
5-Hydroxytryptophan (5-HTP)

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General Features

5-HTP is a naturally occurring agent that is extracted from the seed of an African plant, known as the “Griffonia simplicifolia”. 5-HTP, unlike the amino acid tryptophan, easily crosses the blood-brain barrier. As a result, while only three percent of an oral dose of tryptophan is converted to serotonin in the brain, studies indicate that over seventy percent of an oral dose of 5-HTP is converted to serotonin. As serotonin is a neurotransmitter that elevates mood and improves sleep quality, 5-HTP has been used in clinical trials to treat depression, insomnia and other conditions where a rise in serotonin levels may be desirable.

Some evidence suggests that 5-HTP also increases endorphin and other neurotransmitter levels as well.¹

Supplementation Studies and Clinical Applications

1. Depression

In several clinical trials 5-Hydroxytryptophan has been tested on its own or against other antidepressant drugs, including selective serotonin re-uptake inhibitor drugs (SSRI) such as fluvoxamine (Luvox). Fluvoxamine exerts anti-depressant activity comparable to Prozac, Zoloft, and Paxil.

In general, 5-Hydroxytryptophan has been shown to be as effective as other traditional antidepressants and tends to be associated with fewer and less severe side effects. The usual dosage for this application is 100 mg, three times daily.¹⁻⁵ However, patients with depression should be under the care of a qualified health professional and combining 5-Hydroxytryptophan supplementation with other anti-depressant drugs or supplements is contraindicated and may result in life-threatening side effects (i.e. serotonin syndrome).⁶

2. Insomnia

5-HTP has been shown to improve insomnia and quality of sleep in affected subjects. For insomnia, a single 100 mg dose of 5-HTP, one hour before bedtime has been shown to improve duration and depth of sleep in one placebo-controlled study.⁷

3. Fibromyalgia

Some evidence suggests that 100 mg (5-HTP) taken three times per day may reduce symptoms of fibromyalgia, including pain and insomnia.⁸

4. Migraine

Migraine Headache Studies have provided evidence that patients who suffer from migraine headaches may experience a reduction in frequency and severity of attacks with a dosage range of 400-600 mg per day, in divided doses.⁹⁻¹³

Dosage Ranges

1. Depression: 100 mg, three times daily²
2. Insomnia: a single dose of 25-100 mg, one hour before bedtime.⁴
3. Fibromyalgia: 100 mg, three times daily⁸
4. Migraine headaches: 150 mg, three times per day⁹
5. Anxiety: 100 mg, three times daily⁸

Adverse Side Effects

In clinical studies using the above dosages, some patients experience gastrointestinal upset (i.e. nausea) or, less often, headache, sleepiness, muscle pain, or anxiety.¹⁻¹³

Drug-Nutrient Interactions and Contraindications

5-HTP should not be taken with other antidepressants, weight control drugs, other serotonin-modifying substances, or agents known to cause liver damage. Individuals with liver disease or scleroderma should also avoid 5-HTP.^{2,6,14}

Herb-Nutrient Interactions

St. John's Wort

5-HTP may potentiate the effect of St. John's Wort on brain neurotransmitters and vice versa. These supplements should not be taken concurrently.¹⁷

Toxicity

Animal studies have shown that high doses of 5-HTP can cause muscle jerks in guinea pigs, and when injected has caused kidney damage in rats. To date, these problems and serotonin syndrome have not been reported in humans, but the potential for serotonin syndrome to develop under certain circumstances (i.e. in combination with antidepressant drugs) is very plausible.^{6,15,16}

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1. Van Hiele JJ. L-5 hydroxytryptophan in depression: the first substitution therapy in psychiatry? *Neuropsychobiology* 1980;6:230-40.
 2. Byerley WF, Judd LL, Reimherr FW, Grosser BI. 5-hydroxytryptophan: A review of its antidepressant efficacy and adverse effects. *J Clin Psychopharmacol* 1987;7:127-37 [review].
 3. Van Praaf HM. Management of depression with serotonin precursors. *Biol Psychiatry* 1981;16:291-310.
 4. Poldinger W, Calanchini B, Schwarz W. A functional-dimensional approach to depression: serotonin deficiency as a target syndrome in a comparison of 5-hydroxytryptophan and fluvoxamine. *Psychopathology* 1991;24:53-81.
 5. Praag HM, Lemus C. Monoamine precursors in the treatment of psychiatric disorders. In: Wurtman RJ, Wurtman JJ editors. *Nutrition and the Brain*. New York: Raven Press: 1986. Vol 7. p. 89-139
 6. Martin TG. Serotonin syndrome. *Ann Emerg Med* 1996;28:520-6.
 7. Soulairac A, Lambinet H. Etudes cliniques de liaction du precurseurs de la serotonine le L-5-hydroxytryptophane, sur les troubles du sommeil. *Schweiz Bundaschau Med (Praxis)*. 1998;77(34a):19-23.
 8. Caruso I, Sarzi Puttini P, Cazzola M, Azzolini V. Double-blind study of 5-hydroxytyptophan versus placebo in the treatment of primary fibromyalgia syndrome. *J Int Med Res* 1990;18:201-9.
 9. De Benedittis G, Massei R. 5-HT precursors in migraine prophylaxis: a double-blind cross-over study with L-5 hydroxytryptophan versus placebo. *Clin J Pain* 1986;3:123-9.
 10. Titus F, Davalos A, Alom J, Codina A. 5-hydroxytryptophan versus methysergide in the prophylaxis of magraine. *Eur Neurol* 1986;25:327-9.

11. Maissen CP, Ludin HP. Comparison of the effect of 5-hydroxytryptophan and propranolol in the interval treatment of migraine. *Schweiz. Med Wochen* 1991;121:1585-90.
12. Matlew WT. 5-hydroxytryptophan in the prophylaxis of migraine. *Headache* 1978;18:111-3.
13. De Giorgis G, Miletto R, Iannucelli M, Camuffo M, Scerni S. Headache in association with sleep disorders in children. A psychodiagnostic evaluation and controlled clinical study with L-5HTP versus placebo. *Drugs Exptl Clin Res* 1987;13:425-33.
14. Sternberg EM, Van Woert MH, Young SN, Magnussen I, Baker H, Gauthier S et al. Development of a solar dermatitis-like illness during therapy with L-5-hydroxytryptophan and carbidopa. *New Engl J Med* 1980;303:782-7.
15. Hagan JJ, Hatcher JP, Slade PD. The role of 5-HT_{1D} and 5-HT_{1A} receptors in mediating 5-hydroxytryptophan induced myoclonic jerks in guinea pigs. *Eur J Pharmacol* 1995;294:743-51.
16. Hirai M, Nakajima T. Biochemical studies on the mechanism of difference in the renal toxicity of 5-hydroxy-L-Tryptophan between Sprague Dawley and Wistar rats. *J Biochem (Tokyo)* 1979;86:907-13.
17. Kahn RS, Westenberg HG. L-5-hydroxytryptophan in the treatment of anxiety disorders. *J Affect Disord* 1985;8(2):197-200.