

ly might produce additive effects, including additive adverse effects.

OVERDOSAGE

There are no reports of overdosage with huperzine A.

DOSAGE AND ADMINISTRATION

There are various forms of huperzine A available, including extracts of *Huperzia serrata*, natural (-)-huperzine A and synthetic racemic (\pm)-huperzine A. Natural (-)-huperzine A is approximately three times more potent than the synthetic racemic mixture. The doses of natural (-)-huperzine A used in clinical studies ranged from 60 micrograms to 200 micrograms daily. Huperzine A should only be used with a physician's recommendation and monitoring.

LITERATURE

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Hydrolyzed Collagen

DESCRIPTION

Hydrolyzed collagen refers to enzymatically or chemically processed collagen, which is mainly derived from bovine, ox and pig skin and bone. Hydrolyzed collagen consists of water-soluble peptides of various molecular weights. These peptides are rich in the amino acids found in collagen, including glycine, L-proline and L-hydroxyproline. Nutri-

tional supplements containing hydrolyzed collagen are marketed for bone and joint health purposes. Hydrolyzed collagen and gelatin hydrolysates are similar. See Gelatin.

ACTIONS AND PHARMACOLOGY

ACTIONS

Hydrolyzed collagen has putative activity against degenerative joint disease (DJD). It also may have antiulcer activity.

MECHANISM OF ACTION

The mechanism of the putative anti-arthritis activity of hydrolyzed collagen is a matter of speculation. It is claimed that the amino acids of hydrolyzed collagen contribute to the synthesis of new collagen and new cartilage in joints. If this were the case, then hydrolyzed cartilage would be a disease-modifying substance. The amino acids in hydrolyzed collagen may contribute to joint collagen synthesis. However, if they did, it is unlikely that this contribution would be significant. L-hydroxyproline is not a genetic amino acid. It is formed in collagen post-translationally. Therefore, L-hydroxyproline in hydrolyzed collagen would not contribute to collagen synthesis. Further, both glycine and L-proline are synthesized by the body, and it is entirely unclear how any glycine or L-proline in hydrolyzed collagen would make any significant contribution to collagen synthesis in joints. There is speculation that some oligopeptides that may be found in hydrolyzed collagen might have a stimulatory effect on collagen synthesis. There is some preliminary evidence that collagen hydrolysates may stimulate proliferation of chondrocytes, adipocytes and elements of the extracellular matrix.

PHARMACOKINETICS

The digestion, absorption and metabolism of hydrolyzed collagen are typically slower than that of other dietary proteins and peptides. The reason for this is that the peptides formed from collagen contain a high quantity of L-proline and L-hydroxyproline. Proline and L-hydroxyproline form bonds with other amino acids that are significantly more resistant to enzymatic hydrolysis in the small intestine.

INDICATIONS AND USAGE

It is claimed that hydrolyzed collagen is useful in counteracting degenerative joint diseases. There is some preliminary evidence to support this claim. Hydrolyzed collagen may have antiulcer activity.

RESEARCH SUMMARY

Some preliminary research suggests that hydrolyzed collagen may have effects that could be beneficial in some with degenerative joint diseases. A recent 24-week study (prospective, randomized, placebo-controlled, double-blind) on the use of collagen hydrolysates in athletes with activity-related joint pain was found to show significant improvement of joint pain in the athletes treated with the collagen hydrolysates (10 grams/day). A rat study reported that

collagen hydrolysates provided beneficial effects on bone metabolism, especially in the calcium-deficient condition.

Pig collagen hydrolysate and beef collagen hydrolysate were found to protect rat stomach mucosa against ulcerative lesions caused by ethanol. Some Russian scientists have been interested in the peptides that are produced via hydrolysis of collagen. They have named these peptides glyprolines because they are rich in the amino acids L-proline and glycine. They report that a glyproline with the sequence L-proline-glycine-L-proline has the highest antiulcer activity of all the glyprolines.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Hydrolyzed collagen is contraindicated in those who are hypersensitive to any component of a hydrolyzed collagen-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid the use of supplemental hydrolyzed collagen.

Those with renal failure or liver failure should exercise caution in the use of hydrolyzed collagen.

Those who use hydrolyzed collagen produced from bovine sources should be sure that the products are derived from raw materials (bovine skin and bone) classified as carrying no detectable infectivity. Bovine nervous system parts may carry the bovine spongiform encephalopathy (BSE) organism, the etiological agent of mad cow disease.

INTERACTIONS

There is one report of hydrolyzed collagen enhancing the effect of calcitonin in the treatment of osteoporosis.

DOSAGE AND ADMINISTRATION

Hydrolyzed collagen is available in powder form by itself or in combination with other nutritional supplements, including glucosamine and chondroitin sulfate. A typical dose is 10 grams daily.

LITERATURE

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Hydroxycitric Acid

DESCRIPTION

(-) - Hydroxycitric acid, commonly called hydroxycitric acid, is found in the fruits of the genus *Garcinia*. Supplemental hydroxycitric acid is typically an extract of the rinds of *Garcinia cambogia* fruit, also called Brindle berry. Fruit of this plant has long been used in India as a condiment, and the dried rind is used as a flavoring agent. The dried fruit rind is also used in Indian folk medicine for gastrointestinal complaints and rheumatism. Hydroxycitric acid is the principal acid in the fruits of *Garcinia cambogia* and makes up to 16% of the content of the dried fruit.

Hydroxycitric acid, in addition to being called (-)- hydroxycitric acid, is also known as hydroxycitrate, (-) — threo-hydroxycitric acid and 4S-hydroxycitric acid. It is abbreviated as (-)-HCA and sometimes as HCA. It is a different substance than either citric acid or isocitric acid, which are key intermediates in the tricarboxylic acid or Krebs cycle. The terms for the acid and anion forms, hydroxycitric acid and hydroxycitrate, respectively, are used interchangeably. However, the anion form is the form that occurs under biological conditions.

ACTIONS AND PHARMACOLOGY

ACTIONS

Hydroxycitric acid is a putative antiobesity agent.

MECHANISM OF ACTION

Hydroxycitric acid is a competitive inhibitor of the enzyme adenosine triphosphate-citrate (*pro-3S*) — lyase or ATP citrate lyase. In the cytosol, ATP citrate lyase catalyzes the conversion of citrate and coenzyme A to oxaloacetate and acetyl coenzyme A (acetyl CoA). Acetyl CoA is used in the synthesis of fatty acids, cholesterol and triglycerides and also