Psychoactive Botanicals and Their Constituents: A Brief Review

Antoine Al-Achi
College of Pharmacy and Health Sciences, Campbell University, USA

Received: 22 November 2019
Accepted: 5 December 2019
Version of Record Online: 23 December 2019

Since ancient times botanicals that affected moods and produced a feeling of relaxation have been used as sleep aids (for insomnia), to overcome anxiety, and to induce stillness [1]. A list of these plants, along with their chemical composition, is found in table 1. Specific therapeutic applications of psychoactive botanicals include their use for insomnia, as anti-depressive agents, to induce an anxiolytic action, as a treatment for headaches and migraines, to control menopausal symptoms associated with mood issues, and for various neurodegenerative diseases, among others (Table 2).

| Botanical                      | Chemical composition                                                                                                                                                                                                                     | References |
|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Chamomile (Matricaria recutita) | 1. It contains apigenin, a flavonoid, that is mostly found in its glycosylated form, apigenin-7-glucoside. Overall, chamomile contains 36 flavonoid compounds.                                  | [2]        |
|                               | 2. The mechanism of action of apigenin is through an antagonist effect at α1β1γ2S Gamma-aminobutyric Acid (GABA<sub>A</sub>) receptors and at p1 GABAC receptors.                                                                          | [3]        |
|                               | 3. The essential oil of chamomile contains azulenes and proazulenes.                                                                                                                                         | [4]        |
|                               | 4. The plant other constituents are various sesquiterpenes, terpenoids, flavonoids, coumarins, tannin, and polycetylenges.                                                                                              | [5]        |
|                               | 5. Chamomile contains various minerals including, potassium, magnesium, sodium, and calcium.                                                                                                                                                  | [6]        |
|                               | 6. Matricaria recutita also contains trace elements such as chromium, zinc, iron, and manganese.                                                                                                                                               | [7]        |
|                               | 7. Chamomile may be found contaminated with cadmium, lead, copper, rubidium, vanadium, cobalt, barium, copper, aluminum, and strontium.                                                                                      | [8]        |
|                               | 8. Chamomile inhibits the CYP3A4 hepatic enzymes which are responsible for metabolizing medicinal agents (e.g., Cyclosporine).                                                                                                       | [9]        |
|                               |                                                                ainers such as chromium, zinc, iron, and manganese.                                                                                                                                         | [10]       |
| Ginkgo biloba                  | 1. The leaves of this plant contain ginkgolic acids (alkyl phenols).                                                                                                                                                                        | [11]       |
|                               | 2. Among other compounds found in Ginkgo are the terpenes and trilactones (ginkgolides and bilobalides), and flavonoids (flavonol glycosides). Several ginkgolides are recognized such as the terpene trilactones, ginkgolide A, B, C, and J. | [12]       |
|                               | 3. Other constituents in this herb are the, biflavones, proanthocyanidins, alklyphenols, simple phenolic acids, 6-hydroxykynurenic acid, 4-O-methylpyridoxine, and polyprenols.                                                  | [13]       |

Copyright

Copyright © 2019 Antoine Al-Achi. This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and work is properly cited.

Since ancient times botanicals that affected moods and produced a feeling of relaxation have been used as sleep aids (for insomnia), to overcome anxiety, and to induce stillness [1]. A list of these plants, along with their chemical composition, is found in table 1. Specific therapeutic applications of psychoactive botanicals include their use for insomnia, as anti-depressive agents, to induce an anxiolytic action, as a treatment for headaches and migraines, to control menopausal symptoms associated with mood issues, and for various neurodegenerative diseases, among others (Table 2).
Hops (Humulus lupulus)

1. Over 40 compounds have been isolated from this plant.
2. The major constituents may be classified into three categories: (a) arylethylene-α-pyrone, (b) flavones (chalcones), and (c) conjugated diene ketones.
3. The primary active constituents with the highest psychoactive effects of *Piper methysticum* are known as kavalactones (kavapyrones) (3% to 20% dry weight).
4. Among the 18 kavalactones found in Kava roots are kavain, dihydrokavain, methysticin, dihydromethysticin, yangonin, and desmethoxyyangonin. Those six kavalactones account for about 95% of the biological activity in the plant.
5. Some of the kavalactones are found in other plants as well. For instance, the biologically active kavalactones, desmethoxyyangonin, is present in *Renealmia alpinia*.
6. Kavain was shown to change the sleep characteristics in animal models compared to other sedatives.
7. The mechanisms of action of kavalactones may be summarized as exerting an inhibition on norepinephrine uptake, altering the calcium and sodium channels, and modifying the binding of ligands to GABA$_A$ receptors.
8. Kava also functions by reducing norepinephrine and increasing serotonin levels, similar to benzodiazepines.
9. Pipermethysticine (a hepatotoxic alkaloid) found in Kava leaves and stem peelings.
10. Flavokavain B is a cytotoxic component presents in the plant’s root and is found in the aqueous and organic extracts obtained from Kava.

Kava (Piper methysticum Frost F.)

1. The major two constituents in Lavender are Linalyl acetate and Linalool.
2. Other minor constituents are (Z)-A-Ocimene, Lavandulyl acetate, Terpinen-4-ol, (E)-A-Ocimene, and 3-Octanone, among others.

Lavender (Lavandula officinalis L.)

1. Lemon balm leaves contain caffeic acid, luteolin, monoterpene glycosides, monoterpenoid aldehyde, oleanolic acid, protocatechuic acid, quercetin, rhamnose, rosmarinic acid, sesquiterpenes, tannins, and ursolic acid.
2. Compounds present in the essential oil obtained from this plant are citral (neral and geranial), polyphenols, and flavonoids.
3. Mainly, the essential contained oxygenated monoterpenes, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes.

Lemon balm (Melissa officinalis L.)

1. The plant contains the flavonoids isoschaftoside, schaftoside, isovitexin and isovitexin glucoside as its major constituents.
2. Other components present in this plant are tannins, coumarin alkaloids, flavonoids, glycine, and tyrosine.

Passionflower (Passiflora incarnata L.)

1. The major active constituents in St. John’s wort are the naphthodianthrones hypericin and pseudohypericin and the acylphloroglucinols hyperforin and adhyperforin.
2. Other ingredients present include flavonoids, bioflavonoids, and phenylpropanoids.
3. The plant contains kynurenic acid (an antagonist of ionotropic glutamate receptors) and protocatechuic acid (antioxidant, antibacterial, anticancer, antiallergeic, anti-inflammatory, analgesic, cardiotonic, hepatoprotective, neurological, and nephron-protective activities).
4. *Hypericum perforatum* contains caffeic acid and apigenin.

St. John’s Wort (Hypericum perforatum L.)
It contains essential oils, iridoids, flavonoids, alkaloids, amino acids, and lignanoids. Valerian contains the active components valepotriates, baldrinals, valerenic acid, valerenal, and valeranone. Components in the essential oils include a total of 150 compounds; the main ones are the monoterpenes and sesquiterpenes. The monoterpenes are borneol, bornyl acetate, and isobornyl acetate. Approximately 30 sesquiterpenes (guaiane and valerian types) are also present in valerian.

Table 1: The chemical composition of various psychoactive botanicals.

| Botanical               | Activities/Folk Uses                                                                 | References |
|-------------------------|--------------------------------------------------------------------------------------|------------|
| Valerian (Valeriana officinalis L., s.l.) | 1. It contains essential oils, iridoids, flavonoids, alkaloids, amino acids, and lignanoids.  
2. Valerian contains the active components valepotriates, baldrinals, valerenic acid, valerenal, and valeranone.  
3. Components in the essential oils include a total of 150 compounds; the main ones are the monoterpenes and sesquiterpenes. The monoterpenes are borneol, bornyl acetate, and isobornyl acetate. Approximately 30 sesquiterpenes (guaiane and valerian types) are also present in valerian. | [37] [38] |
| Chamomile (Matricaria recutita) | 1. Anti-anxiety  
2. Antiseptic  
3. Depression  
4. Diaphoretic  
5. Gastrointestinal discomforts  
6. Hay fever,  
7. Hemorrhoids  
8. Inflammatory conditions  
9. Insomnia (sleep aid)  
10. Menstrual disorders  
11. Migraine headaches (essential oil; applied topically)  
12. Muscle spasms (antispasmodic effect)  
13. Rheumatic pain  
14. Ulcers  
15. Wounds (topically; slow- to-heal injuries) | [39] [40] [9] [41] |
| Ginkgo biloba | 1. Acute mountain sickness  
2. Antagonizes the action of platelet activating factor and platelet aggregation is reduced.  
3. Anti-angiogenic  
4. Antioxidant,  
5. Anti-tumor  
6. As an alternative hormone replacement therapy  
7. Cardiovascular dysfunctions  
8. Enhances blood flow  
9. Eye health: Age-related macular degeneration and some types of glaucoma  
10. Gene regulatory effects  
11. Hypertension  
12. Migraine with aura treatment  
13. Neurodegenerative disorders (Alzheimer’s disease) and cognitive impairment (short-term memory loss)  
14. Neurosensory problems (tinnitus)  
15. Peripheral vascular dysfunctions (claudication)  
16. Resolution of ischemia-reperfusion injuries (through scavenging of the excess free radicals)  
17. Stimulates the release of prostacyclines and nitric oxide | [42] [43] [44] [45] |
| Hops (Humulus lupulus) | 1. Antimicrobial activities  
2. Antiparasitic activity (due the chalcones constituents)  
3. As a flavoring agent and preservative in beer (the female flowers)  
4. Hops has sedative effects due the presence of bitter acids  
5. It exhibits an estrogenic activity due to the presence of 8-prenylnaringenin, a phytosterogen | [15] [16] [18] [46] [19] |
### Table 2: Some of the recognizable pharmacological activities of psychoactive botanicals commonly used in folk medicine.

| Kava (*Piper methysticum Frost F.*) | 1. A sleep aid | 47 |
| | 2. An anxiolytic action | 23 |
| | 3. As a ceremonial drink in native Pacific Basin countries |  |
| | 4. For treatment of nervous disorders such as stress and restlessness |  |
| Lavender (*Lavandula officinalis L.*) | 1. An anxiolytic action | 48 |
| | 2. Antidepressant | 49 |
| | 3. Anti-parasitic | 50 |
| | 4. Antispasmodic |  |
| | 5. For relaxation against stress |  |
| | 6. For sternotomy-related pain after open heart surgery (as inhaled lavender oil) |  |
| | 7. Topically, for minor burns and insect bites |  |
| Lemon balm (*Melissa officinalis L.*) | 1. An anxiolytic effect | 51 |
| | 2. Anti-inflammatory | 52 |
| | 3. Antimicrobial |  |
| | 4. Antioxidant |  |
| | 5. Antiviral |  |
| | 6. As a modulator of mood and cognitive function |  |
| | 7. Topically, extracts of lemon balm reduce the amount of intracellular reactive oxygen species and enhance cell viability in human keratinocytes in oxidative stress conditions |  |
| Passionflower (*Passiflora incarnata L.*) | 1. Anti-inflammatory | 53 |
| | 2. Antioxidant | 30 |
| | 3. Anxiety | 31 |
| | 4. Attention-deficit Hyperactivity Disorder (ADHD) |  |
| | 5. Epilepsy |  |
| | 6. Menopausal symptoms |  |
| | 7. Sedative (for insomnia) |  |
| St. John’s Wort (*Hypericum perforatum L.*) | 1. Antidepressant (mild and moderate depression only) | 54 |
| | 2. Antifungal | 55 |
| | 3. Anti-inflammatory | 56 |
| | 4. Antimycobacterial | 57 |
| | 5. Antiviral | 58 |
| | 6. Asthma | 36 |
| | 7. Bronchitis |  |
| | 8. Burns |  |
| | 9. Diseases of the gastrointestinal tract (ulcers, gallbladder diseases, gastritis, diarrhea) |  |
| | 10. Eczema |  |
| | 11. Gout |  |
| | 12. Headaches |  |
| | 13. Hemorrhoids |  |
| | 14. Insomnia |  |
| | 15. Nervous conditions |  |
| | 16. Obsessive-compulsive disorder |  |
| | 17. Premenstrual syndrome |  |
| | 18. Promotes wound healing (slow or delayed wound healing) |  |
| | 19. Rheumatism |  |
| | 20. Skin ulcers |  |
| | 21. Uterine inflammation and endometriosis |  |
| Valerian (*Valeriana officinalis L., s.l.*) | 1. A sleeping aid | 59 |
| | 2. Antimicrobial Activities (essential oil) | 60 |
| | 3. Anxiety | 61 |
| | 4. Restlessness and tremors |  |
| | 5. Skeletal muscle relaxant |  |
The purported pharmacological activities of these herbs are summarized in table 2. Much of these effects are taken advantage of in folk medicine. Potential herb-drug interactions are often recognized, in particular when the herb is taken concurrently with the medications, in large doses, and for prolonged periods. Moreover, the “therapeutic” action of the herb cannot always be explained by the chemistry of the herbal material, a matter that requires further investigations. While some of the activities of the botanicals may be scientifically documented, the majority of these purported effects are folkloric. Folk medicine often relies on traditional ethnic use, anecdotal accounts, and occasional case reports. As shown in table 2, although the actions of the botanicals discussed in this brief editorial are mainly for psychological disorders, these herbs possess tremendous potentials for beneficial applications in many other pathological conditions.

It should be noted that the use of herbal supplements during pregnancy, for children, or while breast-feeding is contraindicated unless prescribed by a physician. Besides, herbal dietary supplements differ significantly in their chemical composition among manufacturers, in particular, those products that are not standardized. The use of standardized preparations, although it does not guarantee efficacy, it assures consistency in the manufactured product.

References

1. Bongartz U, Tan B-K, Seibt S, Bothe G, Uebelhack R, et al. (2019) Sleep Promoting Effects of IQP-AO-101: A Double-Blind, Randomized, Placebo-Controlled Exploratory Trial. Evidence-Based Complementary and Alternative Medicine.

2. Colombo D, Lunardon L, Bellia G (2014) Cyclosporine and Herbal Supplement Interactions. Journal of Toxicology.

3. Dghaim R, Al Khatib S, Rasool H, Ali Khan M (2015) Determination of Heavy Metals Concentration in Traditional Herbs Commonly Consumed in the United Arab Emirates. Journal of Environmental and Public Health.

4. Mahomoodally MF, Sreekeesoon DP (2014) A Quantitative Ethnopharmacological Documentation of Natural Pharmacological Agents Used by Pediatric Patients in Mauritius. BioMed Research International.

5. Haidu D, Párkányi D, Moldovan RI, Savii C, Pinzaru I, et al. (2017) Elemental Characterization of Romanian Crop Medicinal Plants by Neutron Activation Analysis. Journal of Analytical Methods in Chemistry.

6. Lucenteforte E, Gallo E, Pugi A, Giommoni F, Paolletti A, et al. (2012) Complementary and Alternative Drugs Use among Preoperative Patients: A Cross-Sectional Study in Italy. Evidence-Based Complementary and Alternative Medicine.

7. Miguel FG, Henriques Cavalheiro A, Spinola NF, Ribeiro DL, Mazzaron Barcelos GR, et al. (2015) Validation of a RP-HPLC-DAD Method for Chamomile (Matricaria recutita) Preparations and Assessment of the Marker, Apigenin-7-glucoside, Safety and Anti-Inflammatory Effect. Evidence-Based Complementary and Alternative Medicine.

8. Roschchina VV, Kuchin AV, Yashin VA (2017) Application of Autofluorescence for Analysis of Medicinal Plants. International Journal of Spectroscopy.

9. Srivastava JK, Shankar E, Gupta S (2010) Chamomile: A herbal medicine of the past with bright future. Mol Med Report 3: 895-901.

10. Yurcheshen M, Seethuus M, Pigeon W (2015) Updates on Nutraceutical Sleep Therapeutics and Investigational Research. Evidence-Based Complementary and Alternative Medicine.

11. Hamdoun S, Effertth T (2017) Ginkgolic acids inhibit migration in breast cancer cells by inhibition of NEMO sumoylation and NF-κB activity. Oncotarget 8: 35103-35115.

12. Isah T (2015) Rethinking Ginkgo biloba L.: Medicinal uses and conservation. Pharmacogn Rev 9: 140-148.

13. van Beek TA (200) Chemical analysis of Ginkgo biloba leaves and extracts. J Chromatogr A 967: 21-55.

14. van Beek TA, Montoro P (2009) Chemical analysis and quality control of Ginkgo biloba leaves, extracts, and phytopharmaceuticals. J Chromatogr A 1216: 2002-2032.

15. Almaguer C, Schönberger C, Gastl M, Arendt EK, Becker T (2014) Humulus lupulus—a story that begs to be told. A review J Inst Brew 120: 289-314.

16. Chadwick LR, Pauli GF, Farnsworth NR (2006) The pharmacognosy of Humulus lupulus L. (hops) with an emphasis on estrogenic properties. Phytomedicine 13: 119-131.

17. Fortes AM, Santos F, Pais MS (2010) Organogenic Nodule Formation in Hop: A Tool to Study Morphogenesis in Plants with Biotechnological and Medicinal Applications. Journal of Biomedicine and Biotechnology.

18. Frölich S, Schubert C, Bienzle U, Jenett-Siems K (2005) In vitro antiplasmodial activity of prenylated chalcone derivatives of hops (Humulus lupulus) and their interaction with haemin. Journal of Antimicrobial Chemotherapy 55: 883-887.

19. Milligan SR, Kalita JC, Heyerick A, Rong H, De Cooman L, et al. (1999) Identification of a Potent Phytoestrogen in Hops (Humulus lupulus L.) and Beer. The Journal of Clinical Endocrinology & Metabolism 84: 2249-2252.

20. Zhang X-L, Zhang Y-D, Wang T, Guo H-Y, Liu Q-M, et al. (2014) Evaluation on Antioxidant Effect of Xanthohumol by Different Antioxidant Capacity Analytical Methods. Journal of Chemistry.

21. Chandwani KD, Ryan JL, Peppone LJ, Janelbins MM, Sprod LK, et al. (2012) Evidence-Based Complementary and Alternative Medicine.

22. Chaurasiya ND, León F, Ding Y, Gómez-Betancur I, Benjumea D, et al. (2017) Interactions of Desmethoxyyangonin, a Secondary Metabolite from Renealmia alpinia, with Human
Monoamine Oxidase-A and Oxidase-B. Evidence-Based Complementary and Alternative Medicine.

23. Rivers Z, Xing C, Narayanapillai S (2016) Kava as a Pharmacotherapy of Anxiety Disorders: Promises and Concerns. Med Chem 6: 80-107.

24. Rowe A, Zhang L Y, Ramzan I (2011) Toxicokinetics of Kava. Advances in Pharmacological Sciences.

25. Sarris J, Moylan S, Camfield DA, Pase MP, Mischoulon D, et al. (2012) Complementary Medicine, Exercise, Meditation, Diet, and Lifestyle Modification for Anxiety Disorders: A Review of Current Evidence. Evidence-Based Complementary and Alternative Medicine.

26. de Groot A, Schmidt E (2016) Essential Oils, Part V: Peppermint Oil, Lavender Oil, and Lemongrass Oil. DERMATITIS 27: 325-332.

27. Abdellatif F, Boujdella H, Zitouni A, Hassani A (2014) Chemical composition and antimicrobial activity of the essential oil from leaves of Algerian Melissa officinalis L. EXCLI J 13: 772-781.

28. Carnat AP, Carnat A, Fraisse D, Lamanj JL (1998) The aromatic and polyphenolic composition of lemon balm (Melissa officinalis L. subsp. officinalis) tea. Pharmaceutica Acta Helvetiae 72: 301-305.

29. Miraj S, Rafieian-Kopaei M, Kiani S (2017) Melissa officinalis L: A Review Study with an Antioxidant Prospective. Journal of Evidence-Based Complementary & Alternative Medicine 22: 385-394.

30. Elsasa S-M, Rossib DJ, Rabera J, Whitea G, Seeleya C-A, et al. (2010) Passiflora incarnata L. (Passionflower) extracts elicit GABA currents in hippocampal neurons in vitro, and show anxiogenic and anticonvulsant effects in vivo, varying with extraction method. Phytotherapy 17: 940-949.

31. Kim M, Lim H-S, Lee H-H, Kim T-H (2017) Role Identification of Passiflora Incarnata Linnaeus: A Mini Review. J Menopausal Med 23: 156-159.

32. Jiratchariyakul W, Mahady GB (2013) Overview of Botanical Status in EU, USA, and Thailand. Evidence-Based Complementary and Alternative Medicine.

33. Kakkar S, Bais S (2014) A Review on Proteocatechuic Acid and Its Pharmacological Potential. ISRN Pharmacology.

34. Pisoschi AM, Pop A, Cimpeanu C, Predoi G (2016) Antioxidant Capacity Determination in Plants and Plant-Derived Products: A Review. Oxidative Medicine and Cellular Longevity.

35. Turski MP, Turska M, Kocki T, Turski WA, Paluszewkiewicz P (2016) Kynurenic Acid Content in Selected Culinary Herbs and Spices. Journal of Chemistry.

36. Yadollah-Damavandi S, Chavoshi-Nejad M, Jangholi E, Nekouyian N, Hosseini S, et al. (2015) Topical Hypericum perforatum Improves Tissue Regeneration in Full-Thickness Excisional Wounds in Diabetic Rat Model. Evidence-Based Complementary and Alternative Medicine.
51. Ramanauskien K, Stelmakienė A, Majien D (2015) Assessment of Lemon Balm (Melissa officinalis L.) Hydrogels: Quality and Bioactivity in Skin Cells. Evidence-Based Complementary and Alternative Medicine.

52. Scholey A, Gibbs A, Neale C, Perry N, Ossoukhova A, et al. (2014) Anti-Stress Effects of Lemon Balm-Containing Foods. Nutrients 6: 4805-4821.

53. Akhondzadeh S, Mohammadi MR, Momeni F (2005) Passiflora incarnata in the treatment of attention-deficit hyperactivity disorder in children and adolescents. Therapy 2: 609-614.

54. Apaydin EA, Maher AR, Shanman R, Booth MS, Miles JNV, et al. (2016) A systematic review of St. John’s wort for major depressive disorder. Syst Rev 5: 148.

55. Arsić I (2016) Preparation and Characterization of St. John’s Wort Herb Extracts Using Olive, Sunflower and Palm Oils. Acta facultatis medicae Naissensis 33: 119-126.

56. Gaster B, Holroyd J (2000) St John’s Wort for Depression: A Systematic Review. Arch Intern Med 160: 152-156.

57. İlhan M, Süntar I, Ayşe Demirel M, Yeşilada E, Keleş H, et al. (2016) A mixture of St. John’s wort and sea buckthorn oils regresses endometriotic implants and affects the levels of inflammatory mediators in peritoneal fluid of the rat: A surgically induced endometriosis model. Taiwanese Journal of Obstetrics and Gynecology 55: 786-790.

58. Lawvere S, Mahoney MC (2005) St. John’s Wort. Am Fam Physician 72: 2249-2254.

59. Barton DL, Atherton PJ, Bauer BA, Moore DF, Mattar BI, et al. (2011) The Use of Valeriana Officinalis (Valerian) in Improving Sleep in Patients Who Are Undergoing Treatment for Cancer: A Phase III Randomized, Placebo-Controlled, Double-Blind Study: NCCTG Trial, N01C5. J Support Oncol 9: 24-31.

60. Caudal D, Guinobert I, Lafoux A, Bardot V, Cotte C, et al. (2018) Skeletal muscle relaxant effect of a standardized extract of Valeriana officinalis L. after acute administration in mice. J Tradit Complement Med 8: 335-340.

61. Letchamo W, Ward W, Heard B, Heard D (2004) Essential Oil of Valeriana officinalis L. Cultivars and Their Antimicrobial Activity as Influenced by Harvesting Time under Commercial Organic Cultivation. Journal of Agricultural and Food Chemistry 52: 3915-3919.