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PHARMACOLOGICAL EVALUATION OF ANTIDEPRESSANT ACTIVITY OF THE ETHANOLIC EXTRACT OF *BOMBAX CEIBA* FLOWERS IN ALBINO WISTAR RATS

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Abstract

A significant segment of the worldwide population experiences depression, a prevalent mental health issue. Plant extracts are among all Organic compounds gained attention interest due to their possible antidepressant properties. The study's objective is to analyse whether an ethanolic extract of *Bombax ceiba* flowers exhibits antidepressant effects on Albino Wistar rats. Thirty Swiss Albino Wistar rats were divided into five groups, with each group containing six rats, and the study lasted for 42 days. We study three doses of the flower extract of *B. ceiba* (100, 200, 400mg/kg) the effects of both acute and chronic depression were evaluated using two models: the Porsolt forced swim test and the tail suspension test. In the acute trial, drugs (test drug, standard control, and vehicle) were given orally one hour prior to the experiment, and in the chronic research, the drugs were given daily for 14 days. The force swim test and tail suspension test were used in both acute and chronic investigations to show that imipramine had strong antidepressant action. This was evidenced by a decrease in the period of immobility. *B. ceiba* had antidepressant effect that was dose dependant. The antidepressant effect of *B. ceiba* 100 mg/kg was only evident in the acute force swim test. In the force swim test (both acute and chronic), *B. ceiba* 200 mg/kg showed antidepressant action; however, it did not show any effect in the tail suspension test. In investigations conducted on both acute and chronic patients, *B. ceiba* 400 mg/kg demonstrated maximum antidepressant effect that was comparable to that of imipramine, a prescription medication. *B. ceiba* showed dose dependent antidepressant action with BC-400mg/kg showing maximum effect.

Keyword: Antidepressant activities, Force swim & tail suspension test and Phytochemical analysis.

1. Introduction

Neuropsycho pharmacology is an interdisciplinary field of neuroscience that focuses on researching medications and how they affect the nervous system, particularly how they can alter behaviour. This branch of science aims to explore the ways in which drugs can be used to treat

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various conditions such as sleep disorders, pain, mania, anxiety, schizophrenia, and depression (Nemeroff *et al.,* 2007). Three primary signs define depression clinically: acontinuing depressed or melancholy mood, anhedonia (a reduced capacity for pleasure or enjoyment), and exhaustion or low energy. Individuals with depression also commonly experience additional symptoms such as changes in sleep patterns, negative thinking, feelings of guilt, low self-worth, suicidal thoughts, and disruptions in eating and weight regulation. It is noteworthy that depression is more prevalent among women than men, with a diagnosed ratio as high as 5:2 in favour of women (Zis *et al.,* 1979). The excessive demand for natural healthcare has dramatically improved the price of hospital treatment, so humans have used herbal nutritional food, dietary supplements, and nutraceuticals for the usage of phytotherapy or nutritional therapy to replace or get rid of radiotherapy or chemotherapy (Chandra *et al.,* 2022).

The World Health Organisation (WHO) predicts that by 2030, depression will overtake all other diseases as the major cause of illness worldwide (Rot *et al.,* 2009). Currently, depression is diagnosed according to the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). A major depressive episode requires the presence of at least five of the following symptoms: mood fluctuations involving sadness and irritability, diminished interest or pleasure in activities, changes in weight or appetite, alterations in sleep patterns, psychomotor changes, fatigue or loss of energy, feelings of guilt or worthlessness, difficulty concentrating, and recurrent thoughts of death or suicide (Angst *et al.,* 2009). A functional deficit in the brain's levels of monoaminergic neurotransmitters, such as dopamine, serotonin (5-hydroxytryptamine), and norepinephrine, is thought to be the primary cause of depression (Ansseau *et al.,* 2008).

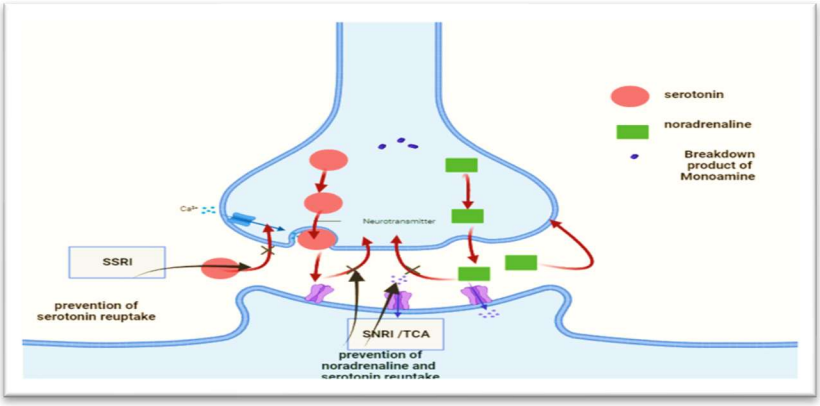

Figure 1: The brain's neurotransmission mechanism.

2. Types of Depression

2.1 Major depressive disorder (MDD): commonly known as clinical depression, is a mental health condition characterized by persistent feelings of sadness and a lack of interest in activities that were previously enjoyed. This severe and debilitating illness affects an individual's mood, thoughts, and behaviors. Common symptoms include depressive mood, changes in eating, sleep patterns, psychomotor agitation or retardation, fatigue, feelings of worthlessness or guilt, difficulty concentrating, and suicidal thoughts. While the precise causes

are unknown MDD is considered to result from a complex interplay of genetic, physiological, environmental, and psychological factors. Potential risk factors include a family history of mental health issues like depression or trauma, chronic medical conditions, substance abuse, and certain prescription medications (Eaton *et al.,* 1997).

2.2 Bipolar Disorder: The hallmark features of bipolar disorder, originally known as manic depressive disorder, are severe mood swings or periods of mania and despair. Manic episodes are distinguished by extreme enthusiasm, strong energy, and impulsiveness. Depressive periods are distinguished by severe dread, hopelessness, and low vitality. Both manic and depressive episodes are experienced by those with bipolar illness. Due to their erratic length and intensity, mood swings can impact daily functioning and interpersonal interactions. Numerous biochemical, environmental, and genetic factors are believed to play a role in the development of bipolar disease, although the exact cause of the disorder remains unknown. Risk factors for bipolar disorder include trauma, high stress circumstances, and family history (Kessler *et al.,* 2003).

2.3 Melancholia: has been used historically to describe a severe form of depression disorder characterized by persistent, strong feelings of melancholy, hopelessness, and despair. This term has virtually been replaced by the diagnosis of Major Depressive Disorder in modern psychiatric categories. However, melancholia sometimes indicated a particular form of despair that was seen to be more acute and incapacitating than regular sadness in literary and historical contexts. Melancholics not only have a profound lack of interest or pleasure in practically all activities, but they can also manifest physical symptoms such extreme weight loss, insomnia, and psychomotor agitation or retardation. Depression was often associated with a pervasive sense of guilt and unworthiness, which raised the risk of suicide (Bourdon *et al.,* 1992).

An annual recurrence of depressive episodes that often happen around the same time each year is the hallmark ofseasonal affective disorder (SAD). Depression usually starts in October and lasts until December, at which point its symptoms usually go away by March. That being said, some people may begin to feel anxious in July or August, which is a few months before a chronic low mood and lack of energy sets in (Xing *et al.,* 2013).

2.4 Postpartum depression (PD): is characterized in psychiatric language as a major depressive disorder (MDD) that begins within one month of childbirth, as indicated by diagnostic criteria. The symptoms of postpartum depression are comparable to those of depression in women who have not given birth. Children who experience difficulties in their interactions with stressed carers are more likely to develop insecure attachment, which can result in behavioral and cognitive problems. Child development is also impacted by the consequences of parental mental illness, such as family strife, financial hardships, and the possibility of placing kids outside the home (Nazario *et al.,* 2016).

2.5 Flavonoids against Depression: Phytochemicals from herbs may reduce risks of disorders like autoimmune, cardiovascular, and neurodegenerative diseases. Compounds like curcumin, ferulic acid, proanthocyanidin, quercetin, and resveratrol exhibit strong anti-inflammatory and antioxidant properties. They have consistently shown neuroprotective effects, indicating

potential to improve depression symptoms. Flavonoids, a type of polyphenol, have been extensively studied. They are present in many foods and drinks and have shown ability to prevent or reverse stress through various mechanisms. Studies on flavonoids have investigated antidepressant activity of natural chemical compounds. In animal models, certain flavonoids demonstrated antidepressant potential by reversing depressive behaviour. They may exert effects by increasing neurotransmitters, neurotrophic factors, and promoting neurogenesis in the brain (Harmer *et al.,* 2017).

Depression pathology is based on biological, physiological and behavioural signals. Low serotonin, neurotransmitter dysfunction and genetic abnormalities have been associated with depression and suicidal behaviour. Plant amounts of flavonoids act on receptors and neurotransmitters. Studies explored flavonoids' potential effects on central nervous system disorders like anxiety and depression. Unlike synthetic medications, natural flavonoids produce antidepressant effects in depression models. Herbal drugs with flavonoids may help patients with depression. Flavonoids have antioxidant and free radical scavenging effects in plants. *Bombax ceiba* flower ethanol extract shows antioxidant activity against reactive oxygen species. This adds the advantage of targeting antioxidants against oxidative stress, as *Bombax Ceiba* flower extract has been proven to help diseases related to oxidative stress (Rubalcava *et al.,* 2016).

3. Material and methods

Figure 2: *Bombax ceiba* **plant with flowers**

3.1 Collection and authentication of plant

Bombax ceiba flowers were collected from the Forest Research Institute (FRI), Dehradun in the month of March. The Botanical Survey of India (BSI) in Dehradun identified and authenticated the plant. The voucher specimen number is: BSI/NRC/Tech/Herb/2023-24/37.

3.2 Chemical and reagent

All of the excellent-grade chemicals and reagents utilised were used exactly as they were, with no purification or further research involved.

3.3 Preparation of extract

After being shade-dried for 40 days, the flowers were coarsely powered. 100 gm of dried flower powder and 400 ml of 95% ethanol were combined, and the mixture was macerated for 7 days to create 95% ethanolic extracts. The extract was passed through Whatman no. 1 filter paper for filtration. The filtrate was then concentrated under reduced pressure to obtain the dry residue. For future usage, the extract was kept at 4^0 c. the sample was dissolved in 0.9 NaCl and utilised to study the antidepressant properties of *Bombax ceiba* ethanolic extracts in rats (Chandra *et al.,* 2016).

Figure 3: *Bombax ceiba* flower extract

3.4 Phytochemical Studies

The extract obtained from the plant material underwent an initial analysis to determine the presence of various phytochemical compounds, including Alkaloids, carbohydrates, flavonoids, phenols, starch, amino acids, proteins, terpenoids, and steroids (Chandra *et al.,* 2019).

3.4.1 Test for Flavonoids

Shinode test: After combining 1-2 fragments of magnesium turning with 3-4 mL of extract, 0.5 mL of concentrated hydrochloric acid (HCl) was introduced into the mixture. Following a 5-minute interval, the solution exhibited distinct color changes indicative of different flavonoid classes. The colours of flavonols were red, flavonones were orange, flavanols were reddish-violet, and flavonols were green.

3.4.2 Phenols were tested using the Ferric chloride test: 1 mL portion of a solution of neutral ferric chloride (2 mL) was added to the plant extract after it had been diluted with distilled water. The resultant tint was bluish-black.

3.4.2 Test for Alkaloids

Mayer's test: A residue was formed when an ethanolic extract was placed on a China plate and evaporated in a water bath. A small quantity of diluted hydrochloric acid was introduced to the residue, and the mixture was filtered to obtain the liquid extract in a

beaker. Mayer's reagent was then added to a test tube containing 2 ml of the filtrate. The formation of a crimson precipitate indicated the presence of alkaloids.

3.4.3 Test for Carbohydrates

Molish test: A 2ml sample was taken and placed in a test tube. 1% alpha-naphthol was then added, followed by 2ml of strong HCl gently poured from the test tube side. A purple-violet ring appeared, suggesting the presence of decreasing sugar (Chandra *et al.,* 2013).

2.4.5 Test for Proteins and amino acids

Million's test: In a test tube, 3 ml of the extract was combined with Million's reagent and boiled for 1 minute. Upon cooling, 1% sodium nitrite solution was added to the mixture, followed by reheating, resulting in the formation of a red-colored precipitate.

3.4.6 Test for Sterols and Triterpenoids

Salkowski test: A test tube containing 5 ml of the extract was treated with sulfuric acid. A red colour indicated the presence of steroids, while a yellow colour indicated the presence of triterpenoids in the extract.

Animals

Procurement of experimental animals Swiss Albino wistar rats of either sex weighing 100-200 grammes were obtained from Shri Guru Ram Rai University's Animal House in Dehradun at 3-4 months of age.

Housing condition

The rats were kept in cages with 3-4 rats per cage, maintained under standard conditions including a temperature of 25°C, 60% relative humidity, and a 12-hour light/12-hour dark cycle. They had unrestricted access to water and a standard pellet diet. The Institutional Animal Ethics Committee approved the protocol, ensuring compliance with CPCSEA regulations.

Methods

4.1 Methods of Induction of Stress

Chronic unpredictable mild stress model (CUMS)

The experimental animals underwent daily stress exposure.

Days → Week ↓	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1	C	T	F	O	N	S	T1
Week 2	C	O	N	S1	T2	C	F

Week 3	O	N	T1	S	C	O	F

Table 1: C represents cold swim (12°C for 5 minutes), T stands for tail pinch (30 seconds), F indicates food and water deprivation (24 hours), and O signifies nocturnal light exposure. N denotes no stress; T1 corresponds to a tail pinch (60 seconds); T2 to a tail pinch (90 seconds); S involves swimming at room temperature (23±2°C for 10 minutes), and S1 involves swimming at room temperature (23±2°C for 15 minutes).

EXPERIMENTAL DESIGN

30 Swiss Albino Wistar rats were allocated into five groups, with each group containing six rats, for a period of 42 days.

Group 1: The control group received normal saline (10 ml/kg, administered orally).

Group 2: Control stressed group was treated with different stressors.

Group 3: Swiss Albino wistar rats received Imipramine (10mg/kg i.p.) + stress

Group 4: Swiss Albino rats received ethanolic extract of *Bombax Ceiba* flower (100mg/kg) + stress

Group 5: Swiss Albino rats received ethanolic extract of *Bombax Ceiba* flower (200mg/kg) + stress

Group 6: Swiss Albino rats received ethanolic extract of *Bombax ceiba* flower (400mg/kg) + stress.

Animals were tested behaviourally and biochemically on day 21 (60 minutes after medication delivery). Rats used in the biochemical test were beheaded and their brains removed (Chandra *et al.,* 2016).

BEHAVIOR ANALYSIS

Porsolt force-swim test (PFST)

The Porsolt forced swim test was conducted in Plexiglas cylinders measuring 20 cm in height and 10 cm in diameter, filled with water at a temperature of 23°C to a depth of 7.5 cm. Rats were placed individually in the cylinders for a 6-minute test session, during which their behavior was observed and recorded. The "immobility period" was defined as the duration when the animals stopped actively moving for at least 1 second.

Figure 4: Porsolt force swim test (PFST)

Tail suspension test (TST)

The immobility period in rats was measured using TST. An adhesive tape was applied roughly 1 cm from the tip of the tail, and at a height of 50 cm above the floor surface, the animals were suspended. The test lasted 6 minutes, and the length of immobility was recorded. In rats, immobility was described as a complete lack of movement.

Figure 5: Tail suspension test

Biochemical Estimation

First, entire brain samples are washed in ice-cold saline (0.9% NaCl, pH 7.4) and then homogenised in cooled phosphate buffer to prepare the brain homogenate. To remove radioactive debris, the homogenates are centrifuged at 800 g for 5 minutes at 4°C. The post-mitochondrial supernatant, which will be utilised for the lipid peroxidation test and catalase activity measurement, is obtained by centrifuging the resultant supernatant one more time at 10,500 g for 20 minutes at 4°C (Yallapu 2012; Xu 2005: Srinivasan 2007; Yogeeta et al., 2006).

Lipid Peroxidation

The extent of lipid peroxidation in brain homogenate was evaluated using the method outlined by Wills (1965). Briefly, 0.5 ml of post-mitochondrial supernatant and 0.5 ml of Tris-HCl buffer were incubated together at 37°C for two hours. Following incubation, 1 ml of 10% trichloroacetic acid was added, and the mixture was centrifuged at 1,000 g for 10 minutes. Next, 1 ml of the resulting supernatant was mixed with 1 ml of 0.67% thiobarbituric acid and heated in boiling water for 10 minutes. After cooling, 1 ml of double-distilled water was added, and the absorbance was measured at 532 nm to determine the concentration of malondialdehyde, expressed as nmol per mg of protein (Mu 2015; Nathan 2006; Kakuda 2002; Uchida *et al.,* 2008).

Analytical Statistics

The data were presented as mean ± S.E.M. One-way analysis of variance (ANOVA) was used to assess differences between groups, and Tukey's test was applied for post-hoc comparisons. Statistical significance was defined as $p < 0.05$ (Chnadra et al., 2016).

Results

Percentage yield of ethanolic extract of *Bombax ceiba*

Weight of dried powder of *Bombax Ceiba* flowers = 100g

Weight of extract obtained =

$$\% \text{ yield} = \frac{\text{weight of extract X 100}}{\text{Weight of dried powder taken}}$$

$$\% \text{ yield} = \frac{8.4 \text{x } 100}{100}$$

%yield of ethanolic extract= 8.4%

Table 2: Physical characteristics of ethanolic extract of *bombax ceiba* flowers

Extract	**Color**	**Odor**	**% Extractive value**
Ethanolic extract	Crimson (darkred)	Characteristics	8.4%

Phytochemical screening

Phytochemical screening of the *Bombax ceiba* flowers extract was done for chemical constituents like phenolic compounds and flavonoids.

Table3: Phytochemical screening of *Bombax ceiba* flowers extract

Phytoconstituents	**Test**	**Inference**	**BCFE**
Alkaloid	Mollish'stest	Development of avioletringat junction.	+
Flavonoids	Shinodetest	Development of reddish to pink colour	+
Glycosides	Kellerkillianitest	The development of a reddish-brown color at the interface.	+

Tannins	Braymer'stest	Development of a solution with a blue or green color.	+
Phenol	Ferricchlori detest	Development ofvioletcolour	+
Carbohydrates	Molischtest	Development ofvioletringat junction.	+

Behavioral Parameters

Impact of *Bombax ceiba* extract on Forced Swim Test

In the FST, ethanolic flower extract of *Bombax Ceiba* (100 mg/kg p.o., 200 mg/kg p.o. & 400mg/kg p.o.) effectively decrease the immobility time in comparison to CUMS. As indicated in table 2 and figure 1, higher dose of ethanolic extract (200 and 400 mg/kg) induce effective decrease in immobility duration when compared to CUMS (**p<0.01,***P<0.001, ****P<0.0001)and were more effective than the lower dose.

Table 4: The impact of BCFE on the Porsolt forced swim test in rats

S. No	Groups	Mean ± S.E.M. of immobility time
1	Control	59.44 ± 0.30
2	Control +Stress	88.00± 0.12
3	Imipramine10mg/kg+stress	55.00 ±0.577
4	BCFE100mg/kg+Stress	69.67± 0.53
5	BCFE200mg/kg+Stress	61.67± 0.49
6	BCFE400mg/kg+Stress	53.67± 0.43

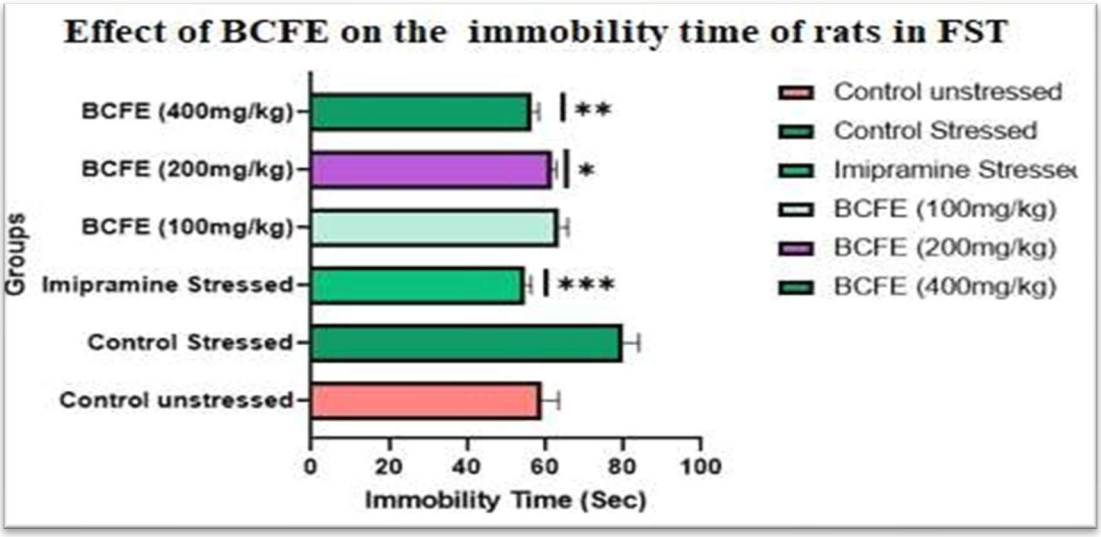

Figure 6: The impact of BCFE on the Porsolt forced swim test in rats

The results, presented as Mean ± SEM, with n = 6 in each group, demonstrate that the ethanolic flower extract of *Bombax ceiba* at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg administered orally significantly reduced immobility time compared to the CUMS group in the TST. Higher doses of the extract (200 mg/kg and 400 mg/kg) were particularly effective (**p<0.01, ***p<0.001) and showed greater efficacy than the lower dose. This information is summarized in Table 2 and Figure 1.

Table 5: Impact of BCFE on Tail Suspension Test in rat

S. No	Groups	Immobilitytime (Mean± S.E.M)
1	Control	59.17 ± 1.759
2	Control +Stress	79.83± 1.759
3	Imipramine10mg/kg+stress	55.00 ±0.577
4	BCFE100mg/kg+Stress	63.67± 0.84
5	BCFE200mg/kg+Stress	61.67± 0.49
6	BCFE400mg/kg+Stress	56.67±0.66

Figure 7: Impact of BCFE on the immobility time of rats in TST

Value is expressed as Mean ± SEM, n = 6 in each group.*p<0.05, **p<0.01, ***p<0.001, compared with CUMS

Biochemical Parameters

Effectof *Bombax Ceiba* on the brain Lipid Peroxidation level instressed rats:

Chronic unpredictable mild stress model produces significant increase in brain oxidative estress as determined by lipid peroxidation level in comparison with vehicle control group. However, BCFE at the dose of(400mg/kgp.o.) showed significant the effects significantly reduced the level of lipid peroxidation (*p<0.05, **p<0.001, ****p<0.0001).

Table 6: Impact of BCFE on Lipid peroxidation level in rat

S. No	Groups	Mean± S.E.M
1	Control	1.12 ± 0.10
2	Control +Stress	1.81 ± 0.08
3	Imipramine10mg/kg+stress	1.23 ± 0.04
4	BCFE100mg/kg+Stress	1.50 ± 0.10
5	BCFE200mg/kg+Stress	1.41 ± 0.04
6	BCFE400mg/kg+Stress	1.32 ± 0.04

The values are presented as Mean ± SEM, with 6 rats in each group. Statistical significance was indicated as *p<0.05, **p<0.01, ***p<0.001, compared to the CUMS group.

DISCUSSION

According to the findings of this study, an ethanolic extract of *Bombax ceiba* flowers has antidepressant qualities in albino Wistar rats. The observed decrease in immobility time in the PFST and TST is suggestive of a potential depressive effect, which is consistent with *Bombax ceiba*'s traditional medical applications. The modification of monoamine levels and the reduction of oxidative stress support the antidepressant effect even more. The results contribute to the growing body of research endorsing the efficacy of plant-derived compounds in addressing mental health disorders. Further investigation is required to comprehensively understand the specific bioactive components responsible for the reported benefits, as well as the safety and long-term usefulness of *Bombax ceiba* extract as an antidepressant medication.

CONCLUSION

This study is designed to evaluate behavioural and biochemical changes in chronic stress. It concluded that *Bombax ceiba* has a potent effect on chronically stressed Mice showed notable effects in behavioural and biochemical change parameters as follows: Using chronicun predictable mild stress models, the antidepressant activity of BCFE (100,200 and 400 mg/kg) was tested in this work. CUMS significantly enhanced the immobility duration in FST and TST in the current investigation, indicating stress-like behaviour. In FST and TST, twenty-one days of pre treatment with *Bombax ceiba* flower extract provided considerable protection against CUMS-induced immobility time. —BCFE dose (100, 200 & 400 mg/kg p.o) significantly reduced lipid peroxidation levels and increase the catalase activity in brain. In comparison to CUMS group, BCFE dose (200 &400mg/kg), shows significant results. BCFE was found highly significant at 400mg/kgp.o in the CUMS model. Hence, it can conclude that the ethanolic flower extract of *Bombax ceiba* is more effective at 400 mg/kg for improving chronic stress symptoms, which can be used in the treatment of chronic stress.

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