

# Nourishing Botanical Nervines to Calm Anxiety, Enhance Sleep, and Promote Relaxation

Co-authored by Donald R. Yance, RH (AHG), CN  
and Suzanne E. Sky, L.Ac., MTOM

## Discussion

### RELAXATION, SLEEP AND RESILIENCE

Relaxation and the ability to sleep well have a reciprocal relationship. Relaxation and deep sleep provide a restorative function to the neuroendocrine system. This enhances resiliency and healthy response to daily life and stressors.

According to the National Institute of Mental Health, 40 million adults, or about 18.1%, of adults in America, suffer from some type of anxiety. This is almost three times the incidence of depression.<sup>1</sup> Many suffer with generalized anxiety disorder, which includes chronic worriers or those who experience low-level chronic anxiety with an inability to relax. Additionally, people with chronic anxiety experience sleep cycle disruption or inability to experience a deep, restorative sleep. Inadequate sleep adversely affects mood, anxiety and the ability to function well at work and socially. This is reported to be an issue for over half of Americans.<sup>2</sup>

Herbal medicine has been successfully and safely used to treat insomnia, calm anxiety and promote a deep restful sleep for thousands of years. The ancient texts of Ayurvedic, Chinese and other ancient medicines discuss the causes and differentiation between types of insomnia in relation to energetic systems and organ systems. These traditions recognized the relationship between physiological or mental/emotional depletion, weakness or overstimulation and the inability to relax or sleep. They identified many causative factors for anxiety, mood and sleep disorders. European and American herbal traditions also work extensively with nervous system disorders, mood and sleep. Today, herbal practitioners utilize this valuable and timelessly pertinent information. In addition, modern science is investigating the efficacy of these herbs and other natural compounds in its search to provide solutions without side effects.

Foundational to any healing process is the ability to sleep well, which is also a key indicator of physical, cognitive and mental health. Sleep, characterized by quiescence and reduced responsiveness, offers a profoundly restorative function.

Though sleep and its cycles are still not fully understood, we do know that it is regulated by complex circadian rhythms and homeostatic mechanisms in concert with the central nervous system.<sup>2</sup> Our metabolism, hormonal levels, cellular healing and repair, nervous system response and other functions perform in a specific chronobiological rhythm.

Circadian biorhythms are natural biological processes common to all living organisms attuned to cycles of night/day. Our body's basic biorhythm, based on cycles of activity and rest, is correlated with our circadian cycle. We spend an average of about 30% of our lives sleeping. Nighttime sleep is when the body does restorative and healing work at the cellular, organ, energetic and other levels of the system.

Many factors influence our ability to sleep well including emotions, trauma, pain, excess exercise, nutrition and lifestyle. It is widely recognized that when our normal, personal circadian rhythm and sleep cycle is disrupted, a myriad array of health issues can ensue. Anxiety or inability to sleep can be temporary or can become a prolonged issue with inability of the nervous system to relax. When this progresses, our system loses its healthy resiliency and ability to deal with stress. Biologically, the cellular, metabolic and neuroendocrine systems become dysfunctional. Mentally and emotionally we can lose touch with our creative ability to deal with life and become weakened.

In traditional medicines, the term neurasthenia is used to describe a weakened state of the nervous system. This weakened state can come about as a result of prolonged stress and further exacerbate conditions of worry, anxiety and sleeplessness. Calming, restorative nervine herbs are renowned for proficiently helping to break this cycle.

Our bodies operate on a foundation of simple biochemical reactions, which either "turn on" (stimulate or arouse) or "turn off" (inhibit or dampen) specific responses. This simple on-

off process, occurring constantly in the cellular, nervous and endocrine systems, creates an ongoing, ever-changing concert of complex biochemical actions and interactions that maintains our homeostasis on a daily basis.

In the neuroendocrine system and brain, this basic binary rhythm involves specific chemicals inducing arousal or activity and other chemicals exerting inhibitory or relaxing response. Glutamate, an excitatory compound, stimulates brain activity. GABA, known as a calming compound, is inhibitory – it calms neural activity. Elevated glutamate, due to increased or chronic sympathetic nervous system activation, can be a root cause of serotonin and GABA imbalance and the excess activation ultimately causes depletion of those beneficial compounds. Along with the amino acid glycine, many of the herbs featured below either act as GABA receptor agonists or enhance GABA levels. Low levels of GABA are associated with anxiety, depression and insomnia. Supporting healthy GABA levels in the nervous system enhances relaxation and the ability to sleep well.<sup>3</sup>

## TYPES & EXAMPLES OF NERVINES

Nervines are a broad group of herbs that calm and restore balance to the nervous system. These herbs prevent or alleviate adverse effects from prolonged stress, overwork, mental/emotional strain or the inability to sleep. They both alleviate symptoms and restore health and resilience to the nervous system.

Nervines can be classified into three main groups, identified by their action.

### 1. Nervine Tonics: Nutritive and Restorative

Two profoundly nutritive tonic nervines that are restorative are:

- Milky Oats (*Avena sativa*)
- Zizyphus Seed (*Zizyphus spinosa*)

### 2. Nervine Relaxants: Promote Relaxation, Alleviate Symptoms

Some relaxing nervines also possess antispasmodic capacity, influencing a relaxation response in the nervous and musculoskeletal system. These herbs include:

- Lemon Balm (*Melissa officinalis*)
- Passion Flower (*Passiflora incarnata*)
- Lavender (*Lavandula angustifolia*)
- Magnolia (*Magnolia officinalis*)
- Saffron (*Crocus sativa*)
- Skullcap (*Scutellaria lateriflora*)
- Kava Root (*Piper methysticum*)

### 3. Nervine Stimulants

Although *Camellia sinensis* is in this category it is also considered a relaxant. Theanine has a positive affinity for the nervous system. L-theanine stimulates the production of alpha brain waves and is a precursor of GABA, helping to promote the relaxation response.

#### A CLASSIC NERVINE FORMULA

*The three herbs below comprise a classic nervine formula that calms the nervous system, induces relaxation and promotes restful sleep.*

##### Passion Flower (*Passiflora incarnata*)

An Eclectic remedy for stress, nervousness and insomnia, especially in conditions of mental overwork or worry.

##### Skullcap (*Scutellaria lateriflora*)

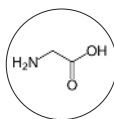
Used by Native Americans and Eclectic physicians to ease stress and anxiety. The Eclectics used it to calm restlessness along with irritability or excitability of the nervous system.

##### Wild Oats (*Avena sativa*)

The milky seed of Wild Oats is known as a restorative tonic both for the nerves and for the adrenal gland system.



## Nourishing Botanical Nervines to Calm Anxiety, Enhance Sleep, and Promote Relaxation



### Glycine

Glycine, a simple, nonessential amino acid and neurotransmitter, is metabolized in the brain. A major inhibitory transmitter, it plays a key role in maintaining healthy function of the central nervous system (CNS). Receptors for glycine are found throughout the vertebral central nervous system, in the brain stem, the spinal cord and throughout the tissues. Highest concentrations of glycine are found in the thalamus, amygdala, and substantia nigra among other areas.<sup>4</sup> Glycine inhibits the release of norepinephrine, exerts a calming influence and is found to modulate anxiety.

GABA, melatonin, serotonin and dopamine play a big part in controlling mood, circadian rhythm, sleep duration and depth. Glycine is a precursor to GABA. Many sedative drugs work by enhancing GABA's inhibitory influence.<sup>5</sup> In some areas of the CNS, glycine is released together with GABA.

Glycine modulates excitatory neurotransmission by potentiating the NMDA (N-methyl-D-aspartate) receptors<sup>5,6</sup> which are glutamate receptors in nerve cells. Glycine is involved with relaxation, detoxification and normal muscle function. It is found to calm aggression and to help reduce manic episodes. Glycine is also known to improve the ability to fall asleep along with quality of sleep.<sup>7</sup>

### Passion Flower (*Passiflora incarnata*)



Passion Flower is grown and used as medicine in Europe, the Americas and in the tropics. There are about 400 species of this perennial vine. The flower's beautiful patterns have been considered symbols of the Passion of Christ for which the plant is named. Native Americans used the plant as food and medicine. Passion Flower seeds were found at Native American sites dating back several thousand years.<sup>8</sup>

Passion Flower is revered by herbalists worldwide to calm stress and anxiety and to support healthy sleep. The Eclectic physicians used Passion Flower for stress, nervousness and insomnia especially in conditions of mental worry or overwork. The Eclectics, American and European herbalists used a formula of three herbs – Passion Flower, Skullcap and Wild Oats – to calm overactive mental, emotional and nervous system conditions.<sup>9,10</sup>

European human and animal studies report that Passion Flower extracts have anti-spasmodic, sedative and anxiolytic properties. It is also found to help normalize blood pressure.<sup>8,10,11</sup> The colorful flowers are high in anthocyanin flavonoids and chrysin. The flavonoid chrysin is found to reduce

inflammation and to help reduce anxiety. It binds to brain receptors known as benzodiazepine receptor sites and exerts a mild relaxing effect.<sup>12,13</sup> Passion Flower also demonstrates anti-inflammatory and antioxidant properties.<sup>14,15</sup>

### Zizyphus Seed (*Zizyphus spinosa*)



Known in Chinese medicine as a nourishing tonic to calm the spirit, Zizyphus Seed is a chief herb in formulas for insomnia especially when due to nervous stress and exhaustion. Zizyphus Seed is a nutritive sedative and is used to calm the nervous system and promote a naturally deep, restorative sleep throughout the night. It is the main ingredient of the famous traditional Chinese formula Suan Zao Ren Tang, which is used for this purpose. A study of this formula confirmed sedative activity of the formula.<sup>16</sup>

Research finds that Zizyphus Seed may act through serotonergic and GABA pathways.<sup>17,18</sup> Zizyphus Seed is found to have a synergistic effect with Magnolia Bark and this combination is reported to be beneficial for mild to moderate sleep disorders.<sup>19</sup>

The main compounds in Zizyphus Seed include saponins, alkaloids and flavonoids. All of these demonstrate the ability to resist lipid oxidation.<sup>20</sup> The triterpenes in Zizyphus Seed, known as jujubosides, are thought to contribute to its calming abilities. A major alkaloid compound, sanjoinine A, is also found to strongly influence sleep. Research shows that Zizyphus binds with both serotonin and GABA receptors, activates the GABA receptor and helps increase GABA synthesis.<sup>3</sup> One of the flavones, spinosin, exerts neuroprotective and anti-inflammatory properties.<sup>20,21</sup> Zizyphus Seeds are found to modulate neurotransmitters in the hypothalamus of rats.<sup>22</sup>

Considered beneficial for the liver in Chinese medicine, research reports hepato-protective benefits from Zizyphus Seeds. The polysaccharides in the seeds are found to benefit markers of liver damage including ALT and AST. The polysaccharide content includes glucose, arabinose, galacturonic acid and galactose. Studies also found elevation of the antioxidant enzyme super oxide dismutase along with glutathione.<sup>23</sup>

### Kava (*Piper methysticum*)



Kava has been cultivated and used for ceremonial and medicinal purposes for over 3,000 years. Widely known throughout the South Pacific, there is also evidence of Kava usage in South America. It is reported that in Fiji, when it seemed the men might

be getting ready to fight, someone would suggest a Kava ceremony. This brought everyone together and the Kava drink calmed and grounded the over-expressive energy. Known for its ability to calm anxiety, Kava helps ground the energy when in an overactive state, to allow for rest. Fishermen and laborers in ancient Hawai'i drank Kava tea at the end of a long day of hard, manual work to relax their muscles and help them sleep well.

Studies report Kava as being very effective for mild anxiety or insomnia, nervousness, stress and tension.<sup>24,25</sup> The superiority of Kava extract over placebo is demonstrated in a number of clinical trials.<sup>25-27</sup> Studies report significant anxiolytic and antidepressant activity.<sup>3,27,28</sup>

Kavalactones are considered to be the main biologically-active compounds in Kava. Some studies report that kavalactones show an affinity for binding with cannabinoid receptors in the nervous system.<sup>29</sup> It is also reported that Kava acts on the GABA receptors.<sup>3</sup> Studies support Kava's benefit in both falling asleep and a healthy sleep pattern.<sup>3</sup>

#### Skullcap (*Scutellaria lateriflora*)



This invaluable member of the Mint family was used by Europeans, Native Americans and by the Eclectic physicians to soothe and calm nerves. The Eclectics utilized it to calm nervous excitability where there is an irritated nervous system, restlessness and inability to sleep. It was also used for nervous disorders with muscular twitching and tremors. It was revered for its soothing influence and for its synergistic benefits with the restorative nervine *Avena sativa*.<sup>30</sup>

American Skullcap contains several amino acids, including glutamate, glutamine and GABA. Glutamine crosses the blood-brain barrier and can be metabolized to GABA in GABAergic neurons. The compound baicalin found in Skullcap binds to the benzodiazepine site of the GABA receptor.<sup>31</sup> Skullcap enhances mood and demonstrates anxiolytic properties. It also shows neuroprotective capacity, which may be attributed to its significant antioxidant influence.<sup>32,33</sup>

#### Lemon Balm (*Melissa officinalis*)



Lemon Balm, also a member of the Mint family, is traditionally used in Europe and the Americas for its ability to calm nervous excitement. This gentle, yet powerful herb also calms digestive upset due to overactivity of the nervous system. The German Commission E formally recommends Lemon Balm for nervous sleep disorders. Studies show Lemon Balm extract significantly reduces the restless state of animals.<sup>34,35</sup> The

manufacturing process of Cyracos, a unique extract of Lemon Balm, preserves all the active components of the aerial parts of Lemon Balm.

#### Fresh Wild Oat Seed (*Avena sativa*)

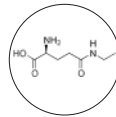


The fresh extract made from the milky seed of *Avena sativa* is well-known as a potent tonic to strengthen and nourish the nervous system. Herbalists use it to calm the nerves and support recovery from neurasthenia – nervous exhaustion and weakness – with its attendant patterns of anxiety, impaired sleep and sensitivity to stimulus.

*Avena*, a classic nervine tonic, supports the nervous system's ability to withstand stress and builds energy. It is traditionally recognized as a nourishing, restorative tonic for the nervous system.<sup>30,36</sup> The milky seed of *Avena* nourishes and harmonizes the sympathetic and parasympathetic nervous systems. It is one of the best herbs to restore vital energy especially in cases of adrenal exhaustion. Herbalists revere it as a primary herb to support healing from various addictions including tobacco, cannabis, alcohol and opiates. The Eclectic physician Dr. Finley Ellingwood considered it a great remedy to alleviate nervous exhaustion due to stress, overwork and nervous anxiety.<sup>30</sup>

Modern research reports that oats exert a wide spectrum of activity including antioxidant, anti-inflammatory and immunomodulating.<sup>36</sup> The milky seed of *Avena* is a rich source of protein, minerals (including calcium and magnesium), flavones, saponins, sterols and tocopherols.<sup>30,36,37</sup>

#### L-Theanine



Theanine is an amino acid (a glutamic acid analog) found in tea leaves (*Camellia sinensis*). Tea has a 5,000 year history as a beverage and medicine in the Chinese culture. In Chinese, Japanese and other Asian cultures tea is used ceremonially and revered for its ability to promote calmness and clarity.

L-theanine is found to stimulate the production of alpha brain waves which promote deep relaxation along with mental clarity and alertness – similar to a meditative state. Theanine promotes the formation of GABA, which influences the levels of dopamine and serotonin, helping to promote the relaxation response.<sup>38,39</sup> Originally discovered in green tea, Theanine is found in red, black and green teas. Studies confirm that it calms nervous agitation, improves mental clarity, acuity and performance, and aids mental concentration. L-theanine antagonizes glutamate receptors and increases brain GABA levels.

Theanine enhances relaxation and improves learning ability and concentration.<sup>40</sup> It is found to be neuroprotective with antioxidant properties.<sup>41</sup> Studies report that Theanine protects neurons from amyloid beta neurotoxicity and significantly reverses glutamate-induced toxicity, a major cause of degenerative brain disease.<sup>42</sup>



#### **Saffron (*Crocus sativus*)**

Since ancient times, the dark red stigmas of Saffron have been used as a medicine and food. It is also used as a dye, offering a rich yellow color to fabrics and foods. In Ayurvedic and Chinese medicine it is revered to enhance healthy blood circulation.

Saffron, high in carotenoids, is known as a potent cell oxygenator. Modern studies report that Saffron shows significant antidepressant-like activity<sup>43</sup> and demonstrates an anxiolytic and calming influence.<sup>44</sup> One study suggests that the carotenoid crocetin can improve sleep quality<sup>45</sup> and help decrease effects of physical fatigue.<sup>46</sup> Saffron extract is found to be a potent antioxidant and free radical scavenger that can help reduce vascular cognitive impairment.<sup>47</sup>



#### **Lavender (*Lavandula angustifolia*)**

Renowned throughout history, Lavender is cultivated for its beautiful aromatic flowers used in teas, potpourri, healing balms and essential oils. Lavender has been recognized for centuries for its ability to calm anxiety, alleviate depression and lift the spirits. In one of the earliest Indian medical texts Lavender was recorded for its use in mental/emotional illness. Lavender exerts a soothing, relaxing influence on the nervous system. Lavender tea is a home remedy to soothe nerves, calm a nervous stomach and relax the busy system for a good night's sleep.

Lavender is licensed in Germany as a medicinal herb for restlessness, sleep disorders and nervous stomach. Lavender flowers are most often used in small amounts, combined with other herbs, in an aqueous tisane. The essential oil of Lavender exerts a relaxant effect used in aromatherapy and is highly-researched. Traditionally in Europe, women placed lavender flowers in their linens and made small "sleep pillows", because Lavender was recognized to gently promote sleep. They used Lavender flowers in baths and teas

as a mild sedative. European herbalists also recognized its spasmolytic, carminative and stomachic actions and it has a long history as a potent antibacterial.

Lavender contains a high concentration of volatile oils, which impart a strong fragrance and possess multiple medicinal properties. These include triterpenes, limonene and camphor. It also contains tannins, flavonoids, phytosterols and coumarins. The level of these constituents varies within its more than 30 species.<sup>48,49</sup>

#### **Magnolia Bark (*Magnolia officinalis*)**



Magnolia Bark is highly-esteemed in the traditional medicines of China and Japan. The Japanese refer to it as saiboku-to and drink Magnolia Bark tea to alleviate anxiety. Magnolia demonstrates anti-stress benefits that allows adaptation to stress and modulates the stress-hormone cortisol.

The highly-aromatic Magnolia Bark is a primary herb in Chinese medicine used for both respiratory and digestive benefits. It is traditionally highly revered to help calm respiratory allergies including asthma. Magnolia Bark is rich in many biologically-active compounds including alkaloids, coumarins, flavonoids, lignans and terpenoids.<sup>50</sup>

One of Magnolia Bark's main constituents is honokiol – a polyphenolic compound that exhibits powerful antioxidative and anti-inflammatory activity. Honokiol is also studied for its neuroprotective influence as it is found to calm oxidative and inflammatory processes in neurons and microglial cells.<sup>50</sup>

Honokiol is the most-researched bioactive constituent of Magnolia Bark. Many studies show that honokiol acts as a potent anti-stress agent and is also powerfully antioxidant. One study found honokiol to be five times stronger than diazepam in reducing anxiety with no side effects, although honokiol has no influence on muscle relaxation.<sup>51</sup>

*For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email [info@naturaedu.com](mailto:info@naturaedu.com).*

## References

1. <http://www.nimh.nih.gov/health/statistics/prevalence/any-anxiety-disorder-among-adults.shtml>
2. Shia Y, Donga JW et al. *Herbal Insomnia Medications that Target GABAergic Systems: A Review of the Psychopharmacological Evidence*. *Current Neuropharmacology*. May 2014. 12(3):289-302
3. Weeks BS. *Formulations of dietary supplements and herbal extracts for relaxation and anxiolytic action: Relarian*. *Med Sci Monit*. 2009 Nov;15(11):RA256-62.

### Glycine

4. Alzheimer's Association. 2014 *Alzheimer's Disease Facts and Figures*, Alzheimer's & Dementia, Volume 10, Issue 2. [http://www.alz.org/downloads/facts\\_figures\\_2014.pdf](http://www.alz.org/downloads/facts_figures_2014.pdf)
5. Zafra F, Aragon C, Gimenez C. *Molecular biology of glycinergic neurotransmission*. *Mol Neurobiol*. 1997. Jun;14(3):117-42.
6. Lopez-Corcuera B, Geerlings A, Aragon C. *Glycine neurotransmitter transporters: an update*. *Mol Membr Biol*. 2001. Jan-Mar; 18(1):13-20.
7. Yamadera W, Inagawa K, Chiba S, et al. *Glycine ingestion improves subjective sleep quality in human volunteers, correlating with polysomnographic changes*. *Sleep and Biological rhythms* 2007. 5 (2): 126-131. doi:10.1111/j.1479-8425.2007.00262.x.

### Passion Flower

8. Steven Foster c 2009: [www.stevenfoster.com/education/monograph/pflower.html](http://www.stevenfoster.com/education/monograph/pflower.html)
9. Felter, HW, Lloyd JU. *King's American Dispensatory*. 2 vols. 1898. reprint ed. 1983.: Eclectic Medical Publications, Portland, Oregon.
10. Speroni, E. and A. Minghetti. *Neuropharmacological Activity of Extracts from Passiflora incarnata*. *Planta Medica* 1988. 54: 488-491.
11. Movafegh A, Alizadeh R, et al. *Preoperative oral Passiflora incarnata reduces anxiety in ambulatory surgery patients: a double-blind, placebo-controlled study*. *Anesth. Analg*. 2008. 106:1728-1732.
12. Paladini AC, Marder M, Viola H, et al. *Flavonoids and the central nervous system: from forgotten factors to potent anxiolytic compounds*. *J Pharm Pharmacol Biochem Behav*. 1999. 51:519-526.
13. Wolfman C, Viola H, Paladini A, et al. *Possible anxiolytic effects of chrysin, a central benzodiazepine receptor ligand isolated from Passiflora coerulea*. *Pharmacol Biochem Behav*. 1994 Jan. 47(1):1-4.
14. Sasikala V, Saravanan S, Parimelazhagan T. *Analgesic and anti-inflammatory activities of Passiflora foetida L*. *Asian Pac J Trop Med*. 2011 Aug. 4(8):600-3.
15. Souza MD, Barbalho SM, et al. *Effects of Passiflora edulis (Yellow Passion) on Serum Lipids and Oxidative Stress Status of Wistar Rats*. *J Med Food*. 2011 Aug 30.

### Zizyphus Seed

16. Li YJ, Bi KS. *Study on the therapeutic material basis of traditional Chinese medicinal preparation suanzaoren decoction*. *Chem Pharm Bull (Tokyo)* 2006. 54: 847-851.
17. Wang LE, Bai YJ, Shi XR, et al. *Spinosin, a C-glycoside flavonoid from semen Ziziphi Spinozae, potentiated pentobarbital-induced sleep via the serotonergic system*. *Pharmacol Biochem Behav*. 2008. 90(3):399-403.

18. Ma Y, Han H, Eun JS, et al. *Sanjoinine A isolated from Ziziphi Spinosi Semen augments pentobarbital-induced sleeping behaviors through the modification of GABA-ergic systems*. *Biol Pharm Bull*. 2007. 30(9):1748-53.
19. Maruyama Y, Kuribara H, et al. *Identification of magnolol and honokiol as anxiolytic agents in extracts of saiboku-to, an oriental herbal medicine*. *J Nat Prod*. 1998. 61:135-138.
20. Chen Kx, Zhao LM et al. *Flavone C-glycosides from seeds of Ziziphus jujuba var. spinosa*. *Zhongguo Zhong Yao Za Zhi*. 2015 Apr. 40(8):1503-7.
21. Ko Sy, Lee He, Park SJ et al. *Spinosin, a C-Glycosylflavone, from Zizyphus jujuba var. spinosa Ameliorates Aβ1-42 Oligomer-Induced Memory Impairment in Mice*. *Biomol Ther (Seoul)*. 2015 Mar. 23(2):156-64. doi: 10.4062/biomolther.2014.110. Epub 2015 Mar
22. Gao Jr, Ji WB et al. *Effects of extracts from ziziphi spinosae semen and schisandrae chinensis fructus on amino acid neurotransmitter in rats with insomnia induced by PCPA*. *Zhong Yao Cai*. 2013 Oct. 36(10):1635-9.
23. Yue, Y, Wu S et al. *Characterization and hepatoprotective effect of polysaccharides from Ziziphus jujuba Mill. var. spinosa (Bunge) Hu ex H. F. Chou sarcocarp*. *Food Chem Toxicol*. 2014 Dec. 74:76-84. doi: 10.1016/j.fct.2014.09.006. Epub 2014 Sep 26.

### Kava Root

24. Lehmann E et al. *Efficacy of a special kava extract (Piper methysticum) in patients with states of anxiety, tension and excitedness of non-mental origin—a double-blind placebo-controlled study of four weeks' treatment*. *Phytomedicine*. 1996. 3:113-119.
25. Pittler MH, Ernst E. *Efficacy of kava extract for treating anxiety: systematic review and meta-analysis*. *J Clin Psychopharmacol*. 2000 Feb. 20(1):84-9.
26. Pittler MH, Ernst E. *Kava extract for treating anxiety*. *Cochrane Database Syst Rev*. 2003. (1):CD003383.
27. Sarris J, Stough C, Bousman CA, et al. *Kava in the treatment of generalized anxiety disorder: a double-blind, randomized, placebo-controlled study*. *J Clin Psychopharmacol*. 2013 Oct. 33(5):643-8. doi: 10.1097/JCP.0b013e318291be67.
28. Sarris J, Kavanagh DJ, Byrne G, et al. *The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of Piper methysticum*. *Psychopharmacology (Berl)*. 2009 Aug. 205(3):399-407. doi: 10.1007/s00213-009-1549-9. Epub 2009 May 9.
29. Ligresti A1, Villano R, et al. *Kavalactones and the endocannabinoid system: the plant-derived yangonin is a novel CB receptor ligand*. *Pharmacol Res*. 2012 Aug. 66(2):163-9. doi: 10.1016/j.phrs.2012.04.003. Epub 2012 Apr 14.

### Skullcap

30. Ellingwood, F MD. *American Materia Medica*, Therapeutics. 1919. Eclectic Medical Publications.
31. Awad R, Arnason JT et al. *Phytochemical and biological analysis of Skullcap (Scutellaria lateriflora L.): A medicinal plant with anxiolytic properties*. 2003. *Phytomedicine* 10: 640-649.
32. Brock C, Whitehouse J, Tewfik I, Towell T. *American Skullcap*

(*Scutellaria lateriflora*): a randomised, double-blind placebo-controlled crossover study of its effects on mood in healthy volunteers. *Phytother Res*. 2014 May. 28(5):692-8. doi: 10.1002/ptr.5044. Epub 2013 Jul 22.

33. Lohani M, Ahuja M, et al. *Suppiramaniam V, Kempainen B, Dhanasekaran M. Anti-oxidative and DNA protecting effects of flavonoids-rich Scutellaria lateriflora*. *Nat Prod Commun*. 2013 Oct. 8(10):1415-8.

#### Lemon Balm

34. Kennedy DO, Scholey AB, et al. *Attenuation of laboratory-induced stress in humans after acute administration of Melissa officinalis (Lemon Balm)*. *Psychosom Med*. 2004 Jul-Aug. 66(4):607-13.
35. Kennedy DO, Wake G, Savelev S, et al. *Modulation of mood and cognitive performance following acute administration of single doses of Melissa officinalis (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties*. *Neuropsychopharmacology*. 2003. 28(10):1871-81.

#### Wild Oat Seed

36. Singh R1, De S, Belkheir A. *Avena sativa (Oat), a potential nutraceutical and therapeutic agent: an overview*. *Crit Rev Food Sci Nutr*. 2013 53(2):126-44. doi: 10.1080/10408398.2010.526725.
37. Chu, YF, Wise, ML, Gulvady AA, et al. *In vitro antioxidant capacity and anti-inflammatory activity of seven common oats*. *Food Chem*. 2013 Aug 15. 139(1-4):426-31. doi: 10.1016/j.foodchem.2013.01.104. Epub 2013 Feb 10.

#### L-Theanine

38. Mason R. *200 mg of Zen; L-theanine boosts alpha waves, promotes alert relaxation*. *Alternative & Complementary Therapies*. 2001 April. 7:91-95.
39. Juneja LR, Chu D-C, Okubo T, et al. *L-theanine a unique amino acid of green tea and its relaxation effect in humans*. *Trends Food Sci Tech*. 1999. 10:199-204.
40. Vuong QV, Bowyer MC, Roach PD. *L-Theanine: properties, synthesis and isolation from tea*. *J Sci Food Agric*. 2011 Aug 30. 91(11):1931-9. doi: 10.1002/jsfa.4373. Epub 2011 Mar 29.
41. Sumathi, T, Shobana C, Thangarajeswari, M, Usha R. *Protective effect of L-Theanine against aluminium-induced neurotoxicity in cerebral cortex, hippocampus and cerebellum of rat brain – histopathological and biochemical approach*. *Drug Chm Toxicol*. 2014 Mar 24.
42. Di X, Yan J, Zhao Y, et al. *L-theanine protects the APP (Swedish mutation) transgenic SH-SY5Y cell against glutamate-induced excitotoxicity via inhibition of the NMDA receptor pathway*. *Neuroscience*. 2010 Jul 14. 168(3):778-86. Epub 2010 Apr 21.

#### Saffron

43. Wang Y, Han T, Zhu Y, et al. *Antidepressant properties of bioactive fractions from the extract of Crocus sativus L.* *J Nat Med*. 2010 Jan. 64(1):24-30. Epub 2009 Sep 29.
44. Hosseinzadeh H, Noraei NB. *Anxiolytic and hypnotic effect of Crocus sativus aqueous extract and its constituents, crocin and safranal, in mice*. *Phytother Res*. 2009 Jun. 23(6):768-74.
45. Kuratsune H, Umigai N, et al. *Effect of crocetin from Gardenia Jasminoides Ellis on sleep: A pilot study*. *Phytomedicine* 2010. 17:11:840-843.

46. Mizuma, H, Tanaka, M, Nozaki, S, et al. *Daily oral administration of crocetin attenuates physical fatigue in human subjects*. *Nutrition research*. Mar 2009. 29 (3):145–50. doi:10.1016/j.nutres.2009.02.003.
47. Hosseinzadeh H, Sadeghnia HR, et al. *Effects of Saffron (Crocus sativus L.) and its Active Constituent, Crocin, on Recognition and Spatial Memory after Chronic Cerebral Hypoperfusion in Rats*. *Phytother Res*. 2011 Jul 19. doi: 10.1002/ptr.3566.

#### Lavender

48. *The Complete German Commission E Monographs Therapeutic Guide to Herbal Medicines*. ed. by M. Blumenthal, W.R. Busse, et al. trans. by S. Klein and R.S. Rister. 1998. Austin: American Botanical Council; Boston: Integrative Medicine Communications.
49. Koulivand PH, Ghadiri MK and Gorji A. *Lavender and the Nervous System. Evidence-Based Complementary and Alternative Medicine*. 2013. Article ID 681304. 10 pages. <http://dx.doi.org/10.1155/2013/681304>

#### Magnolia Bark

50. Chuang DY, Chan MH, Zong Y et al. *Magnolia polyphenols attenuate oxidative and inflammatory responses in neurons and microglial cells*. *Journal of Neuroinflammation* 2013. 10:15.
51. Xu Q, Yi LT, Pan Y, et al. *Antidepressant-like effects of the mixture of honokiol and magnolol from the barks of Magnolia officinalis in stressed rodents*. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007 Nov 28.