administration on $10^{th}$ day, immobility period was recorded. |
| VIII, IX and X | Ethanolic extract of TB (50, 100 and 200 mg/kg, respectively) was administered orally for 10 successive days. At 90 min after administration on $10^{th}$ day, immobility period was recorded. |
| | Tail suspension test (TST) |
| XI to XX | Which group of FST except that immobility period was recorded using TST. |
| XXI | 0.25% CMC (vehicle for aqueous extract) was administered orally for 10 successive days and then sulpiride (50 mg/kg, ip) was injected on $10^{th}$ day after 45 min of last oral administration of vehicle. The animals were subjected to TST after 45 min of sulpiride injection. |
| XXII | Aqueous extract of TB (200 mg/kg) was administered orally for 10 successive days and then sulpiride (50 mg/kg, ip) was injected on $10^{th}$ day after 45 min of last oral administration of TB extract. The animals were subjected to TST after 45 min of sulpiride injection. |
| XXIII | Vehicle for aqueous extract was administered orally for 10 successive days and then prazosin (62.5 μg/kg, ip) was administered on $10^{th}$ day after 45 min of last vehicle administration. The animals were subjected to TST after 45 min of prazosin injection. |
| XXIV | Aqueous extract of TB (200 mg/kg) was administered orally for 10 successive days and then prazosin (62.5 μg/kg, ip) was administered on $10^{th}$ day after 45 min of last oral administration of TB extract. The animals were subjected to TST after 45 min of prazosin injection. |
| XXV | Vehicle for aqueous extract was administered orally for 10 consecutive days. p-CPA (100 mg/kg, ip) was administered from $7^{th}$ day to $10^{th}$ day after 45 min of vehicle administration. The animals were subjected to TST after 45 min of p-CPA injection on $10^{th}$ day. |
| XXVI | Aqueous extract of TB (200 mg/kg) was administered orally for 10 consecutive days. p-CPA (100 mg/kg, ip) was administered from $7^{th}$ day to $10^{th}$ day after 45 min of each oral administration of extract. The animals were subjected to TST after 45 min of p-CPA injection on $10^{th}$ day. |
| XXVII | Fluoxetine (20 mg/kg) was administered orally for 10 successive days to mice. From $7^{th}$ day to $10^{th}$ day, p-CPA (100 mg/kg, ip) was administered after 45 min of injection of fluoxetine. The animals were subjected to TST after 45 min of p-CPA injection on $10^{th}$ day. |
| XXVIII | Vehicle for ethanolic extract + sulpiride; rest was same as in group XXI. |
| XXIX | Ethanolic extract of TB (100 mg/kg) + sulpiride; rest was same as in group XXII. |
| XXX | Vehicle for ethanolic extract + prazosin; rest was same as in group XXIII. |
| XXXI | Ethanolic extract of TB (100 mg/kg) +prazosin; rest was same as in group XXIV. |
| XXXII | Vehicle for ethanolic extract + p-CPA; rest was same as in group XXV. |
| XXXIII | Ethanolic extract of TB (100 mg/kg) + p-CPA; rest was same as in group XXVI. |
| XXXIV | Vehicle for aqueous extract of TB was administered orally for 10 successive days. Reserpine (2 mg/kg) was injected ip on $10^{th}$ day. After 3 hr of reserpine injection, vehicle was administered orally. After 60 min of vehicle administration, animals were subjected to TST. Mice were again tested in TST after 24 hr of reserpine injection. |
| XXXV | Aqueous extract of TB (200 mg/kg) was administered orally for 10 successive days. Reserpine (2 mg/kg) was injected ip on $10^{th}$ day. After 3 hr of reserpine injection, TB extract was administered orally. After 60 min of TB extract administration, animals were subjected to TST. Mice were again tested in TST after 24 hr of reserpine injection. |
| XXXVI | Vehicle for ethanolic extract + reserpine; rest was same as in group XXXIV. |
| XXXVII | Ethanolic extract of TB (100 mg/kg) + Reserpine: Rest was same as in group XXXV. |
| | Locomotor activity |
| XXXVIII and XXXIX | Effect of aqueous extract (200 mg/kg, po) and ethanolic extract (100 mg/kg, po) of TB on locomotor function of mice were studied using photoactometer (INCO, Ambala, India) to rule out the increase in locomotor performance of mice due to the extract. The difference in the locomotor activity scores were noted before and after administration of TB extract. |

*Statistical analysis* — All results are expressed as mean ± SE. Data were analyzed by one-way ANOVA followed by Dunnett's test. The data for reserpine treated groups (Tables 6 and 7) were subjected to Student's unpaired *t*-test, while data for locomotor activity scores were subjected to Student's paired *t*-test. In all the tests, the criterion for statistical significance was $P < 0.05$.

## Results

*Effect of aqueous and ethanolic extracts of TB on immobility periods in TST and FST* — Aqueous extract (50, 100 and 200mg/kg, po) administered for 10 successive days to mice decreased the immobility periods significantly in a dose-dependent manner in both TST and FST, indicating significant antidepressant-like activity. Among three doses administered for 10 days, a dose of 200 mg/kg, po of aqueous extract showed most potent antidepressant-like activity as indicated by highest decrease in immobility period. On the other hand, low dose (50 mg/kg) of ethanolic extract administered for 10 successive days to mice did not show significant effect on immobility period when compared to control group while the highest dose (200 mg/kg) of the ethanolic extract increased the immobility period significantly in both TST and FST. While middle dose (100 mg/kg) of the ethanolic extract significantly reduced the immobility period as compared to control in both TST and FST, indicating significant antidepressant-like activity. Fluoxetine (20 mg/kg, po) and imipramine (15 mg/kg, po) administered for 10 days significantly reduced the immobility period as compared to control. The efficacy of aqueous extract (200mg/kg) and ethanolic extract (100 mg/kg) was found to be comparable to fluoxetine and imipramine in both FST and TST (Tables 2, 3).

*Effect of combination of aqueous and ethanolic extracts of TB with sulpiride, prazosin, p-CPA and reserpine on immobility period in TST* —Sulpiride (50 mg/kg, ip), prazosin (62.5 mg/kg, ip) and p-CPA (100 mg/kg, ip) alone significantly increased the immobility period as compared to control group. Pretreatment of animals with sulpiride or prazosin or p-CPA significantly blocked the decrease of immobility time elicited by aqueous extract (200

Table 2 — Effect of *T. bellirica* (TB) extract on immobility period of mice using forced swim test (FST) [Values are mean ± SE]

| Group No. | Treatment for 10 days, po | Number of animals | Dose ($kg^{-1}$) | Immobility period (sec) |
|---|---|---|---|---|
| I | Vehicle for aqueous extract (0.25% w/v CMC) | 6 | 10 ml | 175.5 ± 3.5 |
| II | Vehicle for ethanolic extract (10% v/v Tween 80) | 7 | 10 ml | 176.7 ± 3.9 |
| III | Fluoxetine | 6 | 20 mg | 149.8 ± 2.7[a] |
| IV | Imipramine | 5 | 15 mg | 138.4 ± 3.3[a] |
| V | TB extract (aqueous) | 6 | 50 mg | 154.0 ± 2.8[a] |
| VI | TB extract (aqueous) | 5 | 100 mg | 151.8 ± 4.9[a] |
| VII | TB extract (aqueous) | 5 | 200 mg | 119.2 ± 3.3[a] |
| VIII | TB extract (ethanolic) | 6 | 50 mg | 176.8 ± 2.1 |
| IX | TB extract (ethanolic) | 5 | 100 mg | 155.0 ± 3.1[b] |
| X | TB extract (ethanolic) | 6 | 200 mg | 196.7 ± 1.9[b] |

Statistical analysis of data was carried out by one-way ANOVA followed by Dunnett's t-test. $F(9, 47) = 46.61$; $P < 0.0001$
$P < 0.05$ when compared with vehicle for [a] aqueous extract group; [b] ethanolic extract group

Table 3 —Effect of TB extract on immobility period of mice using tail suspension test (TST) [Values are mean ± SE]

| Group No. | Treatment for 10 days po | Number of animals | Dose ($kg^{-1}$) | Immobility period (sec) |
|---|---|---|---|---|
| XI | Vehicle for aqueous extract (0.25% w/v CMC) | 6 | 10 ml | 193.3 ± 2.6 |
| XII | Vehicle for ethanolic extract (10% v/v Tween 80) | 7 | 10 ml | 195.7 ± 4.3 |
| XIII | Fluoxetine | 6 | 20 mg | 149.2 ± 6.7[a] |
| XIV | Imipramine | 5 | 15 mg | 146.6 ± 2.2[a] |
| XV | TB extract (aqueous) | 6 | 50 mg | 182.2 ± 2.0[a] |
| XVI | TB extract (aqueous) | 5 | 100 mg | 159.2 ± 3.2[a] |
| XVII | TB extract (aqueous) | 5 | 200 mg | 96.4 ± 3.9[a] |
| XVIII | TB extract (ethanolic) | 6 | 50 mg | 194.7 ± 2.2 |
| XIX | TB extract (ethanolic) | 5 | 100 mg | 152.6 ± 2.6[b] |
| XX | TB extract (ethanolic) | 6 | 200 mg | 221.7 ± 5.4[b] |

Statistical analysis of data was carried out by one-way ANOVA followed by Dunnett's t-test. $F(9, 47) = 77.96$; $P < 0.0001$
$P < 0.05$ when compared with vehicle for [a] aqueous extract group; [b] ethanolic extract group

mg/kg) and ethanolic extract (100 mg/kg). Pretreatment of mice with p-CPA (100 mg/kg) significantly blocked the decrease of immobility period by fluoxetine (Tables 4 and 5).

Reserpine (2 mg/kg, ip) induced significant increase in immobility period after 4 and 24 hr of its administration in TST. Aqueous extract (200 mg/kg) and ethanolic extract (100 mg/kg) administered orally for 10 successive days significantly reversed the reserpine-induced extension of immobility period after 4 and 24 hr as compared to reserpine alone (Tables 6 and 7).

*Effect on locomotor activity* —Aqueous extract (200 mg/kg, po) administered for 10 successive days did not show any significant change in locomotor function of mice (381 ± 9.1) as compared to the control (386.3 ± 8.1). Ethanolic extract (100 mg/kg, po) administered for 10 successive days also did not show any significant change in the locomotor function of mice (251.7 ± 8.9) as compared to the control (254.3 ± 8.0).

## Discussion

In the present study, aqueous extract (200 mg/kg) and ethanolic extract (100 mg/kg) of TB produced significant antidepressant-like effect in mice in both TST and FST and its efficacy was found to be similar to fluoxetine and imipramine. Both the models of depression are widely used to screen new antidepressant drugs[17,20]. These tests are quite

Table 4 — Effect of combination of aqueous extract of TB with sulpiride, prazosin and p-CPA on immobility period in TST
[Values are mean ± SE]

| Group No. | Treatment for 10 days | Number of animals | Dose ($kg^{-1}$) | Immobility period (sec) |
|---|---|---|---|---|
| XI | Vehicle (0.25% w/v CMC) | 6 | 10 ml | 193.3 ± 2.6 |
| XVII | TB extract (aqueous) | 5 | 200 mg | 96.4 ± 3.9[a] |
| XXI | Vehicle + sulpiride | 6 | 10ml 50 mg | 228.3 ± 4.9[a] |
| XXII | TB extract (aqueous)+ sulpiride | 6 | 200mg 50 mg | 226.7 ± 5.3[b] |
| XXIII | Vehicle + prazosin | 6 | 10ml 62.5 µg | 219.8 ±3.9[a] |
| XXIV | TB extract (aqueous) + prazosin | 6 | 200mg 62.5 µg | 215.2 ±3.9[b] |
| XXV | Vehicle + p-CPA | 6 | 10ml 100 mg | 211.8 ± 3.8[a] |
| XXVI | TB extract (aqueous) + p-CPA | 6 | 200mg 100 mg | 196.2 ± 2.8[b] |
| XIII | Fluoxetine | 6 | 20 mg | 149.2 ± 6.7[a] |
| XXVII | Fluoxetine + p-CPA | 6 | 20mg 100 mg | 195.0 ± 3.8[c] |

Statistical analysis of data was carried out by one-way ANOVA followed by Dunnett's t-test. F (9, 49) = 96.88; P< 0.0001
*P*< 0.05 as compared to [a] vehicle [b] TB extract [c] fluoxetine alone

Table 5 — Effect of combination of ethanolic extract of TB with sulpiride, prazosin and p-CPA on immobility period in TST
[Values are mean ± SE]

| Group No. | Treatment for 10 days | Number of animals | Dose ($kg^{-1}$) | Immobility period (sec) |
|---|---|---|---|---|
| XII | Vehicle (10% v/v Tween 80) | 7 | 10 ml | 195.7 ± 4.3 |
| XIX | TB extract (ethanolic) | 5 | 100 mg | 152.6 ± 2.6[a] |
| XXVIII | Vehicle + sulpiride | 6 | 10ml 50 mg | 235.2 ± 4.6[a] |
| XXIX | TB extract (ethanolic) + Sulpiride | 6 | 100mg 50 mg | 231.8 ± 5.3[b] |
| XXX | vehicle + prazosin | 6 | 10ml 62.5 µg | 231.2 ±3.7[a] |
| XXXI | TB extract (ethanolic) + prazosin | 6 | 100mg 62.5 µg | 229.5 ±4.0[b] |
| XXXII | vehicle + p-CPA | 6 | 10ml 100 mg | 215.7 ± 3.6[a] |
| XXXIII | TB extract (ethanolic) + p-CPA | 6 | 100mg 100 mg | 217.0 ± 3.0[b] |

Statistical analysis of data was carried out by one-way ANOVA followed by Dunnett's t-test. F (7, 40) = 42.57; *P*< 0.0001
*P*< 0.05 as compared to [a] vehicle; [b]TB extract

sensitive and relatively specific to all major classes of antidepressant drugs[17,20,22]. In TST, immobility reflects a state of despair which can be reduced by several agents which are therapeutically effective in human depression. Similarly in the FST, mice are forced to swim in restricted space from which they cannot escape. This induces a state of behavioral despair in animals, which is claimed to reproduce a condition similar to human depression[23]. It has been seen that the TST is less stressful and has higher pharmacological sensitivity than FST[24].

Both aqueous and ethanolic extracts did not show significant change in locomotor function of mice as compared to control so they did not produce any motor effects. It confirms the assumption that the antidepressant-like effect of the extracts is specific. The precise mechanisms by which TB extracts produced antidepressant-like effect are not completely understood. However according to the present results, the antidepressant-like effect of TB extracts were significantly reversed by the treatment of animals with prazosin (a $\alpha_1$-adrenoceptor antagonist), sulpiride (a selective dopamine $D_2$-receptor antagonist) and p-CPA (a serotonin synthesis inhibitor) when tested in TST. This suggests that TB extracts may produce antidepressant-like effect by increasing the levels of norepinephrine, dopamine and serotonin in brains of mice. p-CPA significantly reversed the antidepressant effect of fluoxetine (a specific serotonin reuptake inhibitor) in TST, suggesting that fluoxetine has antidepressant effect through serotonergic system. Reserpine, an antihypertensive drug that depleted neuronal storage granules of norepinephrine, serotonin and dopamine, produced clinically significant depression in 15% or more of patients[25]. Reserpine (2mg/kg, ip) produced significant increase in immobility period after 4 and 24 hr of its treatment when tested in TST. Since TB extracts reversed reserpine-induced depression, as indicated by decrease in extension of immobility period in TST, therefore, this suggests that antidepressant-like effect of TB extracts may be through the restoration of brain monoamines, like norepinephrine, 5-hydroxytryptamine and dopamine levels. This is also supported by earlier study that alcoholic extract of TB fruits showed antistress and endurance promoting properties in hypoxia test in mice and swimming performance test in rats[8]. The aqueous extract of TB fruits has antioxidant activity due to the presence of phenolic compounds, particularly gallic acid[15]. There is evidence of derangement of oxidant and antioxidant defense systems in depression[26]. Thus, antidepressant-like activity of TB extracts might be due to its antioxidant activity.

The present results suggest that aqueous and ethanolic extracts of *Terminalia bellirica* produced

Table 6 — Effect of aqueous extract of TB on reserpine-induced extension of immobility period in TST
[Values are mean ± SE]

| Group No. | Treatment for 10 days | Number of animals | Dose ($kg^{-1}$) | Immobility Pperiod (sec) | |
|---|---|---|---|---|---|
| | | | | After 4 hr | After 24 hr |
| XI | Vehicle (0.25% w/v CMC) | 6 | 10 ml | 193.3 ± 2.6 | 193.3 ± 2.6 |
| XXXIV | Vehicle + Reserpine | 6 | 2 mg | 232.3 ± 4.1[a] | 239.2 ± 4.2[a] |
| XXXV | TB extract (aqueous) + Reserpine | 6 | 200 mg<br>2 mg | 150 ± 4.1[b] | 160.7 ± 4.2[b] |

Data was analyzed by Student's unpaired t-test.
$P < 0.01$ when compared with [a]vehicle treated group; [b]respective reserpine control group

Table 7 — Effect of ethanolic extract of TB on reserpine-induced extension of immobility period in TST
[Values are mean ± SE]

| Group No. | Treatment for 10 days | Number of animals | Dose ($kg^{-1}$) | Immobility Period (sec) | |
|---|---|---|---|---|---|
| | | | | After 4 hr | After 24 hr |
| XII | Vehicle (10% v/v Tween 80) | 7 | 10 ml | 195.7 ± 4.3 | 195.7 ± 4.3 |
| XXXVI | Vehicle + reserpine | 6 | 2 mg | 232.5 ± 3.5[a] | 240.3 ± 4.3[a] |
| XXXVII | TB extract (ethanolic) + reserpine | 6 | 200 mg<br>2 mg | 159.3 ± 3.7[b] | 168.5 ± 3.5[b] |

Data were analyzed by Student's unpaired t-test.
$P < 0.01$ when compared with [a]vehicle treated group;. [b]respective reserpine control group.

antidepressant-like effect in mice in both FST and TST, and it was found to be similar to that of fluoxetine and imipramine. The antidepressant-like effects of the extracts seem most likely to be mediated through an interaction with adrenergic, dopaminergic and serotonergic systems. Thus, extracts of *Terminalia bellirica* may have potential therapeutic value for the management of depressive disorders.

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