



## 5-Hydroxytryptophan

### Introduction

5-Hydroxytryptophan (5-HTP) is the intermediate metabolite of the amino acid L-tryptophan (LT) in the serotonin pathway.

It is dedicated to this pathway; i.e., it cannot be converted back into tryptophan, but can only go on to serotonin and its metabolites. This conversion is dependent on the presence of the active form of vitamin B6, pyridoxal-5' phosphate. Therapeutic use of 5-HTP bypasses the conversion of LT into 5-HTP by the enzyme tryptophan hydrolase, which is the rate-limiting step in the synthesis of serotonin. Tryptophan hydrolase can be inhibited by numerous factors, including stress, insulin resistance, vitamin B6 deficiency, insufficient magnesium, and increasing age.<sup>1</sup> In addition, these same factors can increase the conversion of LT to kynurenine via tryptophan oxygenase, making LT unavailable for serotonin production.

5-HTP is used therapeutically to treat depression, obesity, chronic headaches, insomnia, and fibromyalgia, and is commercially produced by extraction from the seeds of the African plant, *Griffonia simplicifolia*.

### Pharmacokinetics

5-HTP is well absorbed from an oral dose, with about 70 percent reaching the bloodstream.<sup>2,3</sup> Absorption of 5-HTP is not affected by the presence of other amino acids; therefore it may be taken with meals without reducing its effectiveness. Unlike LT, 5-HTP cannot be shunted into niacin or protein production.

Serotonin levels in the brain are highly dependent on levels of 5-HTP and LT in the central nervous system (CNS). 5-HTP easily crosses the blood-brain barrier, not requiring the presence of a transport molecule. LT, on the other hand, requires use of a transport molecule to gain access to the CNS. Since it shares this transport molecule with several other amino acids, the presence of these competing amino acids can inhibit LT transport into the brain.

### Mechanisms of Action

5-HTP acts primarily by increasing levels of serotonin within the central nervous system. Other neurotransmitters and CNS chemicals, such as melatonin, dopamine, norepinephrine, and beta-endorphin have also been shown to increase following oral administration of 5-HTP.<sup>4-7</sup>

## Clinical Indications

### *Depression*

Numerous open and double-blind studies of patients with either unipolar or bipolar depression have demonstrated significant clinical response in 2 to 4 weeks at doses of 50-300 mg 5-HTP three times per day.<sup>8-14</sup> In a study comparing 5-HTP and the serotonin reuptake inhibitor fluvoxamine, 5-HTP was as effective as fluvoxamine in relieving depressive symptoms.<sup>15</sup>

### *Fibromyalgia*

Fibromyalgia patients have been found to have low serotonin levels, which can contribute to a low pain threshold. Three clinical trials of 5-HTP administration, totaling 300 patients, demonstrated significant improvement in fibromyalgia symptoms, including pain, morning stiffness, anxiety, and fatigue.<sup>16-19</sup>

### *Obesity*

Decreased caloric intake during dieting can lower serum tryptophan and CNS serotonin levels. Low serotonin levels in obese patients have been associated with carbohydrate cravings and resultant binge eating. Three studies with 5-HTP in obese patients resulted in decreased food intake and subsequent weight loss.<sup>20-22</sup> In a double-blind, placebo-controlled study, patients took either 300 mg 5-HTP three times per day or placebo, and followed no specific dietary regimen for six weeks. During the following six weeks, both groups were instructed to continue supplementation and follow a 1,200-calorie per day diet. The 5-HTP group spontaneously reduced carbohydrate intake and total caloric intake in the first six-week period, and was able to follow the decreased caloric intake in the second six-week period, resulting in significant weight loss compared to placebo.<sup>20</sup>

### *Insomnia*

5-HTP has been shown to be beneficial in treating insomnia, especially in improving sleep quality by increasing REM sleep.<sup>23-26</sup>

### *Chronic Headache*

5-HTP has been used successfully in the prevention of chronic headaches of various types, including migraine, tension headaches, and juvenile headaches.<sup>16,27-34</sup>

## Drug-Nutrient Interactions

Although no reports have been published, it is possible that 5-HTP, when taken in combination with a selective serotonin reuptake inhibitor (SSRI) antidepressant such as Prozac®, Paxil®, or Zoloft®, may cause a condition known as serotonin syndrome. This syndrome is characterized by agitation, confusion, delirium, tachycardia, diaphoresis, and blood pressure fluctuations.

## Side Effects and Toxicity

Because some patients may experience mild nausea when initiating treatment with 5-HTP, it is advisable to begin with a 50 mg dose and titrate upward.

## Dosage

Initial dosage for 5-HTP is usually 50 mg three times per day with meals. If clinical response is inadequate after two weeks, dosage may be increased to 100 mg three times per day. For depression, doses of 50-300 mg 5-HTP three times per day have been used. In fibromyalgia, 100 mg twice or three times per day has been successful. Obesity studies used a higher dose, 300 mg three times per day. For insomnia, the dosage is usually 100-300 mg before bedtime. For chronic headaches, 200 mg three times per day has been used.

## Warnings and Contraindications

5-HTP should not be used in patients currently being treated or who have recently been treated with an SSRI antidepressant.

## References

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