

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

in the synthesis of acetylcholine in the central nervous system.

Oxaloacetate may enter the gluconeogenic pathway, which can lead to the production of glucose and glycogen. It is believed that the putative antiobesity effect of hydroxycitric acid is due to suppression of fatty acid and fat synthesis. In addition, hydroxycitric acid is thought to suppress food intake via an anorectic effect. This is believed to be accounted for by hydroxycitric acid's stimulation of liver gluconeogenesis.

PHARMACOKINETICS

There is little reported on the pharmacokinetics of hydroxycitric acid in humans. Animal studies indicate that it is absorbed via the gastrointestinal tract and transported to the liver and other body tissues. There are no reports indicating if the marketed hydroxycitric acid is transported into liver cells in humans.

INDICATIONS AND USAGE

Claims are made that hydroxycitric acid is an effective weight-loss agent. These claims are not presently supported by well-controlled studies.

RESEARCH SUMMARY

A suggestion from animal work that hydroxycitric acid might be an effective antiobesity agent has not been confirmed in human studies. A recent well-controlled trial of hydroxycitric acid failed to produce any significant weight loss compared with placebo. This was a 12-week double-blind study in which overweight subjects were randomized to receive 1500 milligrams of hydroxycitric acid daily or placebo.

In another recent study, also conducted double-blind, placebo-controlled and randomized, researchers sought to see whether hydroxycitric acid supplementation could increase fat oxidation in human subject. The researchers found no significant effect.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a hydroxycitric acid-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid hydroxycitric acid supplements. Because of the theoretical possibility that hydroxycitric acid might affect the formation of acetylcholine in the brain, those with dementia syndromes, including Alzheimer's disease, should avoid hydroxycitric acid. Those with diabetes should be cautious about using hydroxycitric acid.

ADVERSE REACTIONS

In a 12-week weight loss study comparing hydroxycitric acid, 1500 milligrams daily, against a placebo, the number of reported adverse reactions was not significantly different between the placebo group and hydroxycitric acid groups.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

Hydroxycitric acid is available in *Garcinia cambogia* extracts. Some products contain hydroxycitric acid in the lactone form, which has not shown activity in animal models. There are products available that are free of the lactone form. Typical doses are about 1500 milligrams (as hydroxycitric acid) daily.

LITERATURE

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Hydroxyethylrutosides

DESCRIPTION

Hydroxyethylrutosides (HR) refer to a mixture of semi-synthetic derivatives of the flavonoid rutin. Rutin is a naturally occurring flavonol glycoside comprised of the flavonol quercetin and the disaccharide rutinose (see Rutin). Hydroxyethylrutosides are comprised of the mono-, di-, tri- and tetrahydroxyethyl derivatives of rutin and are prepared by the hydroxyethylation of the phenolic groups of rutin.

Formulations, mainly consisting of the trihydroxyethyl derivative of rutin, are used in Europe, Mexico and other Latin American countries for the treatment of such venous disorders as varicose veins and hemorrhoids. The generic name for these formulations is troxerutin.

Trihydroxyethylrutoside, the principal flavonoid in troxerutin, is also known as 7, 3', 4'-tris [O- (2-hydroxyethyl)]rutin, trioxyethylrutin and 2- [3, 4-bis (2-hydroxyethoxy) phenyl]-3 [[6-O-(6-deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl]oxy]-5-hydroxy-7- (2-hydroxyethoxy) -4H-1-benzopyran-4-one. It is a solid, yellow substance that is soluble