

The Anxiolytic Potential of *Citrus Aurantium* Essential Oil: A focused critical review

Gabriela Silva Bisson ^{1,*}, Francisco Rafael Oliveira da Silva ², Deysen Kerlla Fernandes Bezerra Girão ³

¹ Maternal-Infant and Public Health Nursing Department, University of São Paulo at Ribeirão Preto School of Nursing, Ribeirão Preto, Brazil.

² Centro Universitário de Tecnologia de Curitiba – UNIFATEC, Curitiba, Paraná, Brazil.

³ Centro Universitário Christus, UNICHRISTUS, Fortaleza, Ceará, Brazil.

* Correspondence: gabrielabisson@gmail.com.

Abstract: Anxiety disorders rank among the most common mental health issues globally, prompting extensive research into both traditional and alternative treatments. In this context, *Citrus aurantium* essential oil (bitter orange) has attracted scientific interest due to its anxiolytic properties. This essential oil's pharmacological effects are attributed to its active components, which interact with key neurotransmitter systems, including the serotonergic and GABAergic, to exert anxiolytic, antidepressant, and sedative effects. Recent studies have explored these properties in various models, demonstrating *Citrus aurantium*'s ability to alleviate anxiety-like behaviors in animal models and manage preoperative anxiety in humans. Despite promising preliminary findings, research on *Citrus aurantium* essential oil's efficacy and safety in anxiety treatment presents considerable variability in study design, methodologies, and outcomes. This review aims to synthesize current evidence on the anxiolytic effects of *Citrus aurantium* essential oil, highlighting its potential therapeutic applications and the need for further research to clarify its efficacy and safety in clinical settings. By critically evaluating existing literature, this paper contributes to a deeper understanding of *Citrus aurantium* essential oil as a potential non-pharmacological intervention for anxiety disorders, underscoring the importance of continued investigation in this promising area of complementary and alternative medicine.

Keywords: *Citrus aurantium*; Anxiolytic Effects; Essential Oils; Aromatherapy; Anxiety Treatment.

Citation: Bisson GS, Silva FRO, Girão DKFB. The Anxiolytic Potential of *Citrus Aurantium* Essential Oil: A focused critical review. Brazilian Journal of Aromatherapy and Essential Oil. 2024;1: bjhae11.

doi: <https://doi.org/10.62435/2965-7253.bjhae.2024.bjhae11>

Received: 3 January 2024

Accepted: 7 February 2024

Published: 15 February 2024



Copyright: This work is licensed under a Creative Commons Attribution 4.0 International License (CC BY 4.0).

1. Introduction

Anxiety disorders are among the most prevalent mental health conditions worldwide, affecting a significant portion of the global population [1]. The quest for effective treatment modalities has led researchers to explore both pharmacological and non-pharmacological approaches [2]. In recent years, the potential of aromatherapy and essential oils for alleviating anxiety symptoms has received increased attention [3]. Among the various essential oils studied, *Citrus aurantium*, commonly known as bitter orange, has emerged as a promising candidate due to its purported anxiolytic properties [4, 5].

The pharmacological properties of *Citrus aurantium* essential oil, attributed to its active components, have been the subject of several studies. These investigations have explored its anxiolytic, antidepressant, and sedative effects through various mechanisms of action, including interaction with the serotonergic and GABAergic systems [4, 5]. Preliminary research findings suggest that *Citrus aurantium* can significantly reduce anxiety-like behaviors in animal models and may help in managing preoperative anxiety in clinical settings [3, 2]. Despite the growing body of evidence supporting the anxiolytic effects of *Citrus aurantium* essential oil, the literature is still evolving, with studies varying in design, methodology, and outcomes. This variability underscores the need for a critical

review of the existing evidence to better understand the efficacy, safety, and potential application of *Citrus aurantium* in anxiety treatment [1].

The aim of this narrative critical review is to systematically examine and synthesize the current research on the use of *Citrus aurantium* essential oil for anxiety treatment. This review intends to evaluate the strength of the evidence, identify gaps in the current knowledge, and suggest directions for future research. Through a comprehensive analysis, this paper seeks to clarify the therapeutic value of *Citrus aurantium* essential oil in managing anxiety and contribute to the broader discussion on alternative and complementary approaches to mental health care.

2. *Citrus Aurantium* Essential Oil Use overview in anxiety disorders: a pharmacological approach

The use of *Citrus aurantium* (bitter orange) essential oil has shown promising anxiolytic effects in both preclinical experiments and clinical conditions. This oil has a complex chemical composition, which mainly includes monoterpenes and sesquiterpenes such as limonene, myrcene, linalool, citral, nerol, geraniol, neral, among others [6, 7]. *Citrus aurantium* essential oil has demonstrated beneficial pharmacological effects on the central nervous system, such as anxiolytic, antidepressant, and sedative effects. These effects can be attributed to the interaction of the oil's components with the serotonergic and GABAergic neurotransmitter systems, which are involved in the regulation of mood, sleep, anxiety, and stress [8].

One comprehensive review analyzed preclinical and clinical studies investigating the anxiety effects of *Citrus aurantium* and *Citrus sinensis* essential oils. It concluded that both oils produce anxiolytic effects, highlighting the potential of *Citrus aurantium* aromatherapy to reduce anxiety levels in stressful conditions, including among subjects affected by chronic myeloid leukemia and preoperative patients, although it noted variability in study methodologies and called for more complete clinical studies [9, 10].

Some studies suggest that *Citrus aurantium* essential oil may increase serotonin levels in the brain, a neurotransmitter that promotes well-being and happiness. The oil may also inhibit the reuptake of serotonin by neurons, prolonging its action. In addition, the oil can stimulate 5-HT_{1A} receptors, which are responsible for mediating the anxiolytic and antidepressant effects of serotonin [8]. In a study focused on the anxiolytic-like activity of *Citrus aurantium* essential oil mediated by 5-HT_{1A}-receptors, it was demonstrated that the essential oil could significantly affect anxiety-related behaviors in mice, suggesting the involvement of serotonergic pathways in its mode of action [4]. Another clinical trial evaluated the effect of *Citrus aurantium* aroma (neroli oil) inhalation on patients with acute coronary syndrome (ACS). This double-blind, placebo-controlled randomized trial showed significant reduction in anxiety scores after the intervention with no observed side effects, indicating that aromatherapy with *Citrus aurantium* could be a safe and efficient method to reduce anxiety in ACS patients [5].

Furthermore, a single-blind, randomized controlled trial investigating the effectiveness of *Citrus aurantium* essential oil on anxiety in patients undergoing coronary angiography found significant reductions in anxiety scores and vital signs (such as blood pressure and pulse rate) in the intervention group compared to the control group. This study supports the inhalation of *Citrus aurantium* essential oil as an effective method for reducing anxiety and stress levels in patients undergoing medical procedures [3].

These studies collectively suggest that *Citrus aurantium* essential oil has a notable potential for reducing anxiety through various mechanisms, including interaction with neurotransmitter systems, and providing a calming effect in clinical settings. However, as highlighted in the literature, there is a need for further research to fully establish its efficacy and safety profile across different populations and settings.

3. Anxiety Reduction in Animal Models based on *Citrus Aurantium* Essential Oil Use

Research in animal models and clinical settings has explored its anxiolytic effects and potential applications in treating psychiatric disorders such as depression, anxiety, and insomnia. In animal models, the essential oil of *Citrus aurantium* has shown anxiolytic effects in various behavioral tests, such as the elevated plus maze, open field test, forced swimming test, and social interaction test [11]. These effects may be mediated by the modulation of the serotonergic and GABAergic systems, as well as by the reduction of oxidative stress and inflammation in the brain [10, 11].

In clinical settings, the essential oil of *Citrus aurantium* has been used to reduce preoperative anxiety in patients undergoing minor surgeries, such as colonoscopy, outpatient surgery, and cardiac surgery. Studies have compared *Citrus aurantium* essential oil with placebo, oxazepam, or lavender, and found that *Citrus aurantium* essential oil was effective in lowering anxiety scores measured by scales such as the State-Trait Anxiety Inventory (STAI) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS). Additionally, *Citrus aurantium* essential oil did not cause significant adverse effects, such as excessive sedation or hemodynamic changes [12].

Other clinical applications of *Citrus aurantium* essential oil include the treatment of anxiety associated with depression, irritable bowel syndrome, menopause, and chronic pain [4]. However, these studies are limited in number, sample size, methodological quality, and consistency of results, and further investigation is required to confirm the efficacy and safety of *Citrus aurantium* essential oil in these conditions. Therefore, *Citrus aurantium* essential oil may have anxiolytic properties in animal models and in clinical contexts, especially in reducing preoperative anxiety. However, more clinical studies are needed to assess the optimal dose, route of administration, duration of treatment, and possible side effects of *Citrus aurantium* essential oil for therapeutic use.

4. Safety and Efficacy of *Citrus Aurantium* Essential Oil Use

The essential oil of *Citrus aurantium* is generally considered safe when used in appropriate doses and for short periods of time. However, some adverse effects have been reported, such as skin irritation, photosensitivity, allergy, headache, nausea, tachycardia, hypertension, and interaction with medications [13]. The essential oil of *Citrus aurantium* contains substances like synephrine, octopamine, and tyramine, which can stimulate adrenergic receptors and increase blood pressure, heart rate, and metabolism. These substances can be dangerous for people with cardiovascular diseases, diabetes, hyperthyroidism, glaucoma, enlarged prostate, or those using monoamine oxidase inhibitors (MAOIs) [14].

The essential oil of *Citrus aurantium* may also interfere with the action of some medications, such as antidepressants, anticoagulants, antihypertensives, anticonvulsants, antidiabetics, antifungals, antibiotics, antineoplastics, among others. Therefore, it is recommended to consult a doctor before using *Citrus aurantium* essential oil if you are taking any of these medications or others that may interact [13].

The safety of prolonged use of *Citrus aurantium* essential oil has not been well established. Some studies suggest that chronic use may cause hepatic, renal, cardiac, and neurological toxicity, as well as dependence and tolerance. Therefore, it is advisable to use *Citrus aurantium* essential oil with caution and under medical supervision [13, 14]. Thus, *Citrus aurantium* essential oil may have anxiolytic effects, but it can also present adverse effects and contraindications, depending on the dose, duration of use, and the health conditions of the user. It is important to assess the risks and benefits of *Citrus aurantium* essential oil before using it for the treatment of anxiety.

5. Conclusion

The narrative review presented demonstrates the potential of *Citrus aurantium* essential oil, commonly known as bitter orange, in the treatment of anxiety. Through a comprehensive analysis of the existing literature, it is observed that *Citrus aurantium* essential oil has anxiolytic, antidepressant, and sedative properties attributed to its interaction with the serotonergic and GABAergic neurotransmitter systems. Studies in both animal models and clinical contexts suggest a significant reduction in behaviors associated with anxiety, standing out as a promising alternative for the management of preoperative anxiety and other stressful conditions.

The safety of using this essential oil is considered acceptable in appropriate doses and for short periods, although adverse effects such as skin irritation, photosensitivity, and potential drug interactions have been reported. However, the review also highlights the methodological variability of the studies and the need for more research to conclusively establish the efficacy and safety of using *Citrus aurantium* essential oil in different populations and contexts. Therefore, while *Citrus aurantium* essential oil offers a promising alternative for the treatment of anxiety, it is imperative that future research be directed at elucidating optimal dosages, routes of administration, duration of treatment, and possible side effects. This will ensure a safe and effective application of this therapeutic approach. Additionally, it is recommended that the use of *Citrus aurantium* be accompanied by medical guidance, especially for individuals with pre-existing health conditions or who are taking medications that may interact with its components. In short, *Citrus aurantium* essential oil stands out as a valuable candidate in the spectrum of complementary treatments for anxiety, although its implementation should be cautious and based on robust evidence.

Funding: None.

Research Ethics Committee Approval: None.

Acknowledgments: None.

Conflicts of Interest: None.

Supplementary Materials: None.

References

1. Pimenta FC, Alves MF, Pimenta MB, Melo SA, de Almeida AA, Leite JR, Pordeus LC, Diniz Mde F, de Almeida RN. Anxiolytic Effect of *Citrus aurantium* L. on Patients with Chronic Myeloid Leukemia. *Phytother Res*. 2016 Apr;30(4):613-7. doi: 10.1002/ptr.5566. Epub 2016 Jan 20. PMID: 26787366.
2. Carvalho-Freitas MI, Costa M. Anxiolytic and sedative effects of extracts and essential oil from *Citrus aurantium* L. *Biol Pharm Bull*. 2002 Dec;25(12):1629-33. doi: 10.1248/bpb.25.1629. PMID: 12499653.
3. Moradi K, Ashtarian H, Danzima NY, Saeedi H, Bijan B, Akbari F, Mohammadi MM. Essential Oil from *Citrus aurantium* Alleviates Anxiety of Patients Undergoing Coronary Angiography: A Single-Blind, Randomized Controlled Trial. *Chin J Integr Med*. 2021 Mar;27(3):177-182. doi: 10.1007/s11655-020-3266-5. Epub 2020 Jun 22. PMID: 32572778.
4. Costa CA, Cury TC, Cassettari BO, Takahira RK, Flório JC, Costa M. *Citrus aurantium* L. essential oil exhibits anxiolytic-like activity mediated by 5-HT(1A)-receptors and reduces cholesterol after repeated oral treatment. *BMC Complement Altern Med*. 2013 Feb 23;13:42. doi: 10.1186/1472-6882-13-42. PMID: 23432968; PMCID: PMC3598547.
5. Pultrini Ade M, Galindo LA, Costa M. Effects of the essential oil from *Citrus aurantium* L. in experimental anxiety models in mice. *Life Sci*. 2006 Mar 6;78(15):1720-5. doi: 10.1016/j.lfs.2005.08.004. Epub 2005 Oct 25. PMID: 16253279.
6. Elhawary EA, Nilofar N, Zengin G, Eldahshan OA. Variation of the essential oil components of *Citrus aurantium* leaves upon using different distillation techniques and evaluation of their antioxidant, antidiabetic, and neuroprotective effect against Alzheimer's disease. *BMC Complement Med Ther*. 2024 Feb 2;24(1):73. doi: 10.1186/s12906-024-04380-x. PMID: 38308284; PMCID: PMC10835836.
7. Amala Dev AR, Sonia Mol J. *Citrus* Essential Oils: A Rational View on its Chemical Profiles, Mode of Action of Anticancer Effects/Antiproliferative Activity on Various Human Cancer Cell Lines. *Cell Biochem Biophys*. 2023 Jun;81(2):189-203. doi: 10.1007/s12013-023-01138-z. Epub 2023 Apr 22. PMID: 37086387.

8. Jain S, Arora P, Popli H. A comprehensive review on *Citrus aurantifolia* essential oil: its phytochemistry and pharmacological aspects. *Braz. J. Nat. Sci* [Internet]. 25^o de julho de 2020 [citado 15^o de fevereiro de 2024];3(2):354.
9. Mannucci C, Calapai F, Cardia L, Inferrera G, D'Arena G, Di Pietro M, Navarra M, Gangemi S, Ventura Spagnolo E, Calapai G. Clinical Pharmacology of *Citrus aurantium* and *Citrus sinensis* for the Treatment of Anxiety. *Evid Based Complement Alternat Med*. 2018 Dec 2;2018:3624094. doi: 10.1155/2018/3624094. PMID: 30622597; PMCID: PMC6304613.
10. Moslemi F, Alijaniha F, Naseri M, Kazemnejad A, Charkhkar M, Heidari MR. *Citrus aurantium* Aroma for Anxiety in Patients with Acute Coronary Syndrome: A Double-Blind Placebo-Controlled Trial. *J Altern Complement Med*. 2019 Aug;25(8):833-839. doi: 10.1089/acm.2019.0061. Epub 2019 Jun 18. PMID: 31211612.
11. Mannucci C, Calapai F, Cardia L, Inferrera G, D'Arena G, Di Pietro M, Navarra M, Gangemi S, Ventura Spagnolo E, Calapai G. Clinical Pharmacology of *Citrus aurantium* and *Citrus sinensis* for the Treatment of Anxiety. *Evid Based Complement Alternat Med*. 2018 Dec 2;2018:3624094. doi: 10.1155/2018/3624094. PMID: 30622597; PMCID: PMC6304613.
12. de Sousa DP, de Almeida Soares Hocayen P, Andrade LN, Andreatini R. A Systematic Review of the Anxiolytic-Like Effects of Essential Oils in Animal Models. *Molecules*. 2015 Oct 14;20(10):18620-60. doi: 10.3390/molecules201018620. PMID: 26473822; PMCID: PMC6332383.
13. Zheng L, Guo H, Zhu M, Xie L, Jin J, Korma SA, Jin Q, Wang X, Cacciotti I. Intrinsic properties and extrinsic factors of food matrix system affecting the effectiveness of essential oils in foods: a comprehensive review. *Crit Rev Food Sci Nutr*. 2023;0(0):1-34.
14. Ogunro OB, Richard G, Izah SC, Ovuru KF, Babatunde OT, Das M. *Citrus aurantium*: Phytochemistry, Therapeutic Potential, Safety Considerations, and Research Needs. In: Izah SC, Ogwu MC, Akram M, eds. *Herbal Medicine Phytochemistry*. Reference Series in Phytochemistry. Cham: Springer; 2024. https://doi.org/10.1007/978-3-031-21973-3_69-1.