

## Benefits

### Metabolism and Absorption of 5-HTP

5-HTP (5-hydroxytryptophan) is formed by the addition of a hydroxyl group (-OH) to the 5 carbon of the indole ring of tryptophan. Conversion of tryptophan to 5-hydroxytryptophan is catalyzed by the enzyme tryptophan hydroxylase.<sup>1</sup> 5-HTP functions as the precursor for serotonin, and is converted to serotonin in a pyridoxal phosphate (vitamin B6) dependent reaction catalyzed by the enzyme L-amino acid decarboxylase.<sup>2</sup>

Synthesis of serotonin in the brain requires an adequate supply of either tryptophan or 5-HTP as precursors. The supply of tryptophan available for conversion to 5-HTP depends on a number of factors, including nutritional status and competition between tryptophan and other amino acids for transport across the blood brain barrier.

Disturbances in the serotonin metabolic pathway may disrupt central nervous system functions which utilize serotonin as a neurotransmitter.<sup>2</sup> Administration of 5-HTP bypasses the conversion of tryptophan to 5-HTP. 5-HTP readily crosses the blood brain barrier and becomes available for serotonin synthesis. Serotonergic neurons (nerve cells stimulated by serotonin) regulate sleep, appetite, nociception (the perception of pain), and aggressive behavior.<sup>2</sup>

Serotonin is metabolized to 5-HIAA (5-hydroxyindolacetic acid) which is its primary breakdown product.<sup>3</sup> The concentration of 5-HIAA in cerebrospinal fluid is used as an indicator of serotonin turnover in the CNS serotonin level. Psychiatric patients have been found to have low levels of 5-HIAA in the CNS fluid, suggesting serotonin deficiency.<sup>3</sup>

5-HTP is readily absorbed by the mucosal cells of the gastrointestinal tract. In one study using five subjects, systemic absorption of 5-HTP in combination with carbidopa averaged 69.2 percent.<sup>4</sup> Another absorption study found that carbidopa enhanced the increase in serum 5-HTP concentration 5 to 15 fold.<sup>5</sup> In this study, a single dose of 5-HTP increased the plasma level of 5-HTP only slightly, whereas 5-HIAA increased 9-20 fold. This suggests that the gut mucosa has a storage capacity for 5-HTP, and that plasma increases occur after maximum capacity is reached.<sup>5</sup>

### Improves Well-Being in Depressed Persons

Serotonin in the central nervous system is recognized as a causative factor in some depressed persons.<sup>6,7</sup> A comprehensive review of seven open and seven controlled clinical studies found that oral consumption of 5-HTP improved mental and emotional status in 60 to 70 percent of depressed people. The results varied from "modest" to "marked."<sup>8</sup> Dosages ranged from 50 to 300 mg daily.

The accumulated evidence is inconclusive as to whether 5-HTP is more effective combined with decarboxylase inhibitors than when taken alone. Many of the early trials used the combination, and this has been a frequently used therapeutic strategy for reducing conversion of 5-HTP to serotonin outside the CNS. It is generally accepted that a large portion of absorbed 5-HTP is metabolized to serotonin in peripheral tissues before it can enter the brain.<sup>8</sup>

Peripheral conversion of 5-HTP to serotonin would theoretically limit the usefulness of oral 5-HTP for improving CNS functions and mental health. However, trials in which 5-HTP was given alone do show benefits. A small open trial in which 25 people were given 5-HTP either alone or with a decarboxylase inhibitor found no difference in effectiveness.<sup>9</sup> Thirteen of the patients had "very good" or "good" improvement, 8 had "moderate," and in 4 out of the twenty-five the results were judged to be "poor."

A more recent randomized double-blind study compared the efficacy of oral 5-HTP (100 mg three times daily, without a decarboxylase inhibitor) to that of fluvoxamine, a selective serotonin reuptake inhibitor.<sup>10</sup> (SSRIs block the reabsorption of serotonin by postsynaptic receptors, thus increasing the available supply of serotonin in the synaptic cleft.) The two were found to be equally effective, and 5-HTP was better tolerated. It should be noted that 5-HTP was given in the form of enteric-coated pH-sensitive capsules which dissolve in the small intestine, thus preventing conversion of 5-HTP to serotonin in the stomach.

In contrast to MAO inhibitors and SSRIs, medications which act by blocking normal physiologic functions, 5-HTP supports normal function in its role as a serotonin precursor. Correcting serotonin deficiency has been called a "functional-dimensional approach" in the treatment of depression.<sup>10</sup>

### **Improves Sleep Quality**

Studies have shown that 5-HTP influences the quality of sleep by increasing REM (rapid eye movement) sleep. Administration of 5-HTP in the evening prior to bedtime has been shown to increase the duration of REM sleep and decrease the amount of non-REM sleep.<sup>11,12</sup>

### **5-HTP—A Free-radical Scavenger**

The OH group which is added to tryptophan in the formation of 5-HTP gives 5-HTP antioxidant properties.<sup>13</sup> (Compounds such as vitamin E and flavonoids derive their free-radical quenching ability from OH groups, which donate electrons to oxidants.) 5-HTP quenches a variety of free-radicals. This is in contrast to tryptophan, which is sensitive to oxidation.

### **Adverse Effects of 5-HTP**

Oral administration of 5-HTP in clinical studies has resulted in gastrointestinal disturbances such as nausea, vomiting and diarrhea. According to a review by Byerley, et. al. these effects are tolerated by most patients and tend to lessen over time.<sup>8</sup> Side effects are more marked with higher doses, and may be reduced by the use of enteric-coated, pH sensitive capsules or tablets.<sup>8,10</sup>

### **Safety**

**Suggested Adult Use:** As a dietary supplement, take 1 capsule two or three times daily with or without food.

Notice: Not to be used concurrently with MAO inhibitors, selective serotonin reuptake inhibitors (SSRIs) or other anti-depressant medications. It should also not be used by individuals taking any

of the category of medications known as "triptans".

Free of "Peak X" as verified by assay.

Caution: Keep out of reach of children.

**DOES NOT CONTAIN: *milk, egg, wheat, corn, sugar, sweeteners, starch, salt, or preservatives.***

## Scientific References

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