A REVIEW ON ANXIOLYTIC ACTIVITY OF VARIOUS

ESSENTIAL OILS BY USING LIGHT DARK BOX AND OPEN

FIELD MODELS

Mythili Priyanka. C^{#1}, Noopur Srivastava*²

¹Department of Pharmacology, The Oxford College of Pharmacy, Hongasandra, Bangalore-560068, India.

²Department of Pharmacology, Faculty of Pharmacy, The Oxford College of Pharmacy, Hongasandra, Bangalore-560068, India.

ABSTRACT

Central nerve disorders affect people from all nations, civilizations, and ethnic groups. People suffering from anxiety disorders can benefit from a wide range of treatments and services. Anxiety is a distressing emotion caused by real or anticipated tissue injury. Essential oils are useful in the treatment of central nervous system problems. Essential oils include volatile molecules and are used in a variety of industries including perfume, cuisine, agriculture, taste, and medicine. The aim of the present review is to summarise how essential oils such as Angelica sinensis, Citrus junos, Citrus latifolia, Cymbopogon citratus, Foeniculum vulgare, Lippia alba, Nectandra grandiflora, Ocimum gratissimum L., Spiranthera odoratissima A. St. Hil., Stachys tibetica, and others are used to treat anxiety. The essential oil's anxiolytic effect was investigated in a light dark box and open field test. Essential oils have a wide range of biological effects, including antioxidant, anti-inflammatory, and anti-microbial properties. Essential oils are popular in the foods and cosmetic sectors, as well as in the scope of human health.

Keywords: Essential oil, Anxiety, Antianxiety, Light dark box, Open field

apparatus.

1. INTRODUCTION

Anxiety disorder is a mental condition that has the highest social and individual impact of any mental sickness. Anxiety disorders, according to the World Health Organization (WHO), "are caused by intense constant fear and worry," resulting in physical symptoms such as chest discomfort, headaches, racing heart, and stomach pain ¹.

According to the World Health Organization, one in every four people will have a mental disorder at some point in their lives. Depression and anxiety account for 23% of all mortality worldwide ².

Anxiety disorders are distinguished by an undesirable mental state, unpleasant feelings about the future, or anxiety that stimulates a sense of protection as a warning so that the individual may prepare to face a potentially harmful circumstance. Anxiety may be either a natural or unhealthy emotion. In the latter situation, the person mounts dysfunctional and insufficient responses to any action, actual or imagined, that produces anxiety during daily events or activities³.

Anxiety is one of the mental diseases that manifests itself very early in a patient's life; psychiatric studies show that it shows itself between the ages of 2 and 5 years old. Childhood anxiety affects 2% of the population, and girls are more likely to be nervous than boys ⁴.

Mental illnesses are one of the primary causes of worldwide health-related burden. According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2019, anxiety disorder was one of the top 25 primary causes of burden worldwide in 2019⁵.

2.TYPES OF ANXIETY

There are major six types of anxiety disorders.

2.1.Generalized anxiety disorder (GAD): It is a long-term condition. A person suffering from generalised anxiety disorder has a continual fear that something unpleasant or incorrect may occur. The patients are always worried for no apparent reason. It makes it difficult for them to concentrate.

2.2.Panic disorder: Panic disorder is characterised by a brief and unexpected attack of anxiety that lasts less than 10 minutes and can last for many hours. This assault can be caused by stress or fear ⁶.

2.3.Obsessive-compulsive disorder (OCD): It is a continuous and uncontrolled sensation and conduct in which people frequently examine things ⁷.

2.4.Phobic disorder: It is the broadest category of anxiety, encompassing all types of fear or phobia associated with a particular object or circumstance.

2.5.Social anxiety disorder (SAD): It comprises a strong aversion to social engagement and public humiliation. It is sometimes referred to as social phobia. The most frequent type of social anxiety disorder is performance anxiety⁸.

2.6.Post-traumatic stress disorder (PTS): It is caused by any severe trauma, natural disaster, or life-threatening incident ⁹.

Palpitation, dry mouth, muscle tension, trembling, nausea, unease, sleeplessness, trouble focusing, restlessness, and irritability are common symptoms of all anxiety disorders.

Anxiety can be triggered by genetics, but it can also be triggered by external stimuli or any underlying disease such as sleep apnea, chronic obstructive pulmonary disease, Parkinson's disease, rheumatoid arthritis, cancer or diabetes, a history of trauma, parenting factors, cultural factors, and so on ¹⁰.

Trauma, stress overload, drugs or alcohol, having a blood-related anxiety condition, personality, and illness-

https://doi.org/10.37896/sr9.7/011

Medication and/or psychotherapy are commonly used to treat anxiety disorders. Antidepressants such as serotonin reuptake inhibitors (e.g., fluoxetine and sertraline), tricyclics (e.g., imiptramine and clomiptramine), monoamine oxidase inhibitors (e.g., phenelzine and iso carboxazid), and benzodiazepine anti-anxiety medicines are being administered (e.g., clonazepam, lorazepam, and alprazolam). Many of these medications have negative side effects, many of which are significant or even fatal.

Aromatherapy is a type of complementary and alternative medicine (CAM) that use plant essential oils to improve a patient's mood or health ¹².

3. ESSENTIAL OIL

Essential oils have been utilised for therapeutic and wellness purposes in numerous cultures for thousands of years. Essential oils are a complex blend of volatile elements derived from the secondary metabolism of aromatic and other plant species. The major components of essential oils are volatile terpenes and hydrocarbons. Essential oils have a long history of being used as medicinal agent¹³. Since ancient times, plants containing essential oils have been widely employed in flavouring and medicinal substances in food and pharmaceuticals. Essential oils are also utilised as food preservatives and additives, as well as natural cures, in hygienic, dental, perfume, and beauty applications. A few essential oils have also been claimed to treat organ malfunction or systemic disorders. They are concentrated hydrophobic liquids containing plant-derived volatile (easily evaporated at room temperature) chemical components. They have lately gained appeal as a natural, safe, and cost-effective therapy for a variety of health conditions because to its antidepressant, stimulating, detoxifying, antibacterial, antiviral, and calming properties ¹⁴.

Essential oils (EOs) are aromatic oily liquids collected from various plant components such as leaves, barks, seeds, stems, roots, flowers, and peels ¹⁵.

3.1 CLASSIFICATION OF ESSENTIAL OIL

Essential oils can also be classed based on their aroma/smell.

This oil categorization includes Citrus, Herbaceous, Medicinal, Floral, Resinous oils, and Woody, Earthy, Minty, and Spicy oils ¹⁶.

3.1.1. Citrus Oils: This category includes essential oils with a distinct citrus taste. Citrus oils are produced by plants such as bergamot, grapefruit, lemon, lime, orange, and tangerine ¹⁷.

3.1.2. Herbaceous Oils: Oils produced from plants that are otherwise very beneficial herbs. These oils are derived from plants such as basil, chamomile, Melissa, clary sage, hyssop, marjoram, peppermint, and rosemary ¹⁸.

https://doi.org/10.37896/sr9.7/011

3.1.3. Camphoraceous Oils: These are essential oils that have a specific therapeutic function. Some of these essential oils are from Cajeput, Tea Tree, borneol-like, earthy and mugwort-like, and rosemary-like plants, with a delicious, dried plum-like background.

3.1.4. Floral Oils: This category includes oils derived from flower components or those include the floral essence of plants. Plants that generate these oils include Geranium, Jasmine, Lavender, Rose, Neroli, Chamomile, and Ylang-Ylang¹⁹.

3.1.5. Woody Oils: Essential oils with woody aromas or derived from plant barks and other woody elements. Such oils are produced by plants such as cedar, cinnamon, cypress, juniper berry, pine, and sandalwood, among others ²⁰.

3.1.6. Earthy Oils: Essential oils with an earthy scent or those are derived from plant roots and other earthy elements. Some of these oils are produced by Angelica, Patchouli, Vetiver, and Valerian²¹.

3.1.7. Spicy Oils: Spice and spicy plant oils such as thyme, cloves, aniseed, black pepper, cardamom, cinnamon, coriander, cumin, ginger, and nutmeg ²².

3.2 COMPONENTS OF ESSENTIAL OIL

Every oil has more than a hundred components, however the quantity varies depending on the oil in question. The most significant active molecules, however, are classified as terpenoids (monoterpenoids and sesquiterpenoids) and phenylpropanoids. These two categories are derived from distinct main metabolic substrates and are produced via different metabolic processes. Essential oils, like other organic chemicals, are composed of hydrocarbon molecules and may be further classified as terpenes, alcohols, esters, aldehydes, ketones, and phenols, among others ²³.

3.3 APPLICATION

Essential oils are important natural products that are utilised as raw materials in a variety of industries such as fragrances, cosmetics, aromatherapy, phytotherapy, spices, nutrition, and pesticides. Essential oils exhibit a variety of pharmacological effects, including antibacterial, antifungal, and antiviral properties. Essential oils have medicinal and disinfectant properties ²⁴.

4. SOME ESSENTIAL OIL USED TO TREAT ANXIETY DISORDER

Various essential oils, such as every drug's biological name, are used to relieve anxiety. Ocimum gratissimum L, Angelica sinensis, Citrus junos, Citrus latifolia, Lippia alba, Spiranthera odoratissima, Cymbopogon citratus, Foeniculum vulgare, Stachys tibetica, Nectandra grandiflora Ness, Pelargonium roseum, Gardenia jasminoides Ellis, Citrus aurantium. This paper provides a review of current studies on the anxiolytic and relaxing properties of essential oils. It is not meant for the prescription of anti-anxiety medications. Serious

4.1. Ocimum gratissimum L. (clove basil)

Tankam and Michiho Ito studied the impact of O. gratissimun L essential oil on male mice in light/dark transition experiments. During the behavioural test, the essential oils were administered by inhalation. The number of transitions and duration spent in the light side of the light/dark apparatus increased in the treated animals. The dosage response curve resembled an inverted U. However, treatment of O. gratissimum essential oil reduced motor activity in the open field test, indicating a sedative/depressant effect that might lead to more time in the light side of the light dark apparatus. It is worth noting that thymol, the major component of O. gratissimum essential oil, shows anxiolytic effects ²⁵.

4.2. Angelica sinensis (Dong quai)

Chen and colleagues investigated the effect of A. sinensis essential oil delivered orally in mice assessed for anxiety. A greater dose of A. sinensis essential oil increased the frequency of transitions in the light/dark test, whereas an intermediate dose increased the duration spent in the lighted side. It indicates that Angelica sinensis essential oil has anxiolytic properties ²⁶.

4.3. Citrus junos (Yuzu)

Satou and colleagues investigated the impact of C. junos essential oil from experience similar on isolated male mice in the light/dark test. In the lighting/darkness test Inhaled C. junos essential oil had an anxiolytic-like effect in the light/dark apparatus, with animals increasing the time spent and number of entries in the light side. These findings suggest that C. junos essential oil has an anxiolytic effect ²⁷.

4.4. Citrus latifolia (Persian lime)

Gargano and colleagues investigated the effect of C. latifolia systemic (oral) treatments (containing 58 % limonene and 13% beta-pinene). Male Swiss mice treated with C. latifolia essential oil shown a beneficial impact on light dark parameters. In the light dark test, mice increased their time spent on the light side. According to the results, citrus latifolia has anxiolytic properties ²⁸.

4.5. Lippia alba (Bushy lippia)

Hatano and colleagues gave male rats Lippia alba essential oil (i.p.). In the open-field test, L. alba essential oil had no effect on motor activity ²⁹. An anaesthetic effect research on silver catfish (Rhamdia quelen) revealed a GABAergic action, explaining its anxiolytic-like effect. The results suggest that L. alba essential oil has an anxiolytic effect ³⁰.

4.6. Spiranthera odoratissima A. St. Hil. (manacado cerrado)

Galdino and colleagues investigated the essential oil of Spiranthera odoratissima A. St. Hil. derived from the leaves. Male mice given the essential oil of S. odoratissima A.St. Hil orally (p.o.) displayed an anxiolyticlike profile in a light-dark test. It enhanced transitions between compartments and time spent in the light side, NOLUME 9, ISSUE 7, 2022

https://doi.org/10.37896/sr9.7/011

and it increased center exploration without affecting motor activity in open-field assessments. The anxiolyticlike activity of S. odoratissima was shown to be partially reduced by NAN-190 but not by flumazenil, indicating that it is associated to 5-HT1A receptors rather than the benzodiazepine binding site ³¹.

4.7. Cymbopogon citratus (Lemon grass)

In the light side of the light/dark test, male mice were given orally C. citratus essential oil (leaves) (mostly citral and -myrcene). By administering Cymbopogon citratus essential oil to mice, Costa and colleagues noticed an anxiolytic-like effect in the light/dark test, increasing the duration spent in the lighted side and the number of transitions. The results indicate that Cymbopogon citratus essential oil has anxiolytic properties ³².

4.8. Foeniculum vulgare (Common fennel)

Mesfin and colleagues investigated the potential anxiolytic impact of essential oil extracted from the aerial portions of Foeniculum vulgare in male mice. In the open-field test, acute Foeniculum vulgare essential oil administration increased center exploration. As a consequence, the findings suggested that Foeniculum vulgare essential oil had an anxiolytic effect. This essential oil contains chemicals that have been shown to have anxiolytic properties, including as limonene, -pinene, 1,8-cineole, and linalool ³³.

4.9. Stachys tibetica (Tibetan wound wort)

Kumar and colleagues investigated the potential anxiolytic impact of oral administration of S. tibetica essential oil in rats (male and female). Acute S. tibetica essential oil also had an anxiolytic effect in the light/dark tests, with rats spending more time in the light side and making more transitions. These results suggest anxiolytic effect ³⁴.

4.10. Nectandra grandiflora Ness(Canela amarela)

Garlet and colleagues investigated whether Nectandra grandiflora essential oil and its four separate sesquiterpenoids reduce anxiety-related behaviour in mice through a GABAergic mechanism. In the open field test, Nectandra grandiflora and all four isolated sesquiterpenoids induced anxiolytic-like effects. The essential oils Eremophil-11-en-10-ol (ERM) and selin-11-en-4- α -ol (SEL) contribute to the anxiolytic-like effects. The structures of ERM and SEL include hydroxyl groups. The impact found at low dosages for these two drugs implies that alcohol function is an essential structural element for the anxiolytic action. According to the findings, Nectandra grandiflora essential oil and its isolated sesquiterpenoids ERM and SEL had anxiolytic-like effects in mice behaviour in an open field test ³⁵.

4.11 Pelargonium roseum(Rose geranium)

Tabari and colleagues investigated the anxiolytic and depressive properties of P.roseum intraperitonial injection in male mice. In this investigation, the open field apparatus was used to assess the locomotor activity

of animals and the effects of P.roseum essential oil on them. The number of rearing was significantly reduced in the open field test. These results pointed to an anxiolytic effect ³⁶.

4.12 Gardenia jasminoides Ellis (cape jasmine)

Zhang and colleagues investigated the anxiolytic impact of Gardenia jasminoides Ellis essential oil in mice. In the light dark test, inhaling Gardenia jasminoides had an anxiolytic effect. Mice increased the amount of time spent in the light side as well as the number of transitions in the light dark apparatus. The results pointed to an anxiolytic impact in mouse behaviour in the light-dark test ³⁷.

4.13 Citrus aurantium (Bitter orange)

Costa and colleagues investigated the anti-anxiety efficacy of citrus aurantium essential oil in mice. Citrus aurantium administration produced an anxiolytic effect in the light dark transition model. Citrus aurantium injection, both acute and chronic, enhanced the duration spent in the light side and the frequency of transitions in mice. When compared to greater dosages, the lowest dose is beneficial in both acute and chronic treatment. This results suggest that citrus aurantium has an anxiolytic effect on mouse behaviour in a light-dark test ³⁸.

5.CONCLUSION

Many plants are utilised in traditional medicine to modulate central nervous system activity, and a variety of essential oils are now employed to relieve anxiety. Anxiolytic effects of essential oil have been established in behavioural research employing animal models and species. Volatile oils may have a synergistic impact with medications used to treat central nervous system disorders. Essential oils can be a valuable non-medicinal option or can be supplemented with conventional therapy for some health conditions if safety and quality issues are taken into account. However, despite the fact that essential oils have been used for many years and have numerous biological activities such as antiviral, antibacterial, anti-inflammatory, and have an influence on central neurological diseases. This study concluded that anxiolytic investigations of several essential oils using light dark transition apparatus and open field apparatus showed significant results. This suggests that essential oil treatment can help with anxiety disorders.

ACKNOWLEDGEMENT

This research did not receive any specific grant from funding agencies in public, commercial or non profit sectors. The author acknowledge the support of Parents and The Oxford College Of Pharmacy, Bangalore.

CONFLICTS OF INTEREST

We declare that we have no conflict of interest.

REFERENCE

- 1. AC01696967 A, editor. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. World Health Organization; (1993).
- 2. Sau A, Bhakta I. Screening of anxiety and depression among the seafarers using machine learning technology. Informatics in Medicine Unlocked. (2019) Jan 1;16:100149.
- 3. Castillo AR, Recondo R, Asbahr FR, Manfro GG. Transtornos de ansiedade. Brazilian Journal of Psychiatry. (2000);22:20-3.
- 4. Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen HU. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. International journal of methods in psychiatric research. (2012) Sep;21(3):169-84.
- Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd- Allah F, Abdelalim A, Abdollahi M. Global burden of 369 diseases and injuries in 204 countries and territories, (1990–2019): a systematic analysis for the Global Burden of Disease Study (2019). The Lancet.(2020) Oct 17;396(10258):1204-22.
- 6. Guha M. Encyclopedia of Psychopharmacology. Reference Reviews. (2015) Nov 9.
- 7. Stein DJ. Obsessive-compulsive disorder. The Lancet. (2002) Aug 3;360(9330):397-405.
- 8. Stein MB, Stein DJ. Social anxiety disorder. The lancet. (2008) Mar 29;371(9618):1115-25.
- Gene-Cos N. Post-Traumatic Stress Disorder: The Management of PTSD in Adults and Children in Primary and Secondary Care. National Collaborating Centre for Mental Health. London & Leicester: Gaskell & The British Psychological Society, 2005,£ 50.00, pp. 168 ISBN: 190467125. Psychiatric Bulletin.(2006) Sep;30(9):357.
- Schoenhuber R, Gentilini M. Anxiety and depression after mild head injury: a case control study. Journal of Neurology, Neurosurgery & Psychiatry. (1988) May 1;51(5):722-4.
- 11. Blanco C, Rubio J, Wall M, Wang S, Jiu CJ, Kendler KS. Risk factors for anxiety disorders: common and specific effects in a national sample. Depression and anxiety. **(2014)** Sep;31(9):756-64.
- 12. Koroch AR, Rodolfo Juliani H, Zygadlo JA. Bioactivity of essential oils and their components. Flavours and fragrances. (2007):87-115.
- Bassolé IH, Juliani HR. Essential oils in combination and their antimicrobial properties. Molecules.
 (2012) Apr 2;17(4):3989-4006.
- Mahato N, Sharma K, Koteswararao R, Sinha M, Baral E, Cho MH. Citrus essential oils: Extraction, authentication and application in food preservation. Critical reviews in food science and nutrition. (2019) Feb 21;59(4):611-25.
- 15. Tongnuanchan P, Benjakul S. Essential oils: extraction, bioactivities, and their uses for food preservation. Journal of food science. (2014) Jul;79(7):R1231-49.
- Weyerstahl P, Schneider S, Marschall H, Rustaiyan A. The essential oil of Artemisia sieberi Bess. Flavour and fragrance journal. (1993) May;8(3):139-45.

- Viuda-Martos M, Ruiz-Navajas Y, Fernández-López J, Pérez-Álvarez J. Antifungal activity of lemon (Citrus lemon L.), mandarin (Citrus reticulata L.), grapefruit (Citrus paradisi L.) and orange (Citrus sinensis L.) essential oils. Food control. (2008) Dec 1;19(12):1130-8.
- Yepez B, Espinosa M, López S, Bolanos G. Producing antioxidant fractions from herbaceous matrices by supercritical fluid extraction. Fluid Phase Equilibria. (2002) Mar 30;194:879-84.
- Paulo CD, Marsaioli AJ, Maria do Carmo EA, Bittrich V. The fragrant floral oils of Tovomita species. Phytochemistry. (1998) Oct 27;49(4):1009-12.
- 20. Li CZ, Jiang LJ, Cheng SQ. Study on preparation of bio-diesel with four woody plant oils. Biomass chemical engineering. (2006);40(Z1):51-5.
- 21. Priestap HA, Bandoni AL, Neugebauer M, Rücker G. Investigation of the essential oils from Aristolochia triangularis. Journal of Essential Oil Research. (1990) May 1;2(3):95-8.
- 22. Maurya S, Kushwaha AK, Singh G. Biological significance of spicy essential oils. Advances in Natural Science. (2013) Dec 20;6(4):84-95.
- 23. Berger RG, editor. Flavours and fragrances: chemistry, bioprocessing and sustainability. Springer Science & Business Media; (2007) Mar 6.
- 24. Buchbauer G. The detailed analysis of essential oils leads to the understanding of their properties. CHEMICAL WEEKLY-BOMBAY-. (2000) Mar;45(49):163-5.
- 25. Tankam JM, Ito M. Sedative, anxiolytic and antidepressant-like effects of inhalation of the essential oil of Ocimum gratissimum L. from Cameroon in mice. Journal of Pharmacognosy and Phytochemistry. (2014) Jan 1;2(5).
- 26. Chen SW, Min L, Li WJ, Kong WX, Li JF, Zhang YJ. The effects of angelica essential oil in three murine tests of anxiety. Pharmacology Biochemistry and Behavior. (2004) Oct 1;79(2):377-82.
- Satou T, Miyahara N, Murakami S, Hayashi S, Koike K. Differences in the effects of essential oil from Citrus junos and (+)-limonene on emotional behavior in mice. Journal of Essential Oil Research. (2012) Oct 1;24(5):493-500.
- 28. Gargano AC, Costa CA, Costa M. Essential oils from Citrus latifolia and Citrus reticulate reduces anxiety and prolong ether sleeping time in mice. Tree For Sci Biotech. (2008) Dec;2(Suppl 1):121-4.
- 29. Hatano VY, Torricelli AS, Giassi AC, Coslope LA, Viana MD. Anxiolytic effects of repeated treatment with an essential oil from Lippia alba and (R)-(-)-carvone in the elevated T-maze. Brazilian Journal of Medical and Biological Research. (2012);45:238-43.
- 30. Heldwein CG, Silva LL, Reckziegel P, Barros FM, Bürger ME, Baldisserotto B, Mallmann CA, Schmidt D, Caron BO, Heinzmann BM. Participation of the GABAergic system in the anesthetic effect of Lippia alba (Mill.) NE Brown essential oil. Brazilian Journal of Medical and Biological Research. (2012);45:436-43.
- 31. Galdino PM, Nascimento MV, Florentino IF, Lino RC, Fajemiroye JO, Chaibub BA, de Paula JR, de Lima TC, Costa EA. The anxiolytic-like effect of an essential oil derived from Spiranthera

odoratissima A. St. Hil. leaves and its major component, β -caryophyllene, in male mice. Progress in Neuro-Psychopharmacology and Biological Psychiatry. (2012) Aug 7;38(2):276-84.

- 32. de Almeida Costa CA, Kohn DO, de Lima VM, Gargano AC, Flório JC, Costa M. The GABAergic system contributes to the anxiolytic-like effect of essential oil from Cymbopogon citratus (lemongrass). Journal of ethnopharmacology. **(2011)** Sep 1;137(1):828-36.
- 33. Mesfin M, Asres K, Shibeshi W. Evaluation of anxiolytic activity of the essential oil of the aerial part of Foeniculum vulgare Miller in mice. BMC Complementary and Alternative Medicine. (2014) Dec;14(1):1-7.
- 34. Kumar D, Bhat ZA, Kumar V, Khan NA, Chashoo IA, Zargar MI, Shah MY. Effects of Stachys tibetica essential oil in anxiety. European Journal of Integrative Medicine. **(2012)** Jun 1;4(2):e169-76.
- 35. Garlet QI, Rodrigues P, Barbosa LB, Londero AL, Mello CF, Heinzmann BM. Nectandra grandiflora essential oil and its isolated sesquiterpenoids minimize anxiety-related behaviors in mice through GABAergic mechanisms. Toxicology and Applied Pharmacology. (2019) Jul 15;375:64-80.
- 36. Abouhosseini Tabari M, Hajizadeh Moghaddam A, Maggi F, Benelli G. Anxiolytic and antidepressant activities of Pelargonium roseum essential oil on Swiss albino mice: possible involvement of serotonergic transmission. Phytotherapy research. (2018) Jun;32(6):1014-22.
- 37. Zhang N, Luo M, He L, Yao L. Chemical composition of essential oil from flower of 'Shanzhizi'(Gardenia jasminoides Ellis) and involvement of serotonergic system in its anxiolytic effect. Molecules. (2020) Oct 14;25(20):4702.
- 38. Costa CA, Cury TC, Cassettari BO, Takahira RK, Flório JC, Costa M. Citrus aurantium L. essential oil exhibits anxiolytic-like activity mediated by 5-HT1A-receptors and reduces cholesterol after repeated oral treatment. BMC complementary and alternative medicine. **(2013)** Dec;13(1):1-0.