

APPLICATIONS

- Relax/Sleep Support
- Stress Management Support



INTRODUCTION

Amantilla is a hydro-ethanol extract made from Valerian root (*Valeriana officinalis*), which belongs to the Caprifoliaceae/Valerianaceae family.¹ Various species of Valerian continue to be used for relaxation, sleep support, and stress management in the traditional health practices of China, India, and the Middle East.² Valerian root contains monoterpenes such as borneol; sesquiterpenes such as valerenal and valerenic acid; valepotriates such as valtrate; alkaloids such as actinidine; flavonoids such as linarin; minerals such as copper, zinc, and manganese; lignans; amino acids; and small amounts of GABA.^{1,3,4,5} Valerian root and its constituent valerenic acid may act as a GABA agonist as well as a partial 5-hydroxytryptamine (5-HT5a) agonist.^{2,6-8} It may also act as an adenosine A1 receptor agonist.⁵ Activity at these receptors may account for Valerian root's role in the support of healthy relaxation, sleep, and stress management.*

Amantilla is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

RELAX / SLEEP SUPPORT

According to a recent systematic review and meta-analysis of human studies, Valerian root (*V. officinalis*) may help to support normal relaxation and healthy sleep during times of occasional sleeplessness.⁹ It may also help to support sleep through skeletal muscle relaxation,⁸ and also supports smooth muscle

relaxation.⁹ In a mouse study, researchers notably found that Valerian root helped to support skeletal muscle relaxation while maintaining normal endurance and healthy neuromuscular tone, suggesting that Valerian root may assist with sleep support without the side effects typical of other treatments.⁸

Valerian root (*V. officinalis*) may help to support both quality and quantity of sleep, with fewer nighttime awakenings.¹⁰ It may also help to support a normal sleep onset.⁴ Some of Valerian root's constituents, including the flavonoid linarin and the sesquiterpene valerenic acid, may help to support calm relaxation and healthy sleep.³ Research suggests that blood levels of Valerian root peak from one to two hours after consumption, and because of this, it is recommended to take Valerian root 30 minutes to 2 hours before bed for optimal support.¹¹ While single doses may be helpful, studies lasting 14 days or longer showed more consistent support.^{4,12} A key benefit of Valerian root for sleep support is that it rarely causes next-day drowsiness when used as recommended.⁴

There are several mechanisms by which Valerian root may help with sleep support.* Valerian root is a GABAA receptor agonist, which may help maintain normal central nervous system (CNS) activity; this may facilitate a feeling of calm relaxation.^{2,5,7} Both Valerian root and its constituent valerenic acid may act as a partial 5-HT5a agonist to maintain normal serotonergic function, supporting healthy sleep.⁵ As 5-HT5a receptors are prevalent in the suprachiasmatic nucleus (SCN) and other areas of the brain involved with the circadian rhythm, this may be another avenue for potential sleep support.⁵ Lastly, Valerian root is known to be a partial adenosine A1 agonist, which may help to support and maintain healthy and restorative slow-wave sleep.⁵

In a randomized, double-blind, placebo-controlled, crossover study, 15 healthy participants were given either Valerian root extract or a vitamin E placebo. The Valerian group experienced decreased intracortical facilitation (ICF), or decreased brain excitability, which may also help to support healthy sleep.¹³ Brain excitability returned to the pre-treatment baseline after 6 hours, explaining why morning drowsiness is rare with Valerian extract at the recommended dosages.¹³ In a previous randomized, double-blind, placebo-controlled, crossover study, 14 days of Valerian root showed more consistent support than a single dose, and researchers concluded that Valerian helps maintain healthy slow-wave sleep.¹²

STRESS MANAGEMENT SUPPORT

Many of the same receptors that support healthy sleep (GABAA, 5-HT5a, and adenosine A1) are also involved in stress management. Valerian root (*V. officinalis*) may help support healthy stress management during times of occasional stress through agonist or partial agonist action at these receptors.⁵ One human trial with healthy participants compared the effects of valerian alone, kava alone, and no treatment on mental stress during cognitive testing. All three groups underwent baseline cognitive testing, then were administered either valerian, kava, or no treatment, for 7 days. All three groups then underwent a subsequent session of cognitive testing. While both the valerian and kava groups experienced a decrease in systolic blood pressure after the intervention, only the valerian group experienced a lower heart rate during mental stress. While neither intervention affected performance, it appeared to mitigate the perception of mental stress by maintaining normal physiological reactivity.¹⁴

In a randomized, double-blind, placebo-controlled study with 64 mildly stressed volunteers, participants received Valerian root extract or a placebo three times daily for four weeks. While both groups showed some improvement in stress levels, only the Valerian group had significantly better alpha and theta coherence in the brain.^{*15} The study authors concluded that Valerian root may help maintain normal brain connectivity, supporting a sense of healthy calm.^{*15} There have been similar findings in rodent studies. In a mouse study, valepotriates from Valerian root helped to support normal stress management,⁵ which a rat study attributed to healthy HPA axis support.^{*16}

SAFETY AND CAUTIONS

Valerian root (*V. officinalis*) is generally well tolerated. Common side effects include drowsiness, dizziness, and occasional gastrointestinal effects, though some individuals have reported vivid dreams.^{*17} Because Valerian root may help to support normal relaxation, it may have additive effects when taken with various sedative substances including, but not limited to, alcohol, benzodiazepines, and CNS depressants.^{*18-20}

Because Valerian mildly inhibits glucuronidation, it is possible that it may increase levels of drugs metabolized by UGT1A1 and UGT2B7.21 While rare, there have been isolated case reports of hepatotoxicity, particularly in higher doses, with multi-ingredient formulas, or concurrent with alcohol abuse.¹⁷ Valerian is considered safe at recommended doses for shorter periods, and in extended use, it should be tapered gradually, rather than stopped abruptly, to avoid rebound effects.¹⁷

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

*** This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.**

NutraMedix

SHAKE WELL BEFORE EACH USE:
Put 15 drops in 4 oz (120mL) of water and wait one minute before drinking. May be taken several times per day as needed, or 30 drops at bedtime, or as directed by your physician. Stop use if adverse reactions develop. Keep out of reach of children.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.**

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AMANTILLA

FROM VALERIAN

DAILY STRESS SUPPORT †

Dietary Supplement

1 fl oz. (30mL)

Supplement Facts
Serving Size 15 drops
Servings Per Container 40

Amount Per Serving	
Valerian root extract	0.75 mL*

*Daily Value not established

Other ingredients: mineral water, ethanol (20-24%)

NutraMedix
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www.nutramedix.com
561-745-2917

Lot #
Exp.

REFERENCES

- 1 Pilerood, S. A. & Prakash, J. (2013). *International Journal of Food, Nutrition, and Dietetics*, 1(1), 1-8.
- 2 Gordan, A., Taheri, E., et al. (2019). *Journal of Pharmaceutical Research International*, 292, 1-10.
- 3 Fernández, S., Wasowski, C., et al. (2004). *Pharmacology, Biochemistry, and Behavior*, 77(2), 399-404.
- 4 Hadley, S., & Petry, J. J. (2003). *American Family Physician*, 67(8), 1755-1758.
- 5 Shinjyo, N., Waddell, G., et al. (2020). *Journal of Evidence-based Integrative Medicine*, 25, 2515690X20967323.
- 6 Dietz, B. M., Mahady, G. B., et al. (2005). *Brain Research: Molecular brain research*, 138(2), 191-197.
- 7 Benke, D., Barberis, A., et al. (2009). *Neuropharmacology*, 56(1), 174-181.
- 8 Caudal, D., Guinobert, I., et al. (2017). *Journal of Traditional and Complementary Medicine*, 8(2), 335-340.
- 9 Occhiuto, F., Pino, A., et al. (2009). *The Journal of Pharmacy and Pharmacology*, 61(2), 251-256.
- 10 Abdellah, S. A., Berlin, A., et al. (2019). *Journal of Traditional and Complementary Medicine*, 10(2), 116-123.
- 11 Anderson, G. D., Elmer, G. W., et al. (2005). *Phytotherapy Research: PTR*, 19(9), 801-803.
- 12 Donath, F., Quispe, S., et al. (2000). *Pharmacopsychiatry*, 33(2), 47-53.
- 13 Mineo, L., Concerto, C., et al. (2017). *Neuropsychobiology*, 75(1), 46-51.
- 14 Cropley, M., Cave, Z., et al. (2002). *Phytotherapy Research: PTR*, 16(1), 23-27.
- 15 Roh, D., Jung, J. H., et al. (2019). *Phytotherapy Research: PTR*, 33(4), 939-948.

- 16 Shi, S. N., Shi, J. L., et al. (2014). *Evidence-based Complementary and Alternative Medicine: eCAM*, 2014, 325948.
- 17 Natural Medicines. (2022, August 24). *Valerian* [monograph]. <http://naturalmedicines.therapeuticresearch.com>.
- 18 Chen, D., Klesmer, J., et al. (2002). *The American Journal on Addictions*, 11(1), 75-77.
- 19 Donovan, J. L., DeVane, C. L., et al. (2004). *Drug Metabolism and Disposition: The biological fate of chemicals*, 32(12), 1333-1336.
- 20 Houghton P. J. (1999). *The Journal of Pharmacy and Pharmacology*, 51(5), 505-512.
- 21 Alkharfy, K. M., & Frye, R. F. (2007). *Xenobiotica: The fate of foreign compounds in biological systems*, 37(2), 113-123.