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Anxiolytics and antidepressants properties of roasted agung banana peel: a potential therapeutic approach

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ABSTRACT

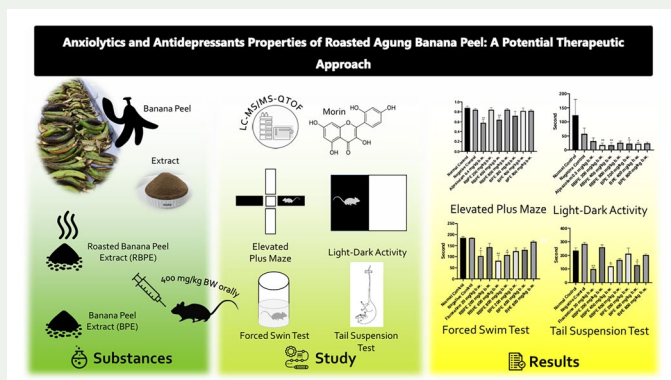
Anxiety and depression are complex neurological disorders that are considered by WHO to be among the most severe health problems. The causes of depression and anxiety disorders are an imbalance between oxidants and antioxidants in favour of the oxidants, resulting in a disruption of redox signalling and control and molecular damage. Banana peels can increase the antioxidants to counteract free radicals. This study explored the effectiveness of several roasted Agung banana peel extract doses, namely 200, 400, and 800 mg/kg b.w., as anxiolytics and antidepressants. The 400 mg/kg b.w. RBPE showed the most consistent anxiolytic and antidepressant effects among the other doses. Due to the roasting process, this pharmacological effect is thought to be caused by the emergence of a new flavonoid compound, morin. Increasing the dose to 800 mg/kg did not cause an increase in pharmacological effects, presumably due to a ceiling effect.

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KEYWORDS

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 antidepressants; SSRIs;
 Roasted banana peels;
 morin



Abbreviations: BPE: banana peel extract; RBPE: roasted banana peel extract; SSRI: selective serotonin reuptake inhibitors; FST: forced swim test; TST: tail suspension test; LDA: light dark activity; EPM: elevated plus maze; LC-MS/MS-QTOF: liquid chromatography-tandem mass spectrometry-quadrupole time of flight; NF-κB: nuclear factor

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kappa-B; SH: glutathione; ROS: reactive oxygen species; ANOVA: analysis of variance; Tukey's HSD: Tukey's honestly significant difference; MAO: Monoamine oxidase; TBA: thiobarbituric acid

1. Introduction

Banana peel is a waste that has been studied by some researcher. Jabeen et al. (2024) have utilise banana peel to isolate the tyrosinase compound. On the other hand, banana peel is also could overcome anxiety and depression (Samad et al. 2017) due to its phytoantioxidant, tryptophan, and flavonoids compound (Tee and Hassan 2011; Siddique et al. 2018). In Hadisoewignyo et al. (2023), Agung var. Semeru banana peel was processed into powder and then roasted at 200°C. Although roasting can remove some compounds with antioxidant properties, new compounds with higher antioxidant activity are potentially formed due to the Maillard reaction. Other findings reported that the RBPE from Agung var. Semeru contains the flavonoid morin, observed using LC-MS/MS-QTOF (Hadisoewignyo et al. 2024). Deepak (2025) found that morin significantly reversed the stress-induced increase in brain TBA-reactive substance (TBARS), plasma nitrite, and increase the stress-induced decrease in brain catalase levels. Morin also inhibited brain MAO-A activity in brain which lead to increase of neurotransmitter in the brain.

Those theoretical hypotheses about the anxiolytic and antidepressant effects of RBPE are explored in this study using behavioural tests such as LDA, EPM, FST, and TST.

2. Results and discussion

Depression and anxiety disorders are among the most common psychiatric disorders; they are highly comorbid with each other and together are considered to belong to the broader category of internalising disorders (Kalin 2020). Several studies have suggested a link between oxidative stress and anxiety-like behaviours. Salim et al. (2010) found that oxidative stress directly contributes to anxiety-like behaviours. In addition, Rammal et al. (2008), using the EPM test to assess anxiety-like behaviour in rodents, discovered a positive association between anxiety-like behaviour and oxidative status in several neuronal and glial cells in brain. This association was observed in the cerebellum, hippocampus, cerebral cortex, and peripheral leukocytes. Collectively, these findings highlight the involvement of oxidative stress in anxiety-like behaviour and suggest a potential therapeutic target for the treatment of anxiety and depression disorders.

When the ROS concentration exceeds an organism's antioxidant capacity, cells enter a state of oxidative stress, where excess ROS induces oxidative damage to cellular components (Hassan et al. 2014). Therefore, a preventive therapy can be given to increase antioxidant levels as a defence mechanism to minimise the effects of increased ROS. An alternative therapy to increase the number of antioxidants in counteracting free radicals is the use of traditional medicine, which is banana peel (Samad et al. 2017).

The profiling metabolites of roasted and unroasted banana peel extract show the presence of flavonoids and phenolic compounds, which are closely related to their antioxidant activity. Moreover, the results of LC-MS/MS-QTOF (Tables S1 and S2) show the flavonoid compound of Kaempferol-3-O-rutinoside. These compounds are included in natural flavonoids, which have anti-anxiety potential (Karim et al. 2018). On the other hand, morin is the main compound of RBPE. Moreover, morin hydrate can reduce anxiety and have an antidepressant effect in mice (Olonode et al. 2018).

Morin is an isomeric structure of quercetin, which is differentiated based on the pattern of hydroxylation meta on morin and ortho on quercetin. Morin has a C15 flavonoid structure, contains three phenolic rings, and has a competitive binding affinity for the serum thyroxine transthyretin transport protein. Morin was ameliorated oxidative stress by reducing malonaldehyde levels and increasing the activities of antioxidant enzymes (glutathione peroxidase, superoxide dismutase) (Rajput et al. 2021). This study performed molecular docking on the morin contained in RBPE binding with the human serotonin transporter (SERT). The known binding affinity for morin (−8.8) and alprazolam (−9.1) strengthens the notion that morin is an active substance in RBPE with anti-anxiety activity.

The tests were conducted on mice, including light-dark activity ($n=4$ mice/group), elevated plus maze ($n=5$ mice/group) for anti-anxiety test, forced swim test ($n=5$ mice/group), and tail suspension test ($n=5$ mice/group) for antidepressant test to evaluate the effect of BPE and RPBE in several doses (200, 400, and 800 mg/kg b.w.).

From the individual test results of both the anxiety test and the depression test (Figures S1–S6), it can be seen that only RBPE 400 mg/kg b.w. provides the most consistent results as an anxiolytic and antidepressant agent. The lack of increased anxiolytic and antidepressant effects was observed when increasing the RBPE dose from 400 to 800 mg/kg b.w. likely reflects a typical dose-response relationship. Generally, a pharmacological effect initiates at a threshold dose and intensifies with escalating doses (Snyder 1984). However, a plateau is eventually reached where further dose increases yield no significant improvement. In some cases, excessively high doses can even diminish or negate the observed response due to the potential toxic effects of the compound. While this dose-response relationship holds across a reasonable concentration range, in this instance, the optimal dose for the observed anxiolytic and antidepressant effects of RBPE was at 400 mg/kg b.w.

3. Experimental

Detailed experimental procedures, are provided in the [supplementary material](#).

4. Conclusion

RBPE 400 mg/kg b.w. has been proven to have an anxiolytic and antidepressant effect. Increasing the dose to 800 mg/kg b.w. Even so, this research doesn't perform long term toxicity assessment. Therefore, it is recommended to test the influence of RBPE on neurotransmitter and toxicity test to assess long term safety so it can be formulated and continued with clinical trials.

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Author contribution statement

CRedit: **Lannie Hadisoewignyo**: Conceptualization, Project administration, Supervision, Writing – review & editing; **Jefri Prasetyo**: Investigation, Methodology; **Kuncoro Foe**: Investigation, Methodology; **Kevin Owen Santoso**: Visualization, Writing – original draft, Writing – review & editing; **Eka Pramyrtha Hestianah**: Formal analysis, Investigation; **Ida Ayu Andri Parwitha**: Formal analysis, Investigation; **Ivonne Soeliono**: Formal analysis, Investigation, Methodology, Software, Supervision, Validation.

Disclosure statement

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