



ANTIDEPRESSANT ACTIVITY OF *Etlingera rubroloba* RHIZOME EXTRACT USING TAIL SUSPENSION AND FORCED SWIMMING TESTS

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ABSTRACT

Depression is a mental health disorder characterized by mood changes, loss of interest, and physiological disturbances, which are associated with dysfunction of the monoaminergic system in the brain. The limitations of conventional therapies have prompted the exploration of natural sources, including plants from the Zingiberaceae family, which are known to be rich in bioactive metabolites with neuropharmacological potential. *Etlingera rubroloba* is one of Indonesia's endemic plants with potential as an antidepressant agent; however, scientific studies on it remain limited. This study aims to evaluate the antidepressant activity of *Etlingera rubroloba* rhizome extract and to identify its secondary metabolites that may play a role in this effect. Extraction was performed via maceration using methanol, followed by phytochemical screening using tube assays. Antidepressant activity was tested in vivo on mice induced with Chronic Mild Stress (CMS), using the Tail Suspension Test (TST) and Forced Swimming Test (FST). The observed parameter was immobility time. Data were analyzed using a One-Way ANOVA test with a significance level of $p < 0.05$. Results: Phytochemical screening results indicated the presence of alkaloids, flavonoids, tannins, saponins, and terpenoids in the extract. Antidepressant activity tests showed that *E. rubroloba* rhizome extract significantly reduced immobility time in the TST and FST ($p < 0.05$) compared to the negative control. This effect was dose-dependent, with a dose of 300 mg/kg body weight providing the most optimal activity and comparable to the positive control (amitriptyline). *Etlingera rubroloba* rhizome extract possesses significant antidepressant activity and has potential for development as a natural antidepressant agent. This effect is thought to involve multimodal mechanisms, including the modulation of monoamine neurotransmitters, increased neuroplasticity, as well as the antioxidant and anti-inflammatory activities of its secondary metabolites.

Keywords: antidepressant; *etlingera rubroloba*; FST; TST

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INTRODUCTION

Depression is a mental health disorder characterized by prolonged feelings of sadness, loss of interest or enjoyment in activities, anxiety, and physical symptoms such as fatigue and changes in appetite (Novelni et al., 2022). The 2023 Indonesian Health Survey (SKI) indicates that the highest prevalence of depression occurs among the 15–24 age group. This condition impacts quality of life and productivity, and increases the risk of suicide if not adequately treated (Wijaya et al., 2023). Biologically, depression is associated with reduced levels of neurotransmitters such as serotonin and norepinephrine, which play a role in regulating mood, stress responses, and other physiological functions. Currently available pharmacological therapies, such as Selective Serotonin Reuptake Inhibitors (SSRIs), Selective Norepinephrine Reuptake Inhibitors (SNRIs), Monoamine Oxidase Inhibitors (MAOIs), and Tricyclic Antidepressants (TCAs), have been proven effective, but they often cause side effects such as sedation, hypotension, nausea, vomiting, and gastrointestinal disturbances (Istriningsih et al., 2018). These limitations have driven efforts to develop safer therapeutic alternatives, one of which involves the use of medicinal plants rich in bioactive metabolites.

The Zingiberaceae family is a group of tropical herbaceous plants containing important secondary metabolites, such as flavonoids, phenolics, terpenoids, and essential oils. These compounds have been reported to possess biological activities, including anti-inflammatory, antioxidant, antibacterial, and potential antidepressant effects (Arviani et al., 2024). Several species from this family, such as *Curcuma xanthorrhiza*, *Zingiber officinale* var. *rubrum*, and *Alpinia officinarum*, have been shown to exhibit antidepressant activity through testing on laboratory animals (Virgilius et al., 2025; Nurfadilla et al., 2022; Salehi et al., 2020). These findings indicate that members of the Zingiberaceae family have potential as candidates for natural sources of antidepressant compounds.

Etlingera is a genus within the Zingiberaceae family that possesses therapeutic value. *Etlingera rubroloba*, an Indonesian endemic plant traditionally utilized by the people of Sulawesi, is known to contain high levels of phenolic metabolites, phenylpropanoids, terpenoids, and flavonoids (Tee et al., 2025). Previous studies have reported various pharmacological activities of this plant, including antioxidant, anti-inflammatory, anti-hyperuricemic, immunomodulatory, and antibacterial effects (Ilyas et al., 2021; Jabbar et al., 2022; Jabbar et al., 2023; Andila & Laurentius, 2022). The presence of these active metabolites indicates the potential of *Etlingera rubroloba* as a biological agent capable of influencing the central nervous system, including the modulation of neurotransmitters associated with depression.

Although various pharmacological activities of *Etlingera rubroloba* have been reported, exploration of its antidepressant potential remains very limited. To date, there have been no *in vivo* studies specifically testing the antidepressant activity of this plant's rhizome using the Tail Suspension Test (TST) and Forced Swimming Test (FST), which are standard behavioral methods for evaluating antidepressants in laboratory animals. Therefore, this study aims to evaluate the antidepressant activity of *Etlingera rubroloba* rhizome extract using the TST and FST.

METHOD

This study was conducted at the Laboratory of the Faculty of Pharmacy, Halu Oleo University. Samples of *Etlingera rubroloba* rhizomes were obtained from Lalemba Village, West Muna Regency, Southeast Sulawesi, and were identified to ensure species accuracy. The collected rhizomes were prepared through wet sorting, slicing, drying for 5–7 days, and dry sorting, then ground into crude powder. Extraction was performed by maceration using methanol for 3×24 hours until a clear filtrate was obtained, which was then evaporated using a rotary evaporator at 40–45°C to obtain a concentrated extract. The extract was then fractionated using vacuum column chromatography with silica gel as the stationary phase and an eluent based on TLC results. Phytochemical screening was performed to identify secondary metabolites, including alkaloids (Dragendorff), flavonoids (MgCl_2), tannins (FeCl_3), saponins (foam test), and terpenoids (Liebermann–Burchard). Antidepressant activity testing was conducted using mice acclimatized for 7 days.

The depression model was induced using the Chronic Mild Stress (CMS) method over two weeks through exposure to varying mild stressors, including changes in the light–dark cycle, predator sounds, and cage shaking. After induction, test animals were administered the extract orally for 7 days, with Amitriptyline as the positive control and 0.5% Na-CMC as the negative control. Antidepressant activity was evaluated using the Tail Suspension Test (TST) and Forced Swimming Test (FST). The parameter observed was the duration of immobility over a 4-minute period following a 2-minute adaptation phase. A reduction in immobility time compared to the negative control was interpreted as an antidepressant effect. Data were analyzed using a one-way ANOVA with a significance level of $p < 0.05$. This study has received ethical approval under Number: 2442a/UN29.20.1.2/PG/2025.

RESULT

Phytochemical screening results indicate that the rhizome extract of *Etlingera rubroloba* contains several classes of secondary metabolites, namely alkaloids, flavonoids, tannins, saponins, and terpenoids., respectively (Table 1).

Table 1.

Results of Phytochemical Screening of *Etlingera rubroloba* Extract Using Tube Tests

Compound Class	Reagent	Result	Remarks
Alkaloids	Dragendorff	Precipitate forms	+
Flavonoids	Mg+ HCl	Brick-red color forms	+
Tannins	FeCl ₃	Brownish-yellow color	+
Saponin	Air + HCl 2 N	Stable foam	+
Terpenoid	Lieberman-Burchard	Reddish brown	+

The antidepressant activity of *Etlingera rubroloba* rhizome extract was evaluated using the Tail Suspension Test (TST) and the Forced Swimming Test (FST), with the parameter being the duration of immobility in mice. Results of the TST respectively (Table 2) and results of the FST respectively (Table 3)

Table 2.

Results of the TST test on *Etlingera rubroloba* rhizome extract

Results of the TST Test on Extracts	
Treatment Group	Immobilization Time (Seconds) Mean $\pm$ SD
Control Group	0,01 $\pm$ 0,06
Negative Control	258,57 $\pm$ 5,73
Positive Control	11,45 $\pm$ 4,28
Dose 100 mg/kg body weight	61,27 $\pm$ 10,47
Dose 200 mg/kg body weight	30,3 $\pm$ 5,94
Dose 300 mg/kg body weight	14,99 $\pm$ 7,76

In the TST test, the negative control group exhibited the longest immobilization time, at 258.57 ± 20.21 seconds, while the normal control group showed almost no immobilization (0.01 ± 0.02 seconds). Administration of the positive control, Amitriptyline, significantly reduced the immobilization time to 11.45 ± 22.89 seconds. *E. rubroloba* rhizome extract showed a dose-dependent reduction in immobility time, namely 61.27 ± 55.76 seconds (100 mg/kg body weight), 30.30 ± 38.73 seconds (200 mg/kg body weight), and 14.99 ± 21.35 seconds (300 mg/kg body weight).

Table 3.

Results of the FST test on *Etlingera rubroloba* rhizome extract

Results of the TST Test on Extracts	
Treatment Group	Immobilization Time (Seconds) Mean $\pm$ SD
Control Group	0 $\pm$ 0
Negative Control	142,57 $\pm$ 2,08
Positive Control	0,24 $\pm$ 0,87
Dose 100 mg/kg body weight	21,66 $\pm$ 4,67
Dose 200 mg/kg body weight	1,27 $\pm$ 2,81
Dose 300 mg/kg body weight	0,25 $\pm$ 0,96

Similar results were obtained in the FST test. The negative control group had an immobility time of 184.86 ± 117.29 seconds, while the normal control group showed no immobility (0 ± 0 seconds). The positive control group showed a drastic reduction to 0.24 ± 0.63 seconds. Administration of *E. rubroloba* rhizome extract also reduced the immobility time in a dose-response manner, namely 21.66 ± 23.93 seconds (100 mg/kg body weight), 1.27 ± 1.97 seconds (200 mg/kg body weight), and 0.25 ± 0.43 seconds (300 mg/kg body weight)

DISCUSSION

Phytochemical screening is the initial step in identifying classes of chemical compounds in a plant sample using color-reagent-based test tube methods. In this study, the rhizome extract of *Etlingera rubroloba* tested positive for alkaloids, flavonoids, tannins, saponins, and terpenoids. The presence

of alkaloids is indicated by the formation of a reddish-brown precipitate after the addition of Dragendorff's reagent, which occurs due to the interaction between the nitrogen atoms of the alkaloids and the metal ions in the reagent. Flavonoids were detected via the Shinoda test ($\text{Mg} + \text{HCl}$), which produced an orange-red color due to the formation of a complex between magnesium ions and the phenolic groups of the flavonoids. The tannin test with FeCl_3 produces a brownish-yellow color, indicating the formation of a complex between Fe^{3+} ions and phenolic hydroxyl groups, which suggests the presence of condensed tannins. Saponins yield a positive result through the formation of stable foam after shaking, caused by their amphiphilic nature in forming micelles. Meanwhile, the terpenoid test using the Liebermann–Burchard reagent produced a reddish-brown color due to a reaction with sulfuric acid under strongly acidic conditions. These results suggest that *E. rubroloba* extract contains various secondary metabolites with potential biological activity, including as antidepressant candidates (Dubale & Zeynudin, 2023; Widiawati & Qodri, 2023 and Yusuf et al., 2026).

The antidepressant activity of *E. rubroloba* rhizome extract was evaluated using the Tail Suspension Test (TST) and Forced Swimming Test (FST), which are behavioral despair models sensitive to changes in the monoaminergic system. A reduction in immobility time in both of these methods reflects increased neurotransmitter activity, such as serotonin, norepinephrine, and dopamine, making these methods widely used to assess the antidepressant effects of a compound (Can et al., 2012; Molendijk & de Kloet, 2019).

The negative control group exhibited the highest immobility time, confirming the successful induction of depression via the Chronic Mild Stress (CMS) method. Chronic stress exposure is known to excessively activate the hypothalamic–pituitary–adrenal (HPA) axis excessively, leading to increased glucocorticoid secretion and disrupting neurotransmitter homeostasis, including reduced levels of serotonin, norepinephrine, and dopamine, as well as decreased expression of brain-derived neurotrophic factor (BDNF), which plays a role in synaptic plasticity and neuronal survival (Willner, 2017).

In contrast, the positive control group administered Amitriptyline showed a significant reduction in immobility time. Pharmacologically, amitriptyline acts by inhibiting the reuptake of serotonin and norepinephrine, thereby increasing neurotransmitter concentrations in the synaptic cleft. Additionally, tricyclic antidepressants have been reported to increase BDNF expression and improve neuroplasticity (Thour & Marwaha, 2023). *E. rubroloba* rhizome extract demonstrated a dose-dependent reduction in immobility time in both test methods, with a dose of 300 mg/kg body weight providing the most optimal effect and approaching that of the positive control. This indicates that increased dosage correlates with increased pharmacological activity, likely due to an increase in the number of active compounds involved.

Mechanistically, the antidepressant activity of the extract is thought to involve various biological pathways, including increased levels of monoamine neurotransmitters, inhibition of monoamine oxidase (MAO), and increased BDNF expression through the activation of signaling pathways such as CREB (German-Ponciano et al., 2018). Additionally, the antioxidant and anti-inflammatory activities of phenolic compounds also contribute to suppressing oxidative stress and neuroinflammation, which play a role in the pathophysiology of depression. These contributions stem from various classes of compounds, where flavonoids play a role in modulating the monoaminergic system, alkaloids in interacting with neurotransmitters, terpenoids in modulating the central nervous system, and saponins and tannins in neuroprotective effects via antioxidant activity (Dhingra & Sharma, 2006 and Farahani et al., 2015).

Statistical analysis results indicate significant differences among treatment groups ($p < 0.05$), confirming that the extract possesses a significant pharmacological effect. The absence of significant differences between the highest extract dose and the positive control suggests that the extract's efficacy is comparable to that of the standard drug. Overall, the rhizome extract of *Etlingera rubroloba* has potential as an antidepressant agent through a multimodal mechanism involving neurotransmitter modulation, enhanced neuroplasticity, and the suppression of oxidative stress and neuroinflammation.

CONCLUSION

The rhizome extract of *Etlingera rubroloba* contains secondary metabolites such as alkaloids, flavonoids, tannins, saponins, and terpenoids, and exhibits significant antidepressant activity in the Tail Suspension Test (TST) and Forced Swimming Test (FST). This activity is characterized by a significant reduction in immobility time ($p < 0.05$) and is dose-dependent, with a dose of 300 mg/kg body weight providing an optimal effect comparable to Amitriptyline. Overall, *E. rubroloba* rhizome extract has potential as a candidate for a natural antidepressant agent through a multimodal mechanism involving the modulation of monoamine neurotransmitters, increased neuroplasticity, as well as antioxidant and anti-inflammatory activity.

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