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L-Tyrosine

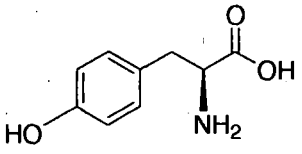
DESCRIPTION

L-tyrosine is a protein amino acid. It is classified as a conditionally essential amino acid.

Under most circumstances, the body can synthesize sufficient L-tyrosine, principally from L-phenylalanine, to meet its physiological demands. However, there are conditions where the body requires a dietary source of the amino acid for its physiological demands. For example, L-tyrosine is an essential amino acid for those with phenylketonuria. L-tyrosine is found in proteins of all life forms. Dietary sources of L-tyrosine 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.

In addition to being involved in protein synthesis, L-tyrosine is a precursor for the synthesis of the catecholamines epinephrine, norepinephrine and dopamine, the thyroid hormones thyroxine and triiodothyronine, and the pigment melanin.

L-tyrosine is also known as beta- (para-hydroxyphenyl) alanine, alpha-amino-para-hydroxyhydrocinnamic acid and *(S)*- alpha-amino-4-hydroxybenzenepropanoic acid. It is abbreviated as either Tyr of by its one-letter abbreviation Y. The molecular formula of L-tyrosine is $C_9H_{10}NO_3$, and its molecular weight is 181.19 daltons. L-tyrosine is an aromatic amino acid with the following structural formula:



L-tyrosine

ACTIONS AND PHARMACOLOGY

ACTIONS

L-tyrosine has putative antidepressant activity.

MECHANISM OF ACTION

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

PHARMACOKINETICS

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

INDICATIONS AND USAGE

Results are mixed, but largely negative, with respect to claims that tyrosine is an effective antidepressant. Claims that it can alleviate some of the mental and physical

symptoms of environmental stress are based on preliminary evidence. Further claims that tyrosine is useful in narcolepsy and attention deficit disorder have been refuted by some studies. Another study found that tyrosine supplementation did not improve neuropsychological performance in subjects with phenylketonuria. Claims that tyrosine is helpful in alleviating symptoms of premenstrual syndrome (PMS) and drug withdrawal are largely anecdotal and unconfirmed. There is no evidence tyrosine has any effect on dementia, Alzheimer's disease or Parkinson's disease.

RESEARCH SUMMARY

Two small, early studies suggested that tyrosine might have useful antidepressant effects. A subsequent follow-up with more subjects and conducted in a randomized, double-blind fashion failed to find any significant antidepressant activity, compared with placebo, in subjects with major depression. The dose used was 100 mg/kg/day of tyrosine for four weeks.

One study has concluded that tyrosine can protect against some forms of environmental stress. Subjects were given a 100 mg/kg dose of tyrosine and then exposed for 4.5 hours to cold and hypoxia in this double-blind, placebo-controlled crossover study. Tyrosine was reported to significantly decrease adverse symptoms, including mood and performance impairment. Follow-up is needed.

In another double-blind, placebo-controlled trial, tyrosine had no significant effect on subjects with narcolepsy and associated cataplexy. Dose used was 9 grams daily for four weeks. Similarly, tyrosine failed to produce lasting, significant improvement in subjects with attention deficit disorder. In this small, open study, tyrosine seemed to improve this condition after two weeks of supplementation, but this improvement was not sustained.

Recently, tyrosine was tested to see if it could improve the neuropsychological test performances of individuals with phenylketonuria. This was a randomized, double-blind, placebo-controlled crossover study. Maximum dosage used was 100 to 150 mg/kg/day. The supplementation increased plasma tyrosine concentrations. Higher tyrosine levels correlated at baseline with improved performance on the neuropsychological tests, yet higher concentrations achieved through supplementation in this trial did not enhance test scores.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

L-tyrosine is contraindicated in those with the inborn errors of metabolism alkaptonuria and tyrosinemia type I and type II. It is also contraindicated in those taking non-selective monoamine oxidase (MAO) inhibitors. L-tyrosine is contraindicated in those hypersensitive to any component of an L-tyrosine-containing supplement.

PRECAUTIONS

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

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

Those with melanoma should avoid L-tyrosine supplements.

ADVERSE REACTIONS

L-tyrosine is generally well tolerated. There are some reports of those taking supplemental L-tyrosine experiencing insomnia and nervousness.

INTERACTIONS

DRUGS

Non-selective MAO inhibitors: including phenelzine sulfate, tranylcypromine sulfate and pargyline HCl—Concomitant use of L-tyrosine and non-selective MAO inhibitors may cause hypertension.

DOSAGE AND ADMINISTRATION

Those who use supplemental L-tyrosine typically take 500 to 1500 mg daily.

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Lactoferrin

DESCRIPTION

Lactoferrin is a glycoprotein that belongs to the iron transporter or transferrin family. It was originally isolated from bovine milk, where it is found as a minor protein component of whey proteins (see Whey Proteins). Lactoferrin contains 703 amino acids and has a molecular weight of 80 kilodaltons. In addition to its presence in milk, it is also found in exocrine secretions of mammals and is released from neutrophil granules during inflammation.

Lactoferrin is considered a multifunctional or multi-tasking protein. It appears to play several biological roles. Owing to its iron-binding properties, lactoferrin is thought to play a role in iron uptake by the intestinal mucosa of the suckling neonate. That is, it appears to be the source of iron for breast-fed infants. It also appears to have antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant and immunomodulatory activities.

Three isoforms of lactoferrin have been isolated: lactoferrin-alpha, lactoferrin-beta and lactoferrin-gamma. Lactoferrin-beta and lactoferrin-gamma have RNase activity, whereas lactoferrin-alpha does not. Receptors for lactoferrin are found in monocytes, lymphocytes, neutrophils, intestinal tissue and on certain bacteria. Lactoferrin is abbreviated LF and Lf. Bovine lactoferrin is abbreviated bLF.

Bovine lactoferrin, derived from whey proteins, is marketed as a nutritional supplement. Supplemental lactoferrin typically contains low amounts of iron.

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental lactoferrin may have antimicrobial, immunomodulatory, antioxidant and anti-inflammatory actions.

MECHANISM OF ACTION

The possible antibacterial activity of supplemental lactoferrin might be accounted for, in part, by its ability to strongly bind iron. Iron is essential to support the growth of pathogenic bacteria. Lactoferrin may also inhibit the attachment of bacteria to the intestinal wall. A breakdown product of lactoferrin is the peptide lactoferricin. Lactoferricin, classified as a bioactive peptide, may also have antibacterial, as well as antiviral, activity. The possible antiviral activity of supplemental lactoferrin may be due to its inhibition of virus-cell fusion and viral entry into cells.

A few mechanisms are proposed for lactoferrin's possible immunomodulatory activity. Lactoferrin may promote the growth and differentiation of T lymphocytes. Lactoferrin appears to bind uniquely in the region of major histocompatability (MHC) proteins and the CD4 and CD8 determinants on T4 (helper) and T8 (suppressor) lymphocytes; it bears sequence homologies with the MHC Class II determinant. Lactoferrin also appears to play a role in the regulation of cytokines and lymphokines, such as tumor necrosis (TNF)-alpha and interleukin (IL)-6. Lactoferrin's possible antioxidant activity may also contribute to its possible immunomodulatory activity.

Lactoferrin's possible antioxidant activity can also be accounted for by its ability to strongly bind iron. Free iron is a major contributor to the generation of reactive oxygen species via the Fenton reaction.

Lactoferrin's possible anti-inflammatory action may be accounted for by its possible antioxidant and immunomodulatory activities.

PHARMACOKINETICS

Little is known of the pharmacokinetics of oral lactoferrin. Lactoferrin appears much more resistant to proteolytic action than most dietary proteins. Lactoferrin is digested in the intestine to the bioactive peptide lactoferricin. Most of the possible actions of oral lactoferrin may be confined to the gut. There is some preliminary evidence that lactoferrin and lactoferricin may be absorbed, in part, from the lumen of the small intestine into enterocytes and that these molecules enter other cells as well. However, this is unclear.

INDICATIONS AND USAGE

There is some preliminary evidence from *in vitro* and animal research that supplemental lactoferrin may have some immune-enhancing effects. There is no evidence that it is effective as a treatment or preventive in any form of cancer. Neither is there any credible evidence to support claims that it helps those with fatigue or allergy.

RESEARCH SUMMARY

A number of *in vitro* and animal studies have shown that lactoferrin has various bactericidal and fungicidal effects. It has exhibited significant activity against *Escherichia coli, Proteus mirabilis, Staphyloccocus aureus, Candida albicans* and other pathogens in these studies. *In vitro*, lactoferrin has similarly shown some significant activity against HIV, herpes simplex virus type 1, hepatitis C virus, cytomegalovirus and some other viruses.

Human studies, however, are almost entirely lacking. One small, recent study showed that oral lactoferrin reduced the duration and severity of bacterial infection in five neutropenic patients receiving chemotherapy for acute myelogenous leukemia, compared with nine matched controls. More research is needed.