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EVALUATION OF ANTIDEPRESSANT ACTIVITY OF ETHANOLIC EXTRACT OF *CISSUS QUADRANGULARIS* IN SWISS ALBINO MICE

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Article History	Abstract
Received: 19-06-2026 Revised: 03-07-2026 Accepted: 17-08-2026	Depression is one of the most common psychiatric disorders affecting people worldwide. It is characterized by persistent sadness, loss of interest or pleasure, feelings of guilt or worthlessness, changes in sleep and appetite, and reduced energy levels. <i>Cissus quadrangularis</i> is a medicinal plant widely recognized in traditional medicine for its diverse therapeutic properties and has been used for managing several health conditions. The present study was undertaken to investigate the potential antidepressant effects of ethanolic extract of <i>Cissus quadrangularis</i> leaves in an animal model. The in vivo antidepressant activity of the ethanolic leaf extract of <i>Cissus quadrangularis</i> was evaluated in Swiss albino mice. The methanolic extract of <i>Cissus quadrangularis</i> leaves (MECQ) was prepared using a Soxhlet extraction method and subjected to preliminary phytochemical screening and acute oral toxicity evaluation. The extract was administered orally at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg body weight to the respective treatment groups. Imipramine hydrochloride (15 mg/kg, p.o.) was used as the standard antidepressant drug, while the control group received normal saline (10 ml/kg body weight). The antidepressant activity was assessed using behavioral models, including the modified Forced Swimming Test (FST) and Tail Suspension Test (TST). The duration of immobility was recorded as an indicator of antidepressant-like activity. Statistical analysis was performed using appropriate methods to determine the significance of the results. The findings demonstrated a significant dose-dependent reduction in immobility time in mice treated with MECQ, indicating notable antidepressant activity in both experimental models. The extract exhibited promising antidepressant effects across all tested doses. However, further studies are required to isolate the active phytoconstituents and elucidate the molecular mechanisms responsible for its antidepressant action before considering potential therapeutic applications in humans.
Keywords: <i>Cissus quadrangularis</i> , antidepressant activity, forced swimming test, tail suspension test, phytochemical screening, Swiss albino mice.	
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INTRODUCTION

Depression is one of the most common psychiatric disorders worldwide and is characterized by persistent sadness, loss of interest, anxiety, sleep disturbances, reduced energy, feelings of guilt, low self-worth, and impaired social functioning. It is a complex and multifactorial illness that affects individuals, families, and society. The increasing burden of depression has created a need for effective therapeutic approaches, including synthetic antidepressant drugs, psychotherapy, electroconvulsive therapy, and herbal medicines with fewer adverse effects. The neurobiology of depression involves complex interactions between different neurotransmitter systems in the central nervous system (CNS) [1-2]. The major neurotransmitters implicated in depression include serotonin (5-hydroxytryptamine; 5-HT), noradrenaline (NA), dopamine (DA), and glutamate. Serotonin plays an important role in regulating mood, memory, appetite, and sexual behavior, while noradrenaline contributes to alertness, stress response, and emotional regulation. Dysfunction of serotonergic and noradrenergic pathways may contribute to the development of depressive symptoms [4-5].

Several biological hypotheses have been proposed to explain the mechanisms underlying depression. The monoamine or biogenic amine hypothesis suggests that depression results from reduced levels or impaired function of monoamine neurotransmitters such as serotonin, noradrenaline, and dopamine. The dopamine hypothesis emphasizes reduced dopaminergic activity, particularly in patients showing reduced motivation and motor activity [6-7]. The permissive hypothesis proposes that serotonin regulates other neurotransmitter systems, and decreased serotonin activity may allow disturbances in noradrenergic and dopaminergic pathways. Recent research has also highlighted the role of glutamatergic dysfunction, particularly involving N-methyl-D-aspartate (NMDA) receptors, and alterations in the kynurenine pathway in the pathophysiology of depression [8-9].

Currently available antidepressant therapies include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs). These drugs act mainly by increasing monoamine neurotransmission but are associated with several adverse effects, including

gastrointestinal disturbances, sedation, weight changes, sexual dysfunction, cardiovascular effects, and neurological complications. The delayed therapeutic response and side effects associated with conventional antidepressants have encouraged researchers to explore safer alternatives from medicinal plants [10]. Medicinal plants have gained significant attention due to their traditional use and potential antidepressant properties [11]. Several plants have demonstrated antidepressant-like effects in animal models such as the Forced Swimming Test (FST), Tail Suspension Test (TST), and Open Field Test (OFT). Plants including *Glycyrrhiza uralensis*, *Curcuma longa*, *Bacopa monnieri*, *Asparagus racemosus*, *Embllica officinalis*, *Rosmarinus officinalis*, *Crocus sativus*, and many others have shown promising effects through modulation of serotonergic, noradrenergic, dopaminergic, antioxidant, and neuroprotective mechanisms [12-13]. Ayurvedic medicine also describes depressive disorders under conditions related to *Manovaha Srotas*, particularly *Avasada* and *Kaphaja Unmada*. Traditional formulations and herbal preparations have been used for managing mental disorders due to their sedative, anxiolytic, and mood-regulating properties [14-15]. The increasing interest in herbal antidepressants is based on their accessibility, traditional acceptance, and potential for reduced toxicity compared with synthetic drugs [16].

METHODOLOGY

The present study was designed to evaluate the antidepressant potential of the ethanolic extract of *Cissus quadrangularis* leaves. The objectives of the study were to prepare the ethanolic extract, perform acute oral toxicity evaluation, and assess antidepressant activity using behavioral models such as the Forced Swimming Test (FST), Tail Suspension Test (TST), and Open Field Test (OFT). Medicinal plants have historically served as an important source of therapeutic agents, particularly in regions where access to modern healthcare facilities is limited. *Cissus quadrangularis* is a well-known medicinal plant belonging to the family Vitaceae and has been traditionally used in Ayurveda and other systems of medicine for its analgesic, anti-inflammatory, and bone-healing properties. However, limited scientific investigations have been conducted regarding its central nervous system effects, particularly its antidepressant activity. Therefore, the present study was undertaken to explore the potential antidepressant effects of ethanolic leaf extract of *Cissus quadrangularis* using experimental animal models. Fresh leaves of *Cissus quadrangularis* were collected, cleaned, shade-dried, powdered, and extracted with ethanol using a Soxhlet extraction method. The prepared extract was subjected to preliminary phytochemical screening for the detection of bioactive constituents such as alkaloids, flavonoids, phenols, tannins, saponins, steroids, and carbohydrates. Swiss albino mice and Wistar rats maintained under standard laboratory conditions were used for the pharmacological evaluation after approval from the Institutional Animal Ethics Committee. Acute oral toxicity studies were performed according to OECD guideline 425, and animals were observed for mortality, behavioral changes, and neurological effects following

administration of the extract up to a dose of 2000 mg/kg body weight. The antidepressant activity of the ethanolic extract was evaluated using FST and TST, with imipramine hydrochloride (15 mg/kg) used as the standard antidepressant drug and normal saline as the control treatment [17]. Animals were divided into different groups and treated orally with extract doses of 100, 200, and 400 mg/kg body weight for the experimental period. In the Forced Swimming Test, animals were placed individually in a water-filled cylindrical tank, and the duration of immobility was recorded as an indicator of behavioral despair [18]. In the Tail Suspension Test, animals were suspended by their tails, and the immobility period was measured to assess antidepressant-like activity. The Open Field Test was performed to evaluate locomotor activity and to exclude possible effects of the extract on general motor function. The experimental data were expressed as mean $\pm$ standard error of mean (SEM) and analyzed statistically using one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test. A p-value of less than 0.05 was considered statistically significant. The overall experimental design aimed to establish the antidepressant potential of *Cissus quadrangularis* leaves and provide scientific evidence supporting its traditional medicinal use. The findings of this study may contribute to the identification of novel plant-based therapeutic agents for the management of depressive disorders.

RESULTS AND DISCUSSION

Preliminary Phytochemical Screening

The ethanolic extract of *Cissus quadrangularis* leaves was subjected to preliminary phytochemical screening to identify the major bioactive constituents. The extract revealed the presence of alkaloids, flavonoids, tannins, saponins, phenolic compounds, steroids, carbohydrates, and glycosides. Among the detected phytoconstituents, flavonoids and alkaloids showed strong positive reactions, whereas tannins and saponins showed moderate presence. The results of the phytochemical analysis are presented in Table 01.

Table 01: Preliminary phytochemical screening of ethanolic extract of *Cissus quadrangularis* leaves

Phytoconstituents	Result
Carbohydrates	+
Tannins	++
Flavonoids	+++
Saponins	++
Phenols	+
Steroids	+
Alkaloids	+++
Glycosides	+

(+ indicates presence; ++ indicates moderate presence; +++ indicates strong presence) [19].

Antidepressant Activity of Ethanolic Extract of *Cissus quadrangularis* Leaves

The antidepressant potential of the ethanolic extract of *Cissus quadrangularis* (EECQ) was evaluated using the Forced Swimming Test (FST) and Tail Suspension Test (TST) in comparison with the standard antidepressant drug

imipramine. The antidepressant activity was assessed based on the reduction in immobility time, which is considered an indicator of antidepressant-like activity. In the acute study (Day 1), administration of imipramine (15 mg/kg) and EECQ at doses of 100, 200, and 400 mg/kg produced a significant reduction in immobility time compared with the normal saline-treated control group in both TST and FST. In the Tail Suspension Test, EECQ at 400 mg/kg showed the maximum reduction in immobility time (116.1 ± 2.24 s), while in the Forced Swimming Test, EECQ 100 mg/kg showed a marked reduction in immobility duration (96.71 ± 5.16 s). The results are summarized in Table 02 and illustrated in Figures 1 and 2.

Table 02: Effect of ethanolic extract of *Cissus quadrangularis* leaves on immobility time in acute antidepressant models (Day 1) [20].

Treatment Group	Dose	Tail Suspension Test (s)	Forced Swimming Test (s)
Normal saline	10 ml/kg	221.3 ± 17.04	136.1 ± 2.17
Imipramine	15 mg/kg	$174.2 \pm 1.21^*$	$101.15 \pm 3.62^*$
EECQ	100 mg/kg	$161.5 \pm 21.5^*$	$96.71 \pm 5.16^*$
EECQ	200 mg/kg	$181.2 \pm 3.19^*$	$108.15 \pm 2.01^*$
EECQ	400 mg/kg	$116.1 \pm 2.24^*$	$106.29 \pm 4.39^*$

Values are expressed as mean $\pm$ SEM. * $p < 0.05$ compared with control group.

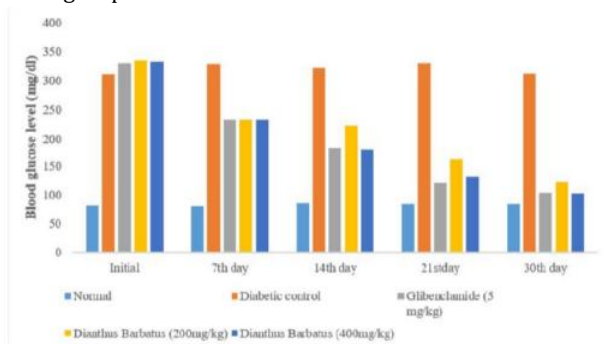


Figure 01. Effect of EECQ on immobility time in Tail Suspension Test (Day 1).

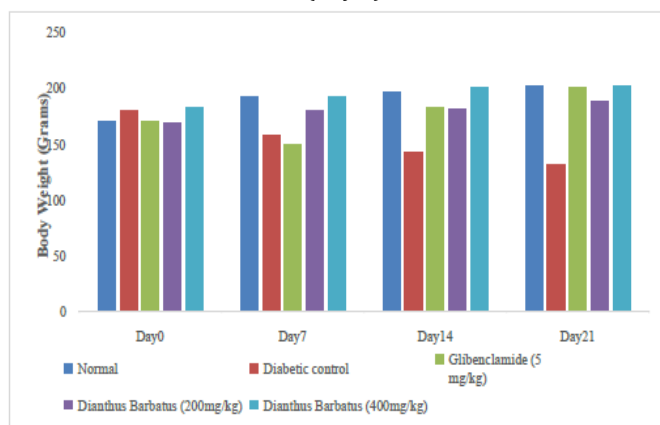


Figure 02: Effect of EECQ on immobility time in Forced Swimming Test (Day 1). [21]

During the subacute study (Day 10), repeated administration of EECQ produced a significant antidepressant-like effect. Treatment with EECQ 100 mg/kg and 400 mg/kg significantly reduced immobility time in both behavioral models compared with the control group [22-23]. The standard drug imipramine also produced a significant reduction in immobility time. The results obtained on Day 10 are presented in Table 3 and Figures 03 and 04.

Table 03: Effect of ethanolic extract of *Cissus quadrangularis* leaves on immobility time in subacute antidepressant models (Day 10)

Treatment Group	Dose	Tail Suspension Test (s)	Forced Swimming Test (s)
Normal saline	10 ml/kg	220.34 ± 11.87	145 ± 1.26
Imipramine	15 mg/kg	$146.52 \pm 26.42^*$	$93.19 \pm 2.95^*$
EECQ	100 mg/kg	$92.87 \pm 2.15^*$	$67.91 \pm 3.24^*$
EECQ	200 mg/kg	$208.18 \pm 11.70^{\#}$	$91.81 \pm 9.16^*$
EECQ	400 mg/kg	$103 \pm 11.62^*$	$86.19 \pm 1.28^*$

Values are expressed as mean $\pm$ SEM. * $p < 0.05$ compared with control group; # statistically non-significant.

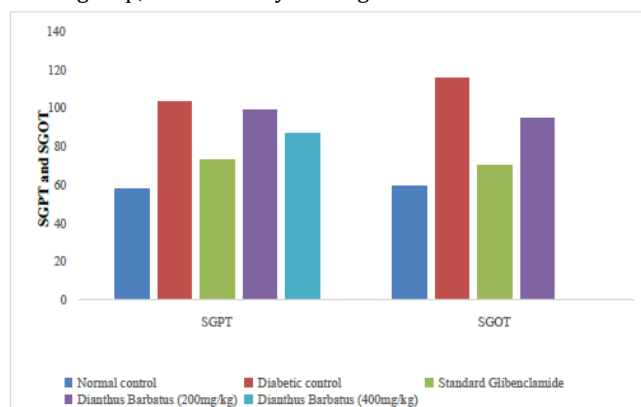


Figure 03: Effect of EECQ on immobility time in Tail Suspension Test (Day 10).

The present study investigated the antidepressant activity of ethanolic extract of *Cissus quadrangularis* leaves using established behavioral models of depression, namely the Forced Swimming Test and Tail Suspension Test. Both models are widely accepted for screening antidepressant agents based on the principle that effective antidepressant compounds reduce stress-induced behavioral despair and decrease immobility duration [24].

In the present investigation, treatment with EECQ produced a significant reduction in immobility time in both acute and subacute experimental conditions. The antidepressant-like effect was observed at all tested doses, with the 100 mg/kg and 400 mg/kg doses showing prominent activity. The effects of EECQ were comparable with the standard antidepressant drug

imipramine, indicating the potential antidepressant activity of the plant extract.

Imipramine exerts its antidepressant action primarily through inhibition of serotonin and noradrenaline reuptake transporters, resulting in increased availability of these neurotransmitters in the synaptic cleft. The antidepressant effect of *Cissus quadrangularis* may involve similar modulation of monoaminergic neurotransmission. Previous phytochemical investigations have demonstrated the presence of alkaloids, flavonoids, tannins, phenolic compounds, and other secondary metabolites in the plant extract. These phytoconstituents may contribute to antidepressant activity through antioxidant effects, regulation of neurotransmitter systems, and neuroprotective mechanisms [25-26].

Flavonoids and phenolic compounds are reported to possess neuroprotective and antioxidant properties, which may play an important role in reducing depressive-like behavior [27-28]. Alkaloids may also contribute through interaction with central neurotransmitter pathways. Therefore, the observed antidepressant activity of EECQ may be attributed to the synergistic action of these bioactive constituents [29].

The findings of the present study provide experimental evidence supporting the traditional medicinal use of *Cissus quadrangularis* and suggest its potential as a source of novel antidepressant agents [30]. However, further investigations involving isolation of active constituents, molecular mechanism studies, and clinical evaluation are required to establish its therapeutic application in depressive disorders.

CONCLUSION

In the present study, the leaves of *Cissus quadrangularis* were evaluated for their potential antidepressant activity. Based on traditional medicinal practices and previous reports suggesting its therapeutic role in neurological disorders, the plant was selected for investigation. The plant material used in the study was commercially procured from a local market, and the antidepressant activity was evaluated using albino rats as experimental models. The findings of the present investigation demonstrated that the ethanolic extract of *Cissus quadrangularis* exhibited significant antidepressant activity in established behavioral models of depression, including the Tail Suspension Test (TST) and Forced Swimming Test (FST). Preliminary phytochemical analysis of the extract revealed the presence of various bioactive constituents, including carbohydrates, tannins, flavonoids, saponins, phenolic compounds, steroids, alkaloids, and glycosides. Among these phytoconstituents, flavonoids and phenolic compounds have been reported to possess several pharmacological properties, including neuroprotective and modulatory effects on the central nervous system. The observed antidepressant-like activity of the extract may be attributed to the synergistic action of these bioactive constituents, which may influence neurotransmitter regulation and oxidative stress pathways associated with depression. The ethanolic leaf extract of *Cissus quadrangularis* also demonstrated significant antidepressant effects along with enhanced behavioral activity, suggesting possible psychostimulant properties. The results of the present study indicate that ethanolic extract of *Cissus quadrangularis* possesses promising antidepressant potential and may serve as

a valuable candidate for the management of depressive disorders. However, further investigations are required to identify the active compounds and elucidate the precise mechanisms responsible for its antidepressant activity before clinical application.

AUTHOR CONTRIBUTIONS

Both authors contributed to equally.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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