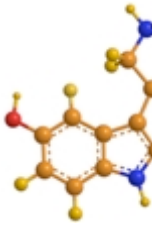
5-HTP (5-Hydroxytryptophan, L-5-Hydroxytryptophan)



While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:

- 5-Hydroxytroptophan, *Griffonia simplicifolia*, L-5-HTP, L-5-Hydroxytroptophan, oxitriptan, Tript-OH®, tryptophan.
- **Note**: Not to be confused with L-tryptophan.

BACKGROUND

- 5-HTP is the precursor of the neurotransmitter serotonin. It is obtained commercially from the seeds of the plant *Griffonia simplicifolia*.
- 5-HTP has been suggested as a treatment for many conditions. There is some research to support the use of 5-HTP in treating cerebellar ataxia, headache, depression, psychiatric disorders, fibromyalgia, and as an appetite suppressant or weight-loss agent. There is not enough scientific evidence to support the use of 5-HTP for any other medical condition.
- 5-HTP may cause gastrointestinal disturbances, mood disturbances, seizure, or abnormal blood counts. Some reported side effects might result from contaminants in 5-HTP products.

SCIENTIFIC EVIDENCE

Uses *These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.*	Grade*
Cerebellar ataxia Cerebellar ataxia results from the failure of part of the brain to regulate body posture and limb movements. 5-HTP has been observed to have benefits in some people who have difficulty standing or walking because of cerebellar ataxia. However, current evidence is mixed.	B
Depression The results of numerous studies in humans suggest that 5-HTP may aid in the treatment of depression. However, it is not known whether 5-HTP is as effective as	B

treatment of depression. However, it is not known whether 5-HTP is as effective as commonly prescribed antidepressant drugs.	
Fibromyalgia There is a small amount of research evaluating the use of 5-HTP for fibromyalgia, and early evidence suggests that 5-HTP may reduce the number of tender points, anxiety, and intensity of pain and may improve sleep, fatigue, and morning stiffness.	**B**
Headaches There is evidence from several studies in both children and adults that 5-HTP may be effective in reducing the severity and frequency of headaches, including tension headaches and migraines. Further research is needed.	**B**
Obesity Studies suggest that 5-HTP may reduce eating behaviors, lessen caloric intake, and promote weight loss in obese individuals.	**B**
Alcoholism (withdrawal symptoms) Early study suggests that 5-HTP may lessen alcohol withdrawal symptoms. Further research is needed to confirm these results.	**C**
Anxiety Although 5-HTP has been proposed as a possible treatment for anxiety disorders, there is not enough human evidence to make a firm recommendation.	**C**
Down's syndrome Preliminary study of 5-HTP in children with Down's syndrome yields insignificant results. Further research is necessary.	**C**
Neurologic disorders (Lesch-Nyhan syndrome) Lesch-Nyhan syndrome (LNS) is a rare, genetic disorder affecting mostly males that often causes mental retardation and self-mutilation. Small studies of 5-HTP in Lesch-Nyhand syndrome show conflicting results. Additional study is needed.	**C**
Psychiatric disorders It has been suggested that 5-HTP may reduce psychotic symptoms and mania or aid	**C**

It has been suggested that 5-HTP may reduce psychotic symptoms and mania or aid in panic disorder, but studies in people with schizophrenia have shown differing results.	
Sleep disorders There is insufficient evidence regarding the use of 5-HTP for sleep disorders. Additional studies are needed before a conclusion can be drawn.	**C**
Seizures/epilepsy (myoclonic disorders) Although 5-HTP has been studied as a treatment for various myoclonic syndromes and epilepsy, available research does not support the use of 5-HTP for these conditions.	**D**
Key to grades: **A: Strong scientific evidence for this use; **B**: Good scientific evidence for this use; **C**: Unclear scientific evidence for this use; **D**: Fair scientific evidence against this use (it may not work); **F**: Strong scientific evidence against this use (it likely does not work).*	

TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Aggression, agoraphobia (fear of open/public spaces), Alzheimer's disease, amyotrophic lateral sclerosis (fatal progressive neurological disease), anorexia, attention deficit hyperactivity disorder (ADHD), autism, bipolar disorder, bulimia nervosa, cough, deficiency (aromatic L-amino acid decarboxylase deficiency; serotonin deficiency), delirium tremens (DTs), diabetes, digestion, dizziness, dystonia (muscle spasms), eating disorders (binge eating), endocrine disorders (Cushing's syndrome), eye disorders (ophthalmoplegia), hepatitis, herpes virus infection (Ramsey-Hunt's syndrome), hormonal disorders, inflammation, insomnia, menopausal symptoms, mood disorder, myoclonic disorders (Lance-Adams syndrome), obsessive compulsive disorder (OCD), pain, panic disorder, Parkinson's disease, phenylketonuria, premenstrual syndrome (PMS), psychosis (LSD-induced), restless leg syndrome, seasonal affective disorder, sexual dysfunction, temperature regulation.

DOSING

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)

- In general, most studies have administered 5-HTP at low doses and for a short duration. A

common dose used is 300 milligrams per day, which has been taken for depression or headache. Doses as high as 1,600 milligrams per day or 16 milligrams per kilogram per day over 12 months have been studied. Starting with low doses (50 milligrams three times daily) and increasing the dosage gradually may minimize side effects such as nausea.

Children (younger than 18 years)

- There is not enough scientific data to recommend 5-HTP for use in children, and 5-HTP is not usually recommended because of potential side effects. However, for headache, 100 milligrams daily for 12 weeks has been used.

SAFETY

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

- Avoid in individuals with a known allergy or hypersensitivity to 5-HTP. Signs of allergy may include rash, itching, or shortness of breath. Urticaria ("hives") has been reported.

Side Effects and Warnings

- Although 5-HTP appears to be generally well tolerated, due to potential serious adverse effects, a physician should supervise the use of 5-HTP. Cases of eosinophilia myalgia syndrome (EMS) have been reported and although the precise role of 5-HTP in these cases remains unclear, it has been suggested that contaminants in certain batches were responsible for these adverse effects. Several thousand cases of EMS and deaths were linked to the ingestion of contaminated L-tryptophan in 1989. Avoid in patients with eosinophilia syndromes.
- Palpitations, lowered blood pressure, myalgia (muscle pain), weakness, rhabdomyolysis (breakdown of skeletal muscle), eosinophilia (increased number of white blood cells), nausea, vomiting, abdominal pain, heartburn, diarrhea, gas, and taste alteration have been reported. Slow initiation of treatment and enteric-coated tablets has decreased gastrointestinal side effects.
- Drowsiness, dizziness, vertigo, somnolence (sleepiness), insomnia, and headache are occasionally reported. Mania and euphoria have also been noted. Seizure syndrome has occurred in patients with Down's syndrome. Despite possible efficacy of 5-HTP for Down's syndrome, 5-HTP is not recommended in Down's syndrome patients.
- Other potential side effects of taking 5-HTP by mouth may include transient disinhibition, euphoria, irritability, depressed mood, restlessness, rapid speech, anxiety, aggressiveness, and agitation. Weight gain has been reported in a few cases. In contrast, loss of appretite has also been reported. Amenorrhea (absence of menstruation) was noted in one case.
- Patients receiving both carbidopa (a drug for Parkinson's disease) and 5-HTP long-term had reductions in total cholesterol, bradycardia (slowed heart rate), hypomania (mild mania), pseudobullous morphea (chronic, degenerative disease that affects the joints, skin, and internal organs), and scleroderma-like illness.
- An intravenous derivative of 5-HTP called gamma-L-glutamyl 5-HTP administered over one hour resulted in sodium retention. It is unknown if this effects was the result of the formulation,

the route of administration, or the rate of infusion.

- Use cautiously in patients with kidney insufficiency, as 5-HTP is eliminated through the kidneys.
- Use cautiously in patients with HIV-1 infection, in patients with existing gastrointestinal disorders, or in patients with a history of mental disorders.

Pregnancy and Breastfeeding

- 5-HTP is not recommended in pregnant or breastfeeding women due to a lack of available scientific evidence. The risk of contaminants found in 5-HTP products further precludes use during pregnancy. 5-HTP may increase prolactin, a necessary hormone for milk production; 5-HTP should be avoided while breastfeeding.

INTERACTIONS

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

Interactions with Drugs

- When 5-HTP is used with drugs that act within the central nervous system, there may be an increased risk of adverse effects. Examples of such drugs include carbidopa, fluoxetine (Prozac®), buspirone (Buspar®), phenelzine (Nardil®), amitriptyline (Elavil®), phenobarbital, trazodone (Desyrel®), venlafaxine (Effexor®), tramadol (Ultram®), sumatriptan (Imitrex®), mirtazapine (Remeron®), and pindolol. If a patient experiences muscle aches, fever, or other abnormalities when taking 5-HTP with other drugs, a healthcare professional should be notified immediately. In contrast, drugs such as methysergide or cyproheptadine may reduce the effects of 5-HTP.
- 5-HTP may enhance the serotonergic effect of selective serotonin reuptake inhibitors (SSRIs). Since 5-HTP increases serotonin levels, when combined with an SSRI, the serotonin level may be increased sufficiently to produce serotonin syndrome. Anecdotally, zolpidem has been associated with exacerbating hallucinations when taken with SSRIs. Its use with 5-HTP may result in a similar effect. Serotonin receptor antagonists, such as methysergide and cyproheptadine, may diminish efficacy of 5-HTP.
- Concomitant use of serotonin specific reuptake inhibitors and monoamine oxidase inhibitors (MAOIs) can cause serotonin syndrome. The addition of 5-HTP may potentiate the antidepressant effect of MAOIs and decrease time to recovery from depression.
- Losartan® (angiotensin receptor blocker) may cause a decrease in pineal serotonin levels.
- Administration of 5-HTP with decarboxylase inhibitors can increase the plasma concentration and half-life of 5-HTP.
- 5-HTP, when taken with fenfluramine, may cause suppression in food intake.
- Lithium carbonate may enhance serotonin receptor sensitivity, whereas tricyclic antidepressants (TCA) and second-generation antidepressants may diminish serotonin receptor sensitivity.
- Anecdotally, concomitant use of reserpine and 5-HTP may result in hypertensive (high blood pressure) reactions.

- The 5-HTP-induced increase in plasma cortisol can be blocked by the administration of ritanserin, a 5-HT2/5-HT1C antagonist.
- Although human evidence is lacking, 5-HTP may interact with angiotensin II receptor antagonist (A2R blockers) and thyroid stimulating hormones. 5-HTP has also been shown to increase luteinizing hormone, although the effects on hormones in humans are unclear.
- In theory, 5-HTP may have additive effects with sedatives or medications taken for epilepsy or seizures.
- 5-HTP has produced weight loss in the obese. In theory, 5-htp may interact additively or synergistically with other weight loss agents. Furthermore, based on animal study, 5-HTP may improve locomotor function and survival in ALS patients when taken with riluzole.
- It has been suggested that 5-HTP may reduce psychotic symptoms and mania or aid in panic disorder, but studies in people with schizophrenia have shown differing results. Caution is advised.
- 5-HTP may alter the concentrations of certain agents metabolized by the liver or interact with agents eliminated through the kidneys

Interactions with Herbs and Dietary Supplements

- In theory, L-tyrosine, adenosyl-L-methionine, tryptophan, vitamin B6, chromium, melatonin, niacin, SAMe, St. John's wort, herbs and supplements with monoamine oxidase inhibitor (MAOI) activity, and magnesium may increase the effects or side effects associated with 5-HTP.
- Although human evidence is lacking, 5-HTP may interact with herbs or supplements with proposed antidepressant effects or thyroid stimulating effects. 5-HTP has also been shown to increase luteinizing hormone, although the effects on hormones in humans are unclear.
- When 5-HTP is used with agents that act within the central nervous system, there may be an increased risk of adverse effects. In theory, use with St. John's wort may increase serotonin levels, resulting in adverse effects, including serotonin syndrome.
- In theory, 5-HTP may have additive effects with sedatives or agents taken for epilepsy or seizures. 5-HTP has produced weight loss in the obese. In theory, 5-HTP may interact additively or synergistically with other weight loss agents.
- It has been suggested that 5-HTP may reduce psychotic symptoms and mania or aid in panic disorder, but studies in people with schizophrenia have shown different results. Caution is advised.
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AUTHOR INFORMATION

- This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

REFERENCES

Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.

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