group); group III: mice received scopolamine and donepezil (as a standard group); and groups IV-VI: mice received scopolamine plus G. inodorum leaf extract 50, 100, and 200 mg/kg BW (GI50, GI100, and GI200), respectively. The behavioural tests, including learning and memory tested by the Morris water maze and passive avoidance, presented the results as time spent in the target quadrant (s) and escape latency time (s), respectively.

Results: The result of learning and memory with the Morris water maze found that the time spent in the target quadrant that mice received donepezil and 200 mg/kg BW of G. inodorum leaf extract had spent in the target quadrant was 21.00 ± 1.84 and 22.83 ± 1.81 sec, respectively, and had statistical significance for more time spent when compared to the scopolamine group (15.83 ± 0.47). This result represented that mice that received donepezil and 200 mg/kg BW of G. inodorum leaf extract demonstrated improved cognitive function relative to those treated with scopolamine. This suggests that both donepezil and the leaf extract may attenuate memory impairment and enhance spatial learning abilities in mice, potentially offering valuable insights for developing treatments for cognitive impairments. However, the fear memory with passive avoidance showed that no statistically significant differences were found in all groups.

Conclusion: Scopolamine-induced memory impairment in ICR mice, particularly in spatial memory, can potentially be attenuated by 200 mg/kg BW of G. inodorum leaf extract. These findings may be related to G. inodorum's acetylcholinesterase-inhibiting activity, indicating the need for further investigation in the future to validate the extract's impact on the prevention or treatment of Alzheimer's disease.

References

[1] Jeytawan N, Yadoung S, Jeeno P, Yana P, Sutan K, Naksen W, et al. Antioxidant and Phytochemical Potential of and Phytochemicals in Gymnema inodorum (Lour.) Decne in Northern Thailand. Plants (Basel). 2022;11 (24):3498. [2] Nunta R, Khemacheewakul J, Sommanee S, Mahakuntha C, Chompoo M, Phimolsiripol Y, et al. Extraction of gymnemic acid from Gymnema inodorum (Lour.) Decne. leaves and production of dry powder extract using maltodextrin. Sci Rep. 2023;13(1):11193. [3] Haideri MH, Phanjaroen T, Khiaolaongam W, Boonchalaem T, Laoung-On J, Chaipoot S, et al. Effect of Different Extraction Techniques on Phenolic Profile and Phytochemical Potential of Gymnema inodorum Leaf Extract. Molecules. 2024;29(22):5475.

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NRF2 AS A NOVEL THERAPEUTIC TARGET FOR DEPRESSION: INSIGHTS FROM PRECLINICAL STUDIES

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Introduction: Depression remains one of the most prevalent and disabling psychiatric conditions worldwide, affecting an estimated 280 million individuals, equivalent to 3.8% of the population, including 5.0% of adults and 5.7% of people over the age of 60 (1). Recent evidence proposes that reduced antioxidant defenses are implicated in the pathophysiology of depression, likely due to a diminished ability to neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS) (2). Nuclear factor erythroid 2–related factor 2 (Nrf2) is a transcription factor that regulates the expression of key antioxidant enzymes (3). The involvement of Nrf2 in depression has received a lot of attention in recent years, reporting the role of oxidative stress and neuroinflammation in depression pathogenesis, placing Nrf2 as a promising target for novel antidepressant strategies.

Aims: This systematic review aimed to critically assess the current preclinical evidence regarding the role of Nrf2 in models of depression. Specifically, we intended to (1) evaluate how Nrf2 expression is affected in depressive conditions, and (2) identify the effect of antidepressant and natural compounds on Nrf2 modulation.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive search of the PubMed database was performed using combinations of the following keywords: "Nrf2", "depression". Boolean operators and MeSH terms were employed to refine the search strategy. Eligible studies met the following inclusion criteria: (1) original peer-reviewed articles published in English; (2) experimental studies involving animal models of depression and/or cell lines; and (3) explicit evaluation of Nrf2 expression, modulation, or related outcomes. Exclusion criteria included: (1) reviews, meta-analyses, or editorials; (2) studies focusing on diseases unrelated to depression; (3) research that did not evaluate Nrf2 directly or lacked molecular data on Nrf2 activity. The study selection process involved two independent reviewers who screened titles and abstracts, followed by full-text assessments of potentially eligible articles.

Results: The results showed that Nrf2 tends to decrease in stress-induced depressive models and increase after treatment with antidepressants as well as compounds that exhibit anti-inflammatory and/or antioxidant properties. Antidepressants such as fluoxetine, bupropion, and duloxetine were found to activate Nrf2 and attenuate depressive-like behaviours. Similarly, natural compounds including sulforaphane, catalpol, resveratrol, and quercetin also elevated Nrf2 levels and improved stress levels and depression in the models evaluated. These alterations were observed in the hippocampus and prefrontal cortex, regions known to be affected in depression. The activation of downstream antioxidant pathways, particularly HO-1 and NQO1, appears to underlie these therapeutic effects, although further elucidation of these mechanisms is required.

Conclusions: The results of this systematic review suggest that Nrf2 expression is downregulated under depressive conditions and can be restored by both conventional antidepressants and natural compounds. These findings reinforce the therapeutic relevance of Nrf2 modulation in depression. Further research is needed to clarify the mechanisms underlying the effects of these compounds and to evaluate their safety and efficacy in clinical trials.

References

(1)Institute for Health Metrics and Evaluation. Global health data exchange. Global Burden of Disease Study 2017 Data Resources. (2)Cui, L., Li, S., Wang, S. et al. (2024). Major depressive disorder: hypothesis, mechanism, prevention and treatment. Sig Transduct Target Ther 9, 30. https://doi.org/10.1038/s41392-024-01738-y (3)Ngo, V., & Duennwald, M. L. (2022). Nrf2 and Oxidative Stress: A General Overview of Mechanisms and Implications in Human Disease. Antioxidants (Basel, Switzerland), 11(12), 2345. https://doi.org/10.3390/antiox11122345

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ANETHOLE DECREASES BODY WEIGHT GAIN DESPITE THE INCREASED FOOD INTAKE AND APPETITE IN RATS ON A HIGH-CALORIE DIET

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Introduction: Loss of appetite can have a detrimental impact on a patient's well-being by reducing physical strength and immune system due to lack of nourishment [1]. Anethole is a natural aromatic compound, which is widely used in food industry, occurring in essential oils such as anise and fennel. Emerging evidence suggests that essential oils and fragrant compounds possess valuable activities, including anti-inflammatory, antioxidant, appetite-enhancing and others [2,3].

Aim: The aim of the present study was to examine the impacts of anethole on food and calorie intake and body weight gain in rats on a high-calorie diet (HCD).

Materials and methods: Fifty male Wistar rats were allocated into five groups: control, HCD, HCD + 62.5A, HCD + 125A, and HCD + 250A. The control group consumed a regular laboratory diet and tap water, whereas the other groups received a high-fat high-fructose diet (lard 17%, fructose 17%) and a 10% fructose solution instead of water. HCD + 62.5A, HCD + 125A and HCD + 250A groups were treated daily orally with anethole dissolved in sunflower oil in a volume of 3 ml/kg at doses of 62.5 mg/kg, 125 mg/kg, and 250 mg/kg, respectively. The solvent was administered to both the control and HCD groups at the same volume and route. Food intake was measured in grams per rat every three days, and the average daily consumption was calculated for the treatment period (10 weeks). Calorie intake was calculated by converting the ingested food and fructose liquid into calories based on established caloric data. Animals' body