

## Original Research Article

# Tryptophan As A Nutraceutical – Clinical And A Critical Review.

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## ABSTRACT:

Nutraceutical is a combination of the words "nutrition" and "pharmaceutics." The term refers to substances separated from herbal products, dietary supplements, and processed foods such as cereal grains, beverages, and soups, which are being used both as a nutrient and medicine. Ginseng, Echinacea, glucosamine, green tea, flavonoids, lycopene, lutein, folate, and cod liver oil are some popular nutraceuticals. Most nutraceuticals have diverse therapeutic attributes. Tryptophan (Trp) is an amino acid that is required in the human diet. It is essential for many metabolic functions. Trp levels can be used by clinicians to diagnose different metabolic disorders and the associated symptoms with those ailments. Furthermore, due to the Trp relationship with the biosynthetic pathways of serotonin (5-HT) and melatonin, dosing with this amino acid is being regarded in the treatment of depressive disorders and sleep disturbances. It is also used to treat cognitive disorders, anxiety, and neurodegenerative diseases. Diminished serotonin secretion has been linked to autism spectrum disorder, obesity, anorexia and many other diseases. The literature strongly suggests that Trp plays an important role in the proper functioning of the brain-gut axis. Chicken, turkey, red meat, milk, pork, eggs fish, beans, nuts, seeds, and oatmeal, are all high in tryptophan. Tryptophan has a reference dietary intake (RDI) of 4mg per kilogramme of body weight. As a result, a 70kg person should require nearly 280mg of tryptophan per day. The chemical is available as 500 mg capsule in the market as medicine. The rare side effect of an abnormal concomitant intake of the nutraceutical with certain antipsychotic drugs is serotonin syndrome. The described eosinophilic myalgia syndrome was later found to be not associated with this nutraceutical. The drug has got a few side effects and should be prescribed by either a qualified physician or a specialist in human nutrition.

**Keywords:** Nutraceutical, amino acid, tryptophan, brain gut axis

## INTRODUCTION:

Stephen De Felice, the founder and chairman of the Foundation for Innovation in Medicine, an American organization that promotes medical health research, originated the term "nutraceutical" in 1989. He further defined a nutraceutical as both a "food, or parts of a food, that can provide health

or medical benefits, including the treatment and prevention of illness<sup>1</sup>. Nutraceuticals are nutrients of pharmaceutical grade which are consumed for health benefits. They are, in fact, herbs, vitamins, minerals, and extracts. Then a doubt will automatically come to the minds of a reader: i.e., the difference between a nutrient, drug, and a nutraceutical.

### **Definitions:**

Pharmaceuticals are FDA-approved (Food and Drug Administration) drugs that are available from primary care physicians and hospitals. Pharmaceutical companies produce them in laboratories and use them to treat diseases or health issues. These drugs have undergone substantial clinical trials and have a large body of scientific evidence to back up their efficacy and safety. To quote an example ant hypertensive drug is being marketed after being synthesized from non-food ingredients.

Dietary supplements are made from food but are available in a non-food format, giving them the appearance of drugs. Dietary supplements contain isolated nutrients with well-documented medical benefits. Innumerable packed supplements with both primary (carbohydrates, proteins and fat) and added secondary metabolites (Phytochemicals) A nutraceutical is a nutrient-dense natural remedy produced from whole foods or parts of foods. (e.g. green tea) The thin line between foods and essential nutrients distinguishes the distinction between nutraceuticals and dietary supplements. Two very different definitions have some overlap. Nutraceuticals<sup>2</sup> are a concentrated version of a nutrient which may avoid the onset of a subclinical sustained pathological condition. It is a whole food, not a separated nutrient concentrated in a non-food format. Food supplements contain micronutrients that can supplement the body's nutritional requirements. Tryptophan is marketed as a nutraceutical. The difference is that the product is from a food source.

The distinction between nutraceutical and functional foods- Nutraceuticals and functional foods are two terms that describe foods that promote health and nutrition. Nutraceuticals are separated, purified, and formulated healthy products that are taken in the form of capsules, pills/tablets and thus are available on the market as medicative forms and are typically not combined with foods. Functional foods, on the other hand, are consumed as regular foods as part of an unusual diet rather than in the form of a dose and provide physiological benefits over and above basic nutrition function. Nutraceuticals are having medical claims that they can both prevent and cure disease; however, functional foods are ordinary foods that only reduce disease rather than prevent and cure disease. Tryptophan (Trp) is an amino acid that is required in the human diet. It is essential for many metabolic functions. Trp levels can be used by clinicians to diagnose various metabolic disorders and the symptoms associated with those diseases. In this review, we shall try to segregate the uses of this nutraceutical in relation to differing systems and disorders. The focus of this article is more towards clinical uses rather than biochemical modulations.

### **Preparation:**

L Tryptophan is available in the commercial product as 125 mg/ capsule or 500 mg/ capsule as a container. As these products are extracted from food and vegetarian sources, these products become nutraceuticals. Serotonin, a vital monoamine neurotransmitter involved in the regulation of central neurotransmission as well as enteric physiological function, is the sole product of tryptophan. The absorption of the nutraceutical is around 90% and it's linked with gut microbiota. Chicken, turkey, red meat, milk, pork, eggs fish, beans, nuts, seeds, and oatmeal, are all high in tryptophan and are designed as dietary sources of this amino acid.

**Daily needs and blood levels:**

Tryptophan has a reference dietary intake (RDI) of 4mg per kilogramme of body weight. As a result, a 70kg person should require nearly 280mg of tryptophan per day. The chemical is available as 500 mg capsule in the market as medicine.

One of the nine described essential amino acids is l-tryptophan. In the peripheral blood stream, tryptophan circulates either free or bound to albumin. Total tryptophan serum levels in healthy blood donors are observed to be  $73 \pm 14.9$  mol/l on an average.

**METABOLISM AND BIOACTIVE DERIVATIVES**

Tryptophan is metabolised through three distinct biosynthetic pathways: (a) the formation of kynurenine derivatives, which is the primary important route, (b) the production of serotonin, a neurotransmitter and a known precursor of melatonin and (c) protein biosynthesis. To produce kynurenine, tryptophan is oxidised by cleavage of the indole ring moiety, which is accomplished either through the enzyme tryptophan 2,3-dioxygenase or by another enzyme<sup>3,4</sup>.

**Infant nutrition:**

The tryptophan-fortified cereals as well as other nutrients managed to improve the sleep of 30 infants aged 8 to 16 months with a sleep disorder associated with excess nocturnal awakenings<sup>5</sup>. Tryptophan is an amino acid that is essential for normal infant growth as well as the generation and maintenance of proteins, musculature, enzymes, and a few neurotransmitters in the body. Tryptophan (Trp) and its metabolites are critical for brain maturation and the development of neurobehavioral regulators of food intake, satiation, and sleep-wake rhythms in new-borns. The blood-brain transport of tryptophan as a precursor of its metabolic by products serotonin and melatonin is preferable due to the high Trp concentration in human breast milk in relation to the total of neutral amino acids. Hence Commercial infant formulas, on the other hand, are lower in Trp and greater in neutral amino acid levels, resulting in comparatively lower Trp serum concentrations.

**CENTRAL NERVOUS SYSTEM:****Migraine:**

Migraineurs have been found to have persistent low serotonin levels, which substantially increase during ictal periods<sup>6</sup>. In terms of the importance of adequate tryptophan consumption in controlling serotonin homeostasis and its consequent impact on migraine attacks, extra tryptophan supplementation is effective in reducing the frequency of attacks.

**Insomnia:**

Tryptophan, at a dose of 1 gram taken 45 minutes before bedtime, reduces the time it takes to fall asleep in people who have minor insomnia or a long sleep latency. At this dose, it has no impact on sleep patterns and has no influence on attentiveness the next day. Tryptophan is not as efficacious as standard hypnotics in patients who have moderate or severe insomnia<sup>7</sup>. Although the influence of tryptophan on sleep has only been researched in the near run, its effect is unlikely to change over time, given that a 1-gram dose taken at bedtime will be completely metabolised before the end of the night. In a systematic review by Sutanto et al<sup>8</sup> have proved that Trp supplementation, especially at more than 1 g can help improve sleep quality. Sleep appears to be hampered by a diet low in tryptophan. Acute tryptophan deficiency affects serotonin synthesis<sup>9</sup> and can decrease REM sleep onset latency in regular sleepers.

**Depression:**

Increasing dietary tryptophan consumption reduced depressive symptoms and anxiety. Although tryptophan may be used to treat affective disorders<sup>10,11</sup>, caution should be exercised before beginning tryptophan supplement treatment options. When taken alone or in combination with a serotonin enhancing drug, only very high dosage of up to 200 mg/kilogram body weight/day of consumed tryptophan can lead to nausea, dizziness, and tremors.

**PARKINSONISM AND ALZHEIMER'S DISEASE**

Trp in the diet dynamically adjusts the (aryl hydrocarbon receptor) AhR pathway to improve muscle function in Parkinson's disease<sup>12</sup>, setting the stage for Trp to become a novel contender for treatment of the disease. Alzheimer's disease (AD) is probably linked to systemic immune activation. Interferon-gamma induces indoleamine 2,3-dioxygenase (IDO), which converts tryptophan to N-formyl kynurenine, which is then converted to kynurenine. Various tryptophan metabolites have been recognised as putative endogenous anti-AD molecules that can inhibit the the described proteopathic-immunopathic cycle of Alzheimer's disease. These findings are consistent with clinical evidence: i.e. serum tryptophan levels decrease significantly with age; the patients with Alzheimer's disease have significantly lower plasma tryptophan levels; and severe tryptophan deficiency significantly worsens cognitive dysfunction in people with Alzheimer's disease<sup>13</sup>.

**Cardiovascular:**

One study describes that observations after controlling for multiple confounders such as nutrients and food habits, there was a significant negative relationship between dietary tryptophan and Metabolic Syndrome incidence. Pathogenetic mechanisms involving central serotonergic mechanisms are implicated in essential hypertension in humans<sup>14</sup>. The reduction in blood pressure caused by tryptophan could be attributed to an increase in central 5-HT synthesis. Vasodilation to the lipophilic, transporter-independent ethyl ester of l-tryptophan was lowered in preeclamptic compared with the healthy placental arteries, consistent with lower IDO1 (Indoleamine 2, 3-dioxygenases) expression<sup>15</sup>. Finally, l-tryptophan stimulates IDO1- and NO-dependent relaxation in placental arteries, which itself is determined by l-tryptophan uptake instead of IDO1 expression. Increased l-tryptophan take - up may recompense for decreased IDO1 expression in preeclamptic placentas. Despite a substantial decline in cardiovascular morbid events as a result of LDL-cholesterol-lowering drugs, patients with CVD continue to be at risk. The sources of this residual risk, which forms the basis of CVD development, are numerous, and their relationships are intricate. Inflammation has been recognized as an important player in various stages of CVD development. This may result in what is known as residual inflammatory risk, which can contribute to CVD irrespective of lipid status. Recent research suggests those drugs which are designed to target inflammation may be promising therapeutic options for reducing acute CV events<sup>16</sup>.

**Miscellaneous:**

IDO mechanism and the metabolites with the neopterin production are elevated in children with allergic asthma, and this could be a potential marker of a dysfunctional immune reaction<sup>17</sup>. Allergic inflammatory response is characterised by an increase in Th2-type cytokines and a decrease in Th1-type cytokines such as IFN-. IDO-1 are well known for its immunoregulatory and tolerance-inducing role in infection, neoplasia, pregnancy, and autoimmunity, but it has also been linked to the control of allergic inflammation. One study discovered that enhanced TpH-1 expression in the gastric mucosa plays a significant role in the development of chronic dyspepsia<sup>18</sup>. A new class of drugs selectively inhibiting TpH-1 is the hope for successful treatment of certain forms of dyspepsia and other disorders of the gastrointestinal tract. Oral TRP consumption reduces the severity of

experimental NAFLD in mice<sup>19</sup>. The underlying principles are unknown, but they most likely involve the stabilization of the upper small intestinal barrier and the possible improvement of the dysfunctional intestinal serotonergic system. Even though the beneficial effects in the kidney disease are not proved, there is some improvement in the progression of coronary disease in kidney failure patients<sup>20</sup>. Tryptophan (Trp) is important in the human body because it functions as a precursor for a variety of bioactive substances, which include major neurotransmitters. According to research, people with ASD (autism spectrum disorders)<sup>21</sup> may be deficient in tryptophan. The deficiency can be determined by looking at Trp levels or its metabolite kynurenine in samples of urine. On a diagnostic eye, we can look Tryptophan as a diagnostic marker in cataract and as a biomarker for diabetic nephropathy<sup>22,23</sup>. The role of tryptophan has been proved in many other diseases like HIV and Crohn's disease<sup>24</sup>.

### **DANGERS**

Overdoes of tryptophan from supplements can cause shivering, overactive reflexes, confusion, fever, vomiting, diarrhoea, and agitation. If the patients are taking antidepressants such as selective serotonin reuptake inhibitors (SSRIs), MAO inhibitors, tricyclic antidepressants, then tryptophan in therapeutic doses is dangerous due to the risk of serotonin syndrome<sup>25</sup>. In 1989, a new syndrome called eosinophilia myalgia syndrome<sup>26</sup> (EMS) emerged and was speedily but doubtfully linked to the use of complementary Trp. Debilitating myalgia and a high peripheral eosinophil count were major symptoms. The culprit was discovered to be a contaminant in certain production batches rather than Trp. Tryptophan catabolism mediated by the gut microbiome appears to be one of the critical regulatory factors important for the Gut Brain Axis<sup>27</sup>, which is supposed to be involved in the progression of multiple neurological diseases. Only long time randomized trials will establish that these are the dangers of the drug or a side effect of a misuse.

### **CONCLUSION:**

L Tryptophan is available in the commercial product as 125 mg/ capsule or 500 mg/ capsule as a container. As these products are extracted from food and vegetarian sources, these products become nutraceuticals. Tryptophan has a reference dietary intake (RDI) of 4mg per kilogramme of body weight. The role and advantage of supplementation of tryptophan as a nutraceutical has been proved to be useful in multiple disease from which the neurodegenerative and cardiometabolic diseases are more significant. The drug has got a few side effects and should be prescribed by either a qualified physician or a specialist in human nutrition.

**CONFLICT OF INTEREST** – NIL for all authors

**FINANCIAL AID** – NIL

MRS has designed the concept, PK has done the data collection and SPS has drafted the manuscript with communication.

**ETHICAL ISSUES** – NIL

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