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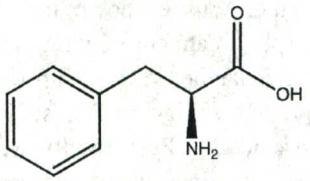
L-Phenylalanine

DESCRIPTION

L-phenylalanine is a protein amino acid. It is classified as an essential amino acid because the body requires a dietary source of the amino acid to meet its physiological demands. L-phenylalanine is found in proteins of all life forms. Dietary sources of the amino acid are principally derived from animal and vegetable proteins. Vegetables and juices contain small amounts of the free amino acid. The free amino acid is also found in fermented foods such as yogurt and miso. The alternative sweetener aspartame is a dipeptide of L-phenylalanine, as is the methyl ester, and L-aspartic acid.

In addition to being involved in protein synthesis, L-phenylalanine is the precursor of L-tyrosine. The conversion of L-phenylalanine to L-tyrosine is via the enzyme L-phenylalanine hydroxylase. It is this enzyme that is virtually absent in those with the inborn error of metabolism phenylketonuria (PKU). L-tyrosine produced from L-phenylalanine is a precursor in the synthesis of the neurotransmitters norepinephrine and dopamine, among other reactions. L-phenylalanine is marketed as a nutritional supplement and used by some for its putative antidepressant activity.

L-phenylalanine is also known as beta-phenylalanine, alpha-aminohydrocinnamic acid, *(S)*-2-amino-3- phenylpropanoic acid and alpha-amino-beta-phenylpropionic acid. It is abbreviated as either Phe or by its one-letter abbreviation F. The molecular formula of L-phenylalanine is $C_9H_{11}NO_2$, and its molecular weight is 165.19 daltons. L-phenylalanine is an aromatic amino acid with the following structural formula:



L-phenylalanine

ACTIONS AND PHARMACOLOGY

ACTIONS

L-phenylalanine has putative antidepressant activity. It may also, when used in conjunction with UVA irradiation, have antivitiligo activity.

MECHANISM OF ACTION

The mechanism of L-phenylalanine's putative antidepressant activity may be accounted for by its precursor role in the synthesis of the neurotransmitters norepinephrine and dopamine. Elevated brain norepinephrine and dopamine levels are thought to be associated with antidepressant effects.

The mechanism of L-phenylalanine's possible antivitiligo activity is not well understood. It is thought that L-phenylalanine may stimulate the production of melanin in the affected skin.

PHARMACOKINETICS

Following ingestion, L-phenylalanine is absorbed from the small intestine by a sodium dependent active transport process. L-phenylalanine is transported from the small intestine to the liver via the portal circulation. In the liver, L-phenylalanine is involved in a number of biochemical reactions, including protein synthesis, the formation of L-tyrosine and oxidative catabolic reactions. L-phenylalanine that is not metabolized in the liver is distributed via the systemic circulation to the various tissues of the body, where it undergoes metabolic reactions similar to those that take place in the liver.

INDICATIONS AND USAGE

L-phenylalanine may be helpful in some with depression. It may also be useful in the treatment of vitiligo. There is some

evidence that L-phenylalanine may exacerbate tardive dyskinesia in some schizophrenic patients and in some who have used neuroleptic drugs.

RESEARCH SUMMARY

Both oral and intravenous administration of L-deprenyl and L-phenylalanine in doses of 5 to 10 milligrams and 250 milligrams per day, respectively, demonstrated significant antidepressant effects in 155 unipolar depressed patients. In another preliminary study, L-phenylalanine was said to have mood-elevating effects in 31 of 40 depressed subjects. Followup is needed.

Several clinical studies have shown that L-phenylalanine may be helpful in the treatment of vitiligo in both children and adults. L-phenylalanine, in doses up to 100 mg/kg/day significantly improved vitiligo in 200 subjects when combined with UVA/sunlight. Best results were achieved in early-stage disease, but significant repigmentation occurred in some with later-stage disease who used the supplement/sunlight combination for prolonged periods. Another study confirmed these effects but found that no added benefit was derived from doses exceeding 50 mg/kg/day.

Recently, other researchers have reported on their six-year experience in treating vitiligo with L-phenylalanine in combination with daily sun exposure. Subjects treated by these researchers received oral L-phenylalanine 50 or 100 mg/kg/day plus topical 10% phenylalanine gel daily. The total average improvement rate was rated at 83.1%, but the improvement rate limited to those judged to have good response was 56.7%, with a 90.3% rate for the face, 42.8% for the trunk and 37.1% for the limbs. This uncontrolled, retrospective study involved 193 patients, male and female, children and adults, with evolving vitiligo of various types. There was no statistically significant difference in response rates between those who received 50 mg/kg/day versus those receiving 100 mg/kg/day or between children and adults.

On the negative side, there is a report that a loading dose of 100 mg/kg of L-phenylalanine exacerbated symptoms of tardive dyskinesia in some neuroleptic-treated depressives. In another study, the same L-phenylalanine challenge exacerbated tardive dyskinesia symptoms in schizophrenic subjects.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

L-phenylalanine is contraindicated in those with phenylketonuria. It is also contraindicated in those taking non-selective monoamine oxidase (MAO) inhibitors. L-phenylalanine is contraindicated in those hypersensitive to any component of an L-phenylalanine-containing supplement.

PRECAUTIONS

Pregnant women and nursing mothers should avoid supplementation with L-phenylalanine.

Tardive dyskinesia has been reported to be exacerbated after ingestion of L-phenylalanine by schizophrenics. Therefore, those with schizophrenia should exercise extreme caution in the use of supplemental L-phenylalanine.

Use of L-phenylalanine for vitiligo must be done under medical supervision.

Those with hypertension should exercise caution in the use of L-phenylalanine.

ADVERSE REACTIONS

L-phenylalanine will exacerbate symptoms of phenylketonuria if used by phenylketonurics. L-phenylalanine was reported to exacerbate tardive dyskinesia when used by some with schizophrenia.

INTERACTIONS

DRUGS

Non-selective monoamine oxidase (MAO) inhibitors: including phenelzine sulfate, tranylcypromine sulfate and pargyline HC1 — Concomitant use of L-phenylalanine and non-selective MAO inhibitors may cause hypertension.

Selegiline: L-phenylalanine and the selective MAO inhibitor selegiline may have synergistic antidepressant activity if used concomitantly.

Neuroleptic Drugs: L-phenylalanine may potentiate the tardive dyskinesia side reactions of neuroleptic drugs if used concomitantly with them.

OVERDOSAGE

There are no reports of Phenylalanine overdosage in the literature.

DOSAGE AND ADMINISTRATION

L-phenylalanine supplements as well as DL-phenylalanine (see DL-Phenylalanine) supplements are available in the nutritional supplement marketplace. Those who use L-phenylalanine supplements typically use 500 milligrams to 1.5 grams daily.

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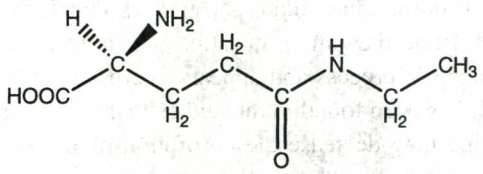
L-Theanine

DESCRIPTION

L-theanine is a non-protein amino acid mainly found naturally in the green tea plant (*Camellia sinensis*). It is also found naturally in only one other known source, the edible mushroom *Boletus badius*, commonly known as the Bay bolete. L-theanine is the predominant amino acid in green tea and makes up 50% of the total free amino acids in the plant. The amino acid constitutes between 1% and 2% of the dry weight of green tea leaves. L-theanine is considered the main component responsible for the taste of green tea, which in Japanese is called umami. Umami, which was first described by a Japanese scientist over a hundred years ago, is now considered one of the five basic tastes: sweet, salty, sour, bitter and umami. Umami is the Japanese term for savory. L-theanine has been marketed in Japan for several years as a nutritional supplement for mood modulation and entered the United States dietary supplement marketplace a few years ago.

L-theanine is a derivative of L-glutamic acid. It is a water-soluble solid substance with the molecular formula $C_7H_{14}O_3N$ and a molecular weight of 160.19 daltons. L-theanine is also known as gamma-ethylamino-L-glutamic acid, gamma-glutamylethylamide, r-glutamylethylamide, L-glutamic acid gamma-ethylamide and L-N-ethylglutamine. The chemical structure is:



L-theanine

ACTIONS AND PHARMACOLOGY

ACTIONS

L-theanine may have activity in modulating the metabolism of cancer chemotherapeutic agents and ameliorating their side effects. It may also have mood-modulating activity and neuroprotective and immunoprotective effects.

MECHANISM OF ACTION

In animal tumor models, L-theanine has been found to increase the antitumor activity of some anthracyline agents (doxorubicin, idarubicin) and to ameliorate some of the side effects of these agents. It appears that L-theanine inhibits the efflux of these agents from tumor cells, increasing the inhibitory concentration of the drugs in the target cells. At the same time, L-theanine appears to decrease the oxidative stress caused by these agents on normal cells. Most of the side effects of these agents are due to oxidative stress. The mechanism by which L-theanine inhibits the efflux of such cancer chemotherapeutic agents as doxorubicin is unclear. L-theanine appears to have modest antioxidant activity, and this may explain, in part, L-theanine's ability to ameliorate some of the side effects of the chemotherapeutic agents. Further, L-theanine, by an unclear mechanism, appears to inhibit the influx of chemotherapeutic normal cells.

The mechanism of L-theanine's possible mood-modulating activity is also unclear. The amino acid might affect the metabolism and the release of some neurotransmitters in the brain, such as dopamine.

Human gamma-delta T cells are known to mediate innate immunity to microbes through T cell receptor-dependent recognition of unprocessed antigens with conserved molecular patterns. The nonpeptide alkylamine antigens are shared by bacteria fungi, parasites, tumor cells and edible plant substances, including mushrooms, apples and green tea. It has been shown that L-theanine, a precursor of the nonpeptide antigen ethylamine, primed peripheral blood gamma-delta T cells to mediate a memory response on reexposure to ethylamine and to secrete interferon (IFN)-gamma in response to bacteria. Such priming may enhance innate