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Anxiolytic Potential of *Scutellaria pinnatifida* Root Methanolic Extract: An Experimental Study in Mice

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ABSTRACT

Background & Objective: Anxiety disorders constitute a significant portion of the global mental health burden, affecting large segments of the population with considerable severity. *Scutellaria pinnatifida*, a medicinal plant belonging to the mint family, has been investigated for its potential anxiolytic effects. In this investigation, we assess the anxiolytic activity of methanolic extract derived from the roots of *S. pinnatifida* in mice, aiming to provide further insights into its neuropharmacological profile.

Materials & Methods: Forty-eight male mice, weighing 20–30 grams, were randomly distributed into six distinct groups, each consisting of eight animals. The groups consisted of: I) control group receiving normal saline; II) positive control given diazepam at 2 mg/kg; III, IV, and V) treatment groups administered S. pinnatifida methanolic extract at doses of 50, 100, and 200 mg/kg, respectively; and VI) a combination group receiving flumazenil at 2 mg/kg along with S. pinnatifida extract at 200 mg/kg. Following intraperitoneal administration of all treatments, behavioral responses indicative of anxiety were evaluated via the elevated plus-maze paradigm. Statistical computations were performed using InStat software. Results are presented as Mean ± SEM, with significance defined at $P < 0.05$.

Results: The results showed that administering diazepam and the highest dose of S. pinnatifida methanolic extract (200 mg/kg) notably raised the number of entries into the open arms and reduced the duration spent in the closed arms. Additionally, the addition of flumazenil to the 200 mg/kg dose of S. pinnatifida did not produce a significant alteration in the observed anxiolytic effects, indicating a comparable response between the two groups.

Conclusion: This study suggests that the methanolic extract of *S. pinnatifida* possesses anxiolytic and sedative properties, with the most pronounced anxiolytic effect observed at the highest dose.

Keywords: *Scutellaria*, Anxiety, Mice, Elevated Plus-Maze Test, Diazepam

1. Introduction

Clinically, anxiety presents as a persistent yet often ambiguous feeling of worry or tension, commonly associated with physical manifestations like chest discomfort, rapid heartbeat, breathlessness, sweating, disorientation, and impaired cognitive performance (1). While mild levels of anxiety can enhance environmental awareness and heighten the perception of potential dangers, severe anxiety can disrupt behavioral consistency and impede rational decision-making (2). The modulation of anxiety involves multiple receptor systems, including serotonin,

gamma-aminobutyric acid (GABA), catecholamines, and sex hormones (3).

GABA, the primary inhibitory neurotransmitter in the brain, reduces neuronal excitability by increasing chloride influx upon receptor binding, resulting in hyperpolarization and a dampening of nerve activity (3). Additionally, estrogen's anxiolytic effects are mediated through two intracellular receptors, ERβ and ERα, which modulate genomic activity (4). Evidence also indicates that oxidative damage to the brain may harm the nervous system, and accumulating evidence suggests that oxidative damage may be a major contributing factor in the pathogenesis of anxiety and depressive disorders, likely through disruption of neuronal homeostasis (5).

Anxiety disorders pose a significant public health issue, impacting around 25% of people in the United States (6). According to national estimates, anxiety disorders affect 15.6% of the Iranian population over 12 months (7). Hence, like other neuropsychiatric disorders, it may cause many complications and burdens on society and the healthcare system (8). Individuals with anxiety disorders frequently seek medical care due to symptoms like chest pain, palpitations, or dizziness, which they often fear are related to physical health problems (1). This increases visits to primary care physicians, specialists, and emergency departments, which strains healthcare resources (9). The economic burden of anxiety is also substantial, as it includes both direct healthcare costs, such as consultations, medications, and hospitalizations, and indirect costs, such as loss of productivity, absenteeism, and long-term disability (10). Moreover, anxiety commonly co-occurs with other mental health disorders, such as depression, and chronic physical conditions like cardiovascular disease (11). This comorbidity complicates treatment, leading to more extensive and complex care plans, which increases the demand for healthcare services and often results in poorer health outcomes (12). Left untreated, anxiety disorders can profoundly deteriorate an individual's quality of life, interfering with their capacity to manage routine responsibilities, sustain employment, and foster meaningful social ties (10). A diminished quality of life in anxious individuals may initiate a negative feedback loop, decreasing their adherence to treatments and engagement in health-promoting activities, thereby exacerbating overall health decline (13). On a broader scale, widespread anxiety within a population can affect public health by increasing the prevalence of mental health issues, reducing workforce productivity, and contributing to social and economic instability (6). This situation may necessitate the expansion of public health initiatives to address the growing mental health needs, diverting resources from other critical areas. Additionally, people with anxiety disorders face a greater risk of developing substance use disorders because they might use alcohol or drugs to self-medicate (14). This exacerbates the public health crisis by increasing the incidence of addiction and related health problems, further straining healthcare services, and intensifying the burden on public health systems (15).

Many conventional anxiolytic medications are associated with adverse effects, including sedation, fatigue, risk of tolerance, and dependence, which limit their long-term usability (16). In recent years, the practice of using natural or herbal remedies for self-managing various stress-related conditions like anxiety has gained significant traction worldwide (17). Today, herbal medicine stands as one of the most commonly adopted complementary or alternative approaches for treating insomnia (17). Due to their favorable safety profiles, herbal treatments are increasingly considered viable substitutes for synthetic anxiolytics (18). However, the effectiveness of traditional medicinal herbs in addressing mental health disorders through complementary and alternative medicine remains insufficiently studied, particularly in terms of understanding the mechanisms by which their phytocomponents act.

Scutellaria pinnatifida (S. pinnatifida), belonging to the Labiatae family, is a plant recognized for its potential therapeutic properties. It is a significant genus of perennial and annual herbs, comprising roughly 360 to 400 species (19). Species of the Scutellaria genus are found extensively in tropical highlands spanning continents such as North America, Europe, Asia, and extending from Siberian regions to South American tropics (19). Commonly called "skullcaps," it is one of the 20 species of the Scutellaria L. genus (Lamiaceae family) native to Iran and has been extensively used in traditional Chinese medicine (19). This plant is known as Boshghabi in Persian (19). The plant usually reaches a height of 20-50 cm or slightly more. Its flowers come in various colors, such as purple, blue, pink, red, yellow, and white, and are arranged axially around the flowering branch (19). The stems are rigid, often square-shaped, and the leaves are opposite, elongated, serrated, and pointed, attaching directly to the stem without petioles (19). The chemical constituents of S. pinnatifida include glucosides, formic acid, cinnamic acid, and silica (19). Both in vitro and in vivo investigations have highlighted the therapeutic promise of Scutellaria-derived phytochemicals, particularly in neurological disorders like anxiety, depression, and neurodegenerative diseases (20). By examining the effects of *S. pinnatifida* root extract on anxiety-like behaviors and its possible interaction with benzodiazepine receptors, this study seeks to uncover a novel phytotherapeutic pathway for managing anxiety disorders.

2. Materials and Methods

2.1 Animals

Male mice weighing 20 to 30 grams were obtained from the animal facility of the University of Medical Sciences in North Khorasan. The animals were kept in a carefully regulated environment, maintaining a temperature of 21±2°C and a 12-hour light-dark cycle. The study received approval from the Ethical Committee of North Khorasan University of Medical Sciences, with Ethical approval ID: IR.NKUMS.REC.1398.038.

2.2 Plant Extraction

The roots of *Scutellaria pinnatifida* were collected, air-dried, and ground into a fine powder. A 100-gram portion of this powder was macerated in 70% hydroethanolic solution at 37°C for 72 hours with periodic agitation. The extract was subsequently filtered and concentrated under reduced pressure at 45°C using a rotary evaporator (Eyela, Heidolph, Germany) (21, 22).

2.3 Experimental Groups

Six experimental groups were formed (n = 8 each), comprising: 1) a saline-treated control group; 2) a diazepam-treated positive control (2 mg/kg); 3–5) groups receiving 50, 100, or 200 mg/kg of S. pinnatifida extract (SP 50, SP 100, SP 200); and 6) a co-treatment group administered flumazenil (2 mg/kg) and SP 200. All injections were performed intraperitoneally 30 minutes before behavioral assessment using the elevated plus maze (EPM).

2.4 Anxiety Assessment

The EPM serves as a standard behavioral paradigm to evaluate anxiety-related behaviors in rodents, capitalizing on their natural aversion to open spaces. It relies on their natural dislike of open and elevated areas and is widely employed in pharmacological and behavioral neuroscience studies (23). The EPM is made of wood and features two open arms opposite two closed arms, all of which are elevated approximately 50 cm above the ground. This model measures innate fear responses without prior animal training or learning. Thirty minutes before the test, each mouse was given its designated treatment and then moved to a study room. Five minutes before testing, each mouse was separately placed into a 30 × 30 × 40 cm box to promote exploratory activity. Subsequently, the mouse was placed in the center of the EPM, and its behavior was recorded for 5 minutes, with a focus on the number of entries and the time spent in both the open and closed arms. The experiment was observed and documented with a video camera positioned above the maze in an adjacent room.

2.5 Statistical Analysis

Quantitative data were reported as mean values with corresponding standard errors (SEM). Statistical significance among groups was determined via one-way analysis of variance (ANOVA), followed by post hoc comparisons using the Tukey-Kramer method. A threshold of $p < 0.05$ was used to denote statistical significance. The analyses were carried out using InStat (GraphPad Software, USA).

3. Result

Treatment with a high dose of *S. pinnatifida* extract (200 mg/kg) and diazepam significantly increased the frequency of entries into the open arms of the maze compared to the control group ($p < 0.05$ and $p < 0.01$, respectively). Interestingly, the number of open arm entries observed across all extract-treated groups did not differ significantly from that of the diazepam group. Furthermore, no meaningful difference was detected between the high-dose extract group and the group receiving both flumazenil and the high extract dose (Figure 1).

Figure 2 illustrates that a high concentration of S. pinnatifida methanolic extract (200 mg/kg), diazepam, and flumazenil with S. pinnatifida methanolic extract (200 mg/kg) significantly reduced the number of entries into the closed arms of the maze, compared to the control group. The effect of the lowest extract concentration (50 mg/kg) was significantly lower than that of diazepam. No notable differences were observed between the high extract concentration group and the treated flumazenil group (Figure 2).

Administration of diazepam significantly prolonged the time mice spent in the open arms relative to the control group. Although the methanolic extract of *S. pinnatifida* demonstrated a dose-dependent increase in open-arm exploration, none of the tested concentrations matched the effect of diazepam. Furthermore, the duration spent in the open arms did not differ significantly between the group receiving 200 mg/kg of the extract alone and the group co-administered with flumazenil and the same extract dose (Figure 3).

Treatment with the extract, diazepam, or flumazenil resulted in a significant decrease in the amount of time spent in the closed arms compared to the control group, with the most pronounced effects observed at the highest dose of the extract ($p < 0.001$ across all comparisons; see Figure 4). Among the extract-treated groups, the 200 mg/kg dose resulted in a significantly greater reduction in closed-arm duration compared to the 50 and 100 mg/kg doses ($p < 0.05$ and $p < 0.001$, respectively). In contrast, the lower doses of the extract had a less significant impact than diazepam ($p < 0.001$ for both). Importantly, no significant difference was detected between the group receiving 200 mg/kg of the extract alone and the group co-treated with flumazenil and the same extract dose.

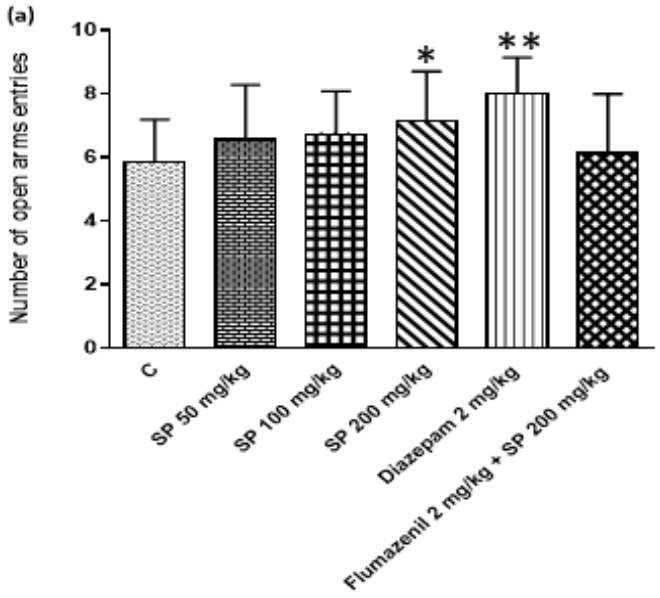

Figure 1. The number of entering into the open arms in elevated plus-maze of control (C), *S. pinnatifida* (SP, 50, 100, and 200 mg/kg), diazepam (D), and SP 200 mg/kg with flumazenil, (n=8 in each group). Data are presented as mean ± SEM values. * $p<0.05$ and ** $p<0.01$ shows significant differences compared to group C. Statistical analyses were performed using ANOVA with Tukey-Kramer's post-test. (**Designed by Authors, 2025**).

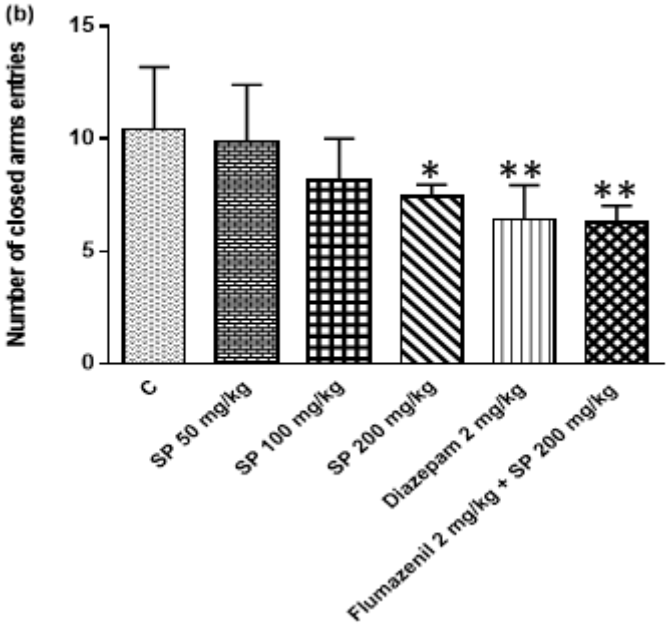

Figure 2. The number of entering into the closed arms in elevated plus-maze of control (C), *S. pinnatifida* (SP, 50, 100, and 200 mg/kg), diazepam (D), and SP 200 mg/kg with flumazenil, (n=8 in each group). Data are presented as mean ± SEM values. * $p<0.05$ and ** $p<0.01$ show significant differences compared to group C. + $p<0.05$ shows significant differences between the three concentrations of SP and D. Statistical analyses were performed using ANOVA with Tukey-Kramer's post-test. (**Designed by Authors, 2025**).

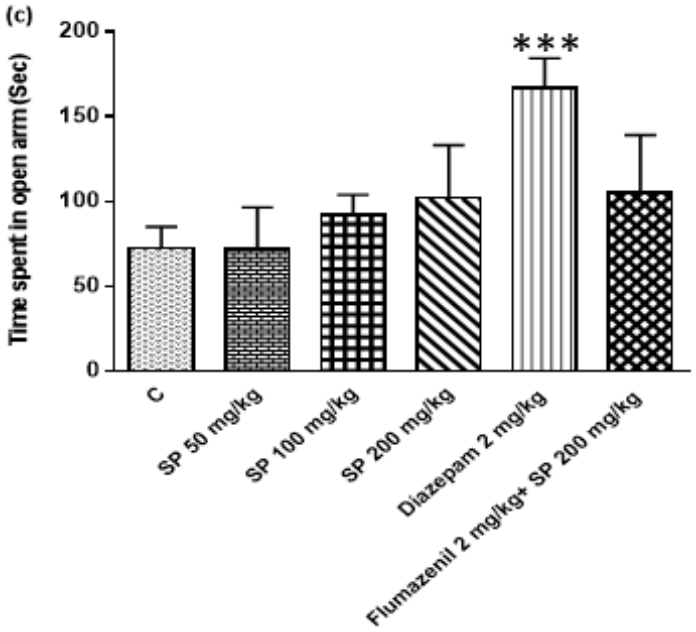

Figure 3. The time spent in the open arms in elevated plus-maze of control (C), *S. pinnatifida* (SP, 50, 100, and 200 mg/kg), diazepam (D), and SP 200 mg/kg with flumazenil, (n=8 in each group). Data are presented as mean ± SEM values. *** p<0.001 shows significant differences compared to group C. +++ p<0.001 show significant differences between the three concentrations of SP and D. Statistical analyses were performed using ANOVA with Tukey-Kramer's post-test. (**Designed by Authors, 2025**).

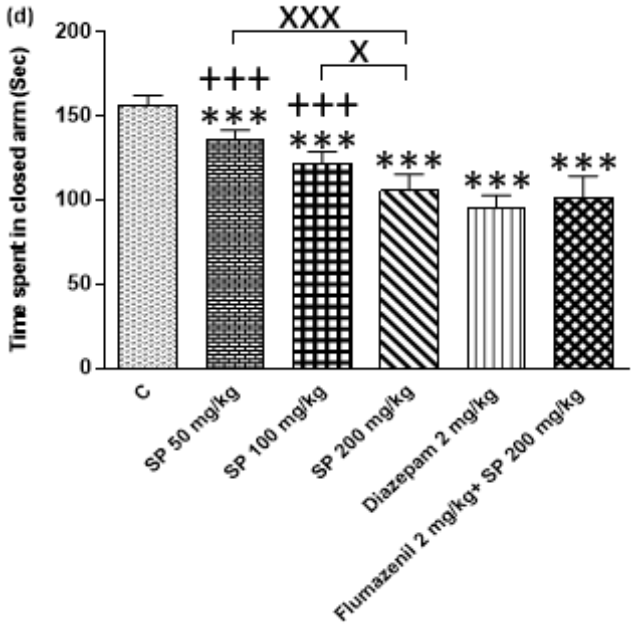

Figure 4. The time spent in the closed arms in elevated plus-maze of control (C), *S. pinnatifida* (SP, 50, 100, and 200 mg/kg), diazepam (D), and SP 200 mg/kg with flumazenil, (n=8 in each group). Data are presented as mean ± SEM values. *** p<0.001 shows significant differences compared to group C. +++ p<0.001 show significant differences between the three concentrations of SP and D. x p<0.05 and xxx p<0.001 show significant differences between the three concentrations SP. Statistical analyses were performed using ANOVA with Tukey-Kramer's post-test. (**Designed by Authors, 2025**).

4. Discussions

This work explored whether the methanolic extract of S. pinnatifida exhibits anxiety-modulating effects in mice. Notably, the behavioral effects were more prominent at higher administered doses. To evaluate anxiety-related behavior, the EPM test was utilized, an established paradigm in behavioral pharmacology. This test leverages rodents' aversion to open spaces, and its predictive validity is demonstrated by increased exploration of the

open arms following administration of known anxiolytic agents such as diazepam (23).

In the current study, as expected from earlier studies, diazepam significantly increased both the frequency and duration of visits to the open arms in the EPM, confirming its known anxiolytic properties. Similarly, treatment with high concentrations of the *S. pinnatifida* methanolic extract resulted in a significant increase in open arm entries and a decrease in closed arm entries, suggesting an anxiolytic effect comparable to that of diazepam (20, 24-29). Furthermore, all treatment groups, including those receiving high doses of the extract, diazepam, and high-dose extract with flumazenil, spent significantly less time in the closed arms than the control group, underscoring the potential efficacy of the extract. Interestingly, the study found no significant interaction between high extract concentrations and flumazenil, a benzodiazepine receptor antagonist. This suggests that the anxiolytic effects of *S. pinnatifida* are likely mediated through pathways independent of the GABAergic system, particularly benzodiazepine receptors. Several investigations have proposed that the antidepressant effects of *S. pinnatifida* may be mediated through the inhibition of brain monoamine oxidases A and B, offering a plausible neurochemical mechanism underlying its action (20, 29). Thus, it appears that the methanolic extract of *S. pinnatifida* may exert its anti-anxiety effects through alternative receptor mechanisms. Previous studies have linked experimentally induced anxiety with oxidative stress, characterized by the overproduction of free radicals, lipid peroxidation, and subsequent neuronal damage. This connection has been supported by findings such as those from Merzoug et al., which highlighted the role of oxidative stress in anxiety, as well as from Ying Xu's study, which suggested that antioxidant therapies could offer a novel approach to anxiety treatment (30, 31). Antioxidant effects have been discussed in previous studies (26, 32). According to Del Azar and colleagues, the methanolic extract of the aerial parts of the plant exhibited vigorous antioxidant activity, as quantified by an RC_{50} value of 350 ± 0.044 mg/mL, supporting its potential as a natural source of free radical scavengers (33). Golmakani et al. conducted a study that found a link between the phenolic content and the antioxidant activity of S. pinnatifida. These observations suggest that *S. pinnatifida* serves as a promising reservoir of naturally occurring antioxidant and flavonoid constituents (26). Subsequent phytochemical analyses using DPPH and FRAP techniques confirmed that *S. pinnatifida* contains significant quantities of antioxidant compounds, including various flavonoids, anthocyanins, and carotenoids. These findings suggest that the anxiolytic effects seen in this study may partly result from the antioxidant properties of S. pinnatifida, which could help reduce anxiety caused by oxidative stress.

The study on *Scutellaria pinnatifida* demonstrates several significant strengths. Firstly, it addresses a relatively unexplored area within the Scutellaria genus. While species like Scutellaria baicalensis have been extensively researched for their anxiolytic properties, this study on *S. pinnatifida* offers new insights into the potential of lesser-known species. This contributes valuable information to the field of herbal medicine, particularly in the context of identifying alternative or complementary treatments for anxiety disorders. Another strength of the study is its systematic approach to dose-dependent analysis. The research provides robust evidence of its anxiolytic potential by systematically examining the effects of varying doses of *S. pinnatifida*. This detailed approach not only strengthens the validity of the findings but also offers practical guidance for determining appropriate dosing in future clinical settings. Including flumazenil, a benzodiazepine receptor antagonist, is a powerful aspect of this research. The involvement of benzodiazepine receptors in the extract's anxiolytic response enhances our understanding of the neuropharmacological basis of *S. pinnatifida*'s effects. This is important because it indicates that S. pinnatifida could be a safer option than traditional benzodiazepines, which are often linked to side effects like sedation. Another notable strength of the study is its potential for clinical application. The findings suggest that *S. pinnatifida* exhibits anxiolytic effects without significant sedation, making it a promising candidate for the development of new anxiolytic therapies. This is especially crucial due to the continuous demand for better and more reliable therapies to address anxiety conditions. By expanding the pharmacological understanding of *S. pinnatifida*, this research lays the groundwork for future innovations in anxiety treatment modalities.

However, the study has its limitations. While the current findings support the anxiolytic potential of S. pinnatifida extract based on behavioral parameters, we acknowledge the preliminary nature of these results. Through biochemical and histological analyses, future studies must explore the underlying molecular mechanisms, including receptor-level interactions and oxidative stress pathways. One limitation is the reliance on a single behavioral test, the elevated plus-maze, to assess anxiety. Although this method is well-established, additional behavioral assays, such as the light-dark box test or open-field test, could have provided a more comprehensive evaluation of the anxiolytic effects. This would have strengthened the robustness of the findings and offered a broader understanding of the behavioral effects of S. pinnatifida. Another limitation is the lack of long-term efficacy data. The study primarily focuses on the acute effects of S. pinnatifida. Without long-term studies, assessing the extract's chronic effects, potential development of tolerance, or long-term safety is difficult. Future research would benefit from extending the treatment periods and incorporating follow-up studies to better understand the long-term implications of S. pinnatifida use.

Additionally, while the study successfully demonstrates the anxiolytic effects of S. pinnatifida, it does not identify the specific active compounds responsible for these effects. Identifying and isolating these compounds would lead to a clearer understanding of the pharmacological mechanisms and could guide the development of more

targeted anxiolytic therapies. Lastly, the study's findings, though promising, are based on animal models. The differences in biology and psychology between mice and humans could limit the direct applicability of these findings to human medical outcomes. Given the encouraging outcomes observed in this study, future investigations, especially clinical trials, are warranted to determine whether *S. pinnatifida* can be safely and effectively used in the clinical treatment of anxiety disorders.

5. Conclusion

This study demonstrates that high doses of methanolic extract from *S. pinnatifida* significantly attenuate anxiety-like behaviors in mice, yielding outcomes analogous to those produced by diazepam. While flumazenil was used to explore the possible role of benzodiazepine receptors, the lack of a notable antagonistic effect indicates that the anxiolytic effects of S. pinnatifida are probably mediated via pathways other than benzodiazepine receptors. Collectively, the data suggest that *S. pinnatifida* may serve as an effective plant-based agent for managing anxiety-related conditions. Nevertheless, further biochemical, molecular, and receptor-level investigations are essential to elucidate the exact mechanisms underlying its effects and to assess the efficacy and safety of its active constituents in both preclinical and clinical settings.

6. Declarations

6.1 Acknowledgments

Not applicable.

6.2 Ethical Considerations

This study has been approved by the North Khorasan University of Medical Sciences Ethical Committee (Ethical approval ID: IR.NKUMS.REC.1398.038). Relevant guidelines and regulations are carried out for all methods. Furthermore, informed consent was obtained from all subjects.

6.3 Authors' Contributions

YE, FS, and ZB contributed to the designing and running of the model. YE, ZK, AND SP gathered the required data for the model, including literature review, cost, and efficacy data. AMT and MV contributed to the study's statistical and epidemiological parts and double-checked all analyses. YE, FS, and MS wrote the manuscript. FS and YE reviewed the manuscript and double-checked all the analyses. All authors participated in reviewing the manuscript and its revision, and they were involved in research, interpretation, and finalizing the manuscript.

6.4 Conflict of Interest

The authors have no conflict of interest.

6.5 Fund or Financial Support

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

6.6 Using Artificial Intelligence Tools (AI Tools)

The authors were not utilized AI Tools.

6.7 Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. Dixon T. Anxiety Disorders: Mental Illness Or Normal?: Help-For; 2020.
2. Adams D, Malone S. The impact of anxiety on decision making in individuals with intellectual and developmental disabilities or a diagnosis on the autism spectrum. Decision making by individuals with intellectual and developmental disabilities: Integrating research into practice: Springer; 2021. p. 173-96. [DOI:10.1007/978-3-030-74675-9_8]
3. Tongta S, Daendee S, Kalandakanond-Thongsong S. Anxiety-like behavior and GABAergic system in ovariectomized rats exposed to chronic mild stress. Physiol Behav. 2023;258:114014. [PMID] [DOI:10.1016/j.physbeh.2022.114014]
4. Kundakovic M, Rocks D. Sex hormone fluctuation and increased female risk for depression and anxiety disorders: From clinical evidence to molecular mechanisms. Front Neuroendocrinol. 2022;66:101010. [PMCID] [DOI:10.1016/j.yfrne.2022.101010] [PMID]
5. Bhatt S, Nagappa AN, Patil CR. Role of oxidative stress in depression. Drug Discov Today. 2020;25(7):1270-6. [DOI:10.1016/j.drudis.2020.05.001] [PMID]
6. Szuhany KL, Simon NM. Anxiety Disorders: A Review. JAMA. 2022;328(24):2431-45. [DOI:10.1001/jama.2022.22744] [PMID]

7. Hajebi A, Motevalian SA, Rahimi-Movaghar A, Sharifi V, Amin-Esmaeili M, Radgoodarzi R, et al. Major anxiety disorders in Iran: prevalence, sociodemographic correlates and service utilization. BMC Psychiatry. 2018; 18(1):261. [DOI:10.1186/s12888-018-1828-2] [PMID] [PMCID]
8. Tajik A, Nikfar S, Elyasi S, Rajabi O, Varmaghani M. Cost-effectiveness and budget impact analysis of lisdexamfetamine versus methylphenidate for patients under 18 with attention-deficit/hyperactivity disorder in Iran. Child Adolesc Psychiatry Ment Health. 2023; 17(1):115. [PMID] [PMCID] [DOI:10.1186/s13034-023-00664-1]
9. Horenstein A, Heimberg RG. Anxiety disorders and healthcare utilization: A systematic review. Clin Psychol Rev. 2020;81:101894. [DOI:10.1016/j.cpr.2020.101894] [PMID]
10. Benson C, Singer D, Carpinella CM, Shawi M, Alphs L. The Health-Related Quality of Life, Work Productivity, Healthcare Resource Utilization, and Economic Burden Associated with Levels of Suicidal Ideation Among Patients Self-Reporting Moderately Severe or Severe Major Depressive Disorder in a National Survey. Neuropsychiatr Dis Treat. 2021;17:111-23. [PMID] [PMCID] [DOI:10.2147/NDT.S229530]
11. Gomez KU, McBride O, Roberts E, Angus C, Keyes K, Drummond C, et al. The clustering of physical health conditions and associations with co-occurring mental health problems and problematic alcohol use: a cross-sectional study. BMC Psychiatry. 2023;23(89):1-14. [DOI:10.1186/s12888-023-04577-3] [PMID] [PMCID]
12. Rogers AH, Wieman ST, Baker AW. Anxiety comorbidities: mood disorders, substance use disorders, and chronic medical illness. Clinical handbook of anxiety disorders: From theory to practice2019. p. 77-103. [DOI:10.1007/978-3-030-30687-8_5]
13. Hohls JK, König HH, Quirke E, Hajek A. Anxiety, Depression and Quality of Life-A Systematic Review of Evidence from Longitudinal Observational Studies. Int J Environ Res Public Health. 2021;18(22): 12022. [DOI:10.3390/ijerph182212022] [PMID] [PMCID]
14. Bartoli F, Carretta D, Carrà G. Comorbid anxiety and alcohol or substance use disorders: an overview. Textbook of Addiction Treatment: International Perspectives. 2020: 1315-25. [DOI:10.1007/978-3-030-36391-8_92]
15. Chandler TL, Dombrowski F. Mood and Anxiety Disorders. Co-occurring Mental Illness and Substance Use Disorders. 1 ed2022. p. 17-28. [DOI:10.4324/9781003220916-3]
16. Bandelow B. Current and Novel Psychopharmacological Drugs for Anxiety Disorders. Adv Exp Med Biol. 2020;1191:347-65. [DOI:10.1007/978-981-32-9705-0_19] [PMID]
17. Zhang W, Yan Y, Wu Y, Yang H, Zhu P, Yan F, et al. Medicinal herbs for the treatment of anxiety: A systematic review and network meta-analysis. Pharmacol Res. 2022;179: 106204. [DOI:10.1016/j.phrs.2022.106204] [PMID]
18. Dave PH, Vishnupriya V, Gayathri R. Herbal remedies for anxiety and depression-a review. Res J Pharm Technol. 2016;9(8):1253-6. [DOI:10.5958/0974-360X.2016.00237.7]
19. Mozaffarian V. Biodiversity of poisonous plants in Iran. Iran Nature. 2021;6(4):47-82.
20. EghbaliFeriz S, Taleghani A, Tayarani-Najaran Z. Central nervous system diseases and Scutellaria: a review of current mechanism studies. Biomed Pharmacother. 2018;102:185-95. [DOI:10.1016/j.biopha.2018.03.021] [PMID]
21. Zhang QW, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: a comprehensive review. Chin Med. 2018;13:20. [DOI:10.1186/s13020-018-0177-x] [PMID] [PMCID]
22. Gharari Z, Bagheri K, Sharafi A. Chemical Composition of Methanolic Extracts of Scutellaria orientalis L.: Digitoxin and Neocurdione Detection by Gas Chromatography/Mass Spectrometry. Pharm Biomed Res. 2022;8(1):53-6. [DOI:10.18502/pbr.v8i1.9388]
23. Acikgoz B, Dalkiran B, Dayi A. An overview of the currency and usefulness of behavioral tests used from past to present to assess anxiety, social behavior and depression in rats and mice. Behav Processes. 2022;200:104670. [DOI:10.1016/j.beproc.2022.104670] [PMID]
24. Scult MA, Paulli AR, Mazure ES, Moffitt TE, Hariri AR, Strauman TJ. The association between cognitive function and subsequent depression: a systematic review and meta-analysis. Psychol Med. 2017;47(1):1-17. [DOI:10.1017/S0033291716002075] [PMID] [PMCID]
25. Zehravi M, Karthika C, Azad AK, Ahmad Z, Khan FS, Rahman MS, et al. A Background Search on the Potential Role of Scutellaria and Its Essential Oils. Biomed Res Int. 2022;2022:

7265445. [DOI:10.1155/2022/7265445] [PMID] [PMCID]

26. Golmakani E, Mohammadi A, Sani TA, Kamali H. Phenolic and flavonoid content and antioxidants capacity of pressurized liquid extraction and perculation method from roots of Scutellaria pinnatifida A. Hamilt. subsp alpina (Bornm) Rech. f. J Supercrit Fluids. 2014;95: 318-24. [DOI:10.1016/j.supflu.2014.09.020]
27. Brock C. American skullcap (Scutellaria lateriflora L): a study of its effects on mood in healthy volunteers: University of Westminster; 2012. [DOI:10.1186/ISRCTN48078312]
28. Sripathi R, Ravi S. Ethnopharmacology, phytoconstituents, essential oil composition and biological activities of the genus Scutellaria. J Pharm Sci & Res. 2017;9(3):275-8. [DOI:10.25258/phyto.v9i5.8140]
29. Huen MS, Leung JW, Ng W, Lui WS, Chan MN, Wong JT, et al. 5,7-Dihydroxy-6-methoxyflavone, a benzodiazepine site ligand isolated from Scutellaria baicalensis Georgi, with selective antagonistic properties. Biochem Pharmacol. 2003;66(1):125-32. [PMID] [DOI:10.1016/S0006-2952(03)00233-8]
30. Merzoug S, Toumi ML, Boukhris N, Baudin B, Tahraoui A. Adriamycin-related anxiety-like behavior, brain oxidative stress and myelotoxicity in male Wistar rats. Pharmacol Biochem Behav. 2011;99(4):639-47. [DOI:10.1016/j.pbb.2011.06.015] [PMID]
31. Xu Y, Wang C, Klabnik JJ, O'Donnell JM. Novel therapeutic targets in depression and anxiety: antioxidants as a candidate treatment. Curr Neuropharmacol. 2014;12(2):108-19. [DOI:10.2174/1570159X11666131120231448] [PMID] [PMCID]
32. Saboura A, Ahmadi A, Zeinali A, Parsa M. Comparison Between the Contents of Phenolic and Flavonoid Compounds and Aerial Part Antioxidant Activity in Scutellaria pinnatifida in Two NorthIranian Populations. J Rafsanjan Univ Med Sci. 2014;13(3):249-66.
33. Delazar A, Nazemiyeh H, Afshar FH, Barghi N, Esnaashari S, Asgharian P. Chemical compositions and biological activities of Scutellaria pinnatifida A. Hamilt aerial parts. Res Pharm Sci. 2017;12(3):187-95. [PMCID] [DOI:10.4103/1735-5362.207199] [PMID]

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