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D-Glucarate

DESCRIPTION

D-glucarate is the anionic form of D-glucaric acid, a dicarboxylic sugar acid derived from the oxidation of D-gluconic acid. It is naturally found in some vegetables and fruits, including cruciferous vegetables, bean sprouts and apples. D-glucarate may have cancer-chemopreventive activity.

D-glucarate is also known as D-saccharate. D-glucarate, in the form of its calcium salt, calcium D-glucarate, is marketed as a nutritional supplement. The molecular formula of calcium D-glucarate is $C_6H_8C_9O_8$, and its molecular weight is 248.20 daltons.

ACTIONS AND PHARMACOLOGY

MECHANISM OF ACTION

The mechanism of D-glucarate's possible anticarcinogenic activity is not entirely clear. One possibility is the inhibition of beta-glucuronidase via the D-glucarate derivative D-glucaro-1, 4-lactone (1, 4-GL). A major mechanism for the detoxification of certain carcinogens is via glucuronidation, which is catalyzed by glucuronyl transferase. The glucuro-

nide conjugates are excreted in the urine and bile. However, deconjugation can occur via the enzyme beta-glucuronidase. Inhibition of beta-glucuronidase prevents deconjugation. D-glucarate may have anticarcinogenic activity independent of 1, 4-GL. D-glucarate has been demonstrated to inhibit protein kinase, and this is a possible mechanism for a direct anticarcinogenic effect of the substance.

D-glucarate has been shown to lower cholesterol in rats. The mechanism of this effect is unknown.

PHARMACOKINETICS

There is little on the pharmacokinetics of D-glucarate in humans. Rat studies indicate that D-glucarate is converted to 1, 4-GL in the stomach. 1, 4-GL, again in rats, appears to be absorbed, transported by the blood to various tissues and excreted in the urine and, to a lesser extent, in the bile. Calcium-D-glucarate is claimed to be a sustained or slow release precursor of 1, 4-GL, but there are few human data to substantiate this.

INDICATIONS AND USAGE

Animal and *in vitro* work suggest that D-glucarate may have some anticancer and lipid-lowering effects. Clinical data, however, are lacking.

RESEARCH SUMMARY

D-glucarate has exhibited significant anticarcinogenic effects in numerous *in vitro* and animal experiments. It has shown some efficacy when used alone or in combination with some other putative anticancer substances, notably some of the retinoids. It has shown preventive and therapeutic activity against a number of cancers, including mammary, liver, prostate and colon cancer. There is evidence it may protect against a number of chemical carcinogens.

In one experiment, D-glucarate was found to be particularly effective in inhibiting chemically induced cancer in animals when fed during the promotional phase of carcinogenesis, but it was also effective when fed during the initiation phase. A more recent study also found that D-glucarate seems to be most effective in the post-initiation phases of cancer, as assessed, in this study by its inhibiting effects on carcinogen-induced aberrant crypt foci in the colons of rats. Research is ongoing.

Data related to claims that D-glucarate is an effective lipid-lowering agent are not as plentiful as the cancer data. Some animal data, however, suggest that D-glucarate may reduce total cholesterol and LDL-cholesterol. It does not appear to affect HDL-cholesterol. More research is needed.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

D-glucarate is contraindicated in those hypersensitive to any component of a D-glucarate-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid D-glucarate supplementation pending long-term safety studies.

INTERACTIONS

DRUGS

Retinoids: D-glucarate has shown synergistic chemopreventive effects with retinoids in some tumor models.

5-Fluorouracil: D-glucarate and 5-fluorouracil exhibited synergistic antitumor activity in a rat-tumor model.

DOSAGE AND ADMINISTRATION

D-glucarate is available in supplemental form as calcium-D-glucarate. A usual dose is 200 mg once or twice daily.

LITERATURE

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