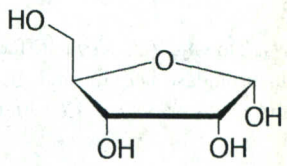
D-Ribose

DESCRIPTION

D-ribose is a naturally occurring five-carbon sugar found in all living cells, as well as in RNA-containing viruses. It is not an essential nutrient, since it can be made in the body from other substances, such as glucose. D-ribose, however, is very essential for life. Some of the most important biological molecules contain D-ribose, including ATP (adenosine triphosphate), all the nucleotides and nucleotide coenzymes and all forms of RNA (ribonucleic acid). D-ribose, in the form of ribonucleoside diphosphates, is converted to deoxyribonucleoside diphosphates, precursor molecules for DNA. D-ribose in RNA and D-deoxyribose in DNA may be considered genetic sugars.

Since D-ribose is ubiquitous in living matter, it is ingested in our diets. Such nutritional substances as brewers yeast are rich in RNA and are thus rich sources of D-ribose. Some recent research suggests that supraphysiological amounts of this sugar may have cardioprotective effects, particularly for the ischemic heart.

D-ribose is a sweet, solid, water-soluble substance that is also known as alpha-D-ribofuranoside. L-ribose does not have biological activity. D-ribose is sometimes referred to as just ribose. Supplemental D-ribose is produced from the fermentation of corn syrup. D-ribose has the following structural formula:



D-ribose

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental D-ribose may have metabolic cardioprotective activity. It may also enhance *de novo* purine biosynthesis.

MECHANISM OF ACTION

Following a cardiac ischemic event, ATP levels in the heart decline rapidly and are slow to rebound. 5-Phosphoribosyl 1-pyrophosphate (PRPP) is a key intermediate in the *de novo* and salvage pathways of purine nucleotide formation, as well as a key intermediate in synthesis of pyrimidine nucleotides. PRPP is the biochemically activated form of D-ribose and is synthesized from D-ribose-5-phosphate, which is produced in the oxidative pentose phosphate pathway (PPP). The limiting step in the PPP is the glucose-6-phosphate dehydrogenase (G-6-PD) reaction. The G-6-PD reaction can be bypassed with D-ribose. In supraphysiological amounts, D-ribose may serve as a precursor to PRPP, which then allows for *de novo* synthesis of purine nucleotides, including ATP. D-ribose infusion has been shown to significantly enhance the recovery of energy levels in the post-ischemic myocardium in animal models.

PHARMACOKINETICS

About 88% to 100% of an oral dose of D-ribose, up to 200 milligrams per kilogram per hour, is absorbed from the small intestine, from whence it is distributed to various tissues of the body, including cardiac muscle and skeletal muscle. Very little first-pass metabolism occurs in the liver. Following transport into cells, D-ribose is phosphorylated to D-ribose-5-phosphate. D-ribose-5-phosphate is metabolized via a number of pathways, including the pentose phosphate pathway and glycolytic pathway. Its metabolism is complex. It is also metabolized to PRPP, which is the precursor to purine nucleotides, as well as L-histidine and pyrimidine nucleotides. Those receiving very high doses of D-ribose excrete a small fraction of the administered dose unchanged in the urine.

INDICATIONS AND USAGE

D-ribose may have some protective effects in cardiac ischemia. Claims that it is an effective "energizer" and exercise-performance enhancer are not substantiated by credible evidence. D-ribose may also be beneficial in some rare genetic diseases, such as adenylosuccinase deficiency and myoadenylade deaminase deficiency.

RESEARCH SUMMARY

In a study of 20 men (aged 45 to 69 years) with documented severe coronary artery disease and a history of angina induced by normal daily activities, 60 grams of ribose (in four doses of 15 grams each) were tested against placebo. Treated subjects exhibited improvement as measured electrocardiographically, and time to onset of moderate angina (during exercise testing) increased significantly in those ribose-treated subjects. There was no significant electrocardiograph improvement in the placebo group, and there was no significant difference between the groups in time to onset of moderate angina. The authors concluded: "In patients with CAD, administration of ribose by mouth for three days improved the heart's tolerance to ischemia. The presumed effects on cardiac energy metabolism offer new possibilities for adjunctive medical treatment of myocardial ischemia."

Claims that supplemental ribose is an energy booster and exercise/athletic-performance enhancer are unfounded. Studies sometimes cited in support of these claims fall far short of being substantiating. It has been shown that administration of ribose in patients with myoadenylate deaminase deficiency disease can reduce cramping and stiffness caused by exercise. On the other hand, in a double-blind, placebo-

controlled crossover trial of ribose in McArdle's disease, 60 grams of ribose daily for seven days failed to improve exercise tolerance in these subjects. Finally, there is one case report of a patient with adenylosuccinate deficiency whose neurological symptoms (behavior and seizure frequency) improved with supplemental D-ribose.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a D-ribose-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid supplemental D-ribose.

Supplemental D-ribose may cause hypoglycemia and elevation in uric acid levels. Those with gout should avoid supplemental D-ribose, and those with elevated uric acid levels and hypoglycemics should exercise extreme caution in its use. Those with diabetes should also exercise extreme caution in its use. And those diabetics who decide to try D-ribose must be under a physician's supervision and have their blood glucose levels closely monitored and their antidiabetic medications appropriately adjusted, if necessary.

ADVERSE REACTIONS

Reported adverse reactions include hypoglycemia, hyperuricemia, hyperuricosuria, diarrhea, nausea and headache.

INTERACTIONS

Antidiabetic drugs: D-ribose may cause hypoglycemia. Diabetics who use D-ribose must have their blood glucose levels closely monitored and their antidiabetic medicines appropriately adjusted, if necessary.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

No typical dosage. Most experimental studies with ribose used very high doses, usually about 60 grams daily.

LITERATURE

Gross M, Dormann B, Zollner N. Ribose administration during exercise: effects on substrates and products of energy metabolism in healthy subjects and a patient with myoadenylate deaminase deficiency. *Klin Wochenschr.* 1991; 69:151-155.

Priml W, von Arnim T, Stablein A, et al. Effects of ribose on exercise-induced ischaemia in stable coronary artery disease. *Lancet.* 1992; 340:507-510.

Salerno C, D'Eufermia P, Finocchiaro R, et al. Effect of D-ribose on purine synthesis and neurological symptoms in a patient with adenylsuccinase deficiency. *Biochim Biophys Acta.* 1999; 1453:135-140.

Steele IC, Patterson VH, Nicholls DP. A double-blind, placebo-controlled, crossover trial of D-ribose in McArdle's disease. *J Neurol Sci.* 1996; 136:174-177.

Tullson PC, Terjung RL. Adenine nucleotide synthesis in exercising and endurance-trained skeletal muscle. *Am J Physiol.* 1991; 261:C342-C347.

Zimmer HG. The oxidative pentose phosphate pathway in the heart: regulation, physiological significance and clinical implications. *Basic Res Cardiol.* 1992; 87:3003-316.

Zimmer HG. Regulation of and intervention into the oxidative pentose phosphate pathway and adenine nucleotide metabolism in the heart. *Mol Cell Biochem.* 1996; 160/161:101-109.

Zimmer HG. Significance of the 5-phosphoribosyl-1-pyrophosphate pool for cardiac purine and pyrimidine nucleotide synthesis: studies with ribose, adenine, inosine, and orotic acid in rats. *Cardiovasc Drugs Ther.* 1998; 12 Suppl 2:179-187.

Zollner N, Reiter S, Gross M, et al. Myoadenylate deaminase deficiency: successful symptomatic therapy by high dose oral administration of ribose. *Klin Wochenschr.* 1986; 64:1281-1290.

Daidzein

DESCRIPTION

Daidzein belongs to the isoflavone class of flavonoids. It is also classified as a phytoestrogen since it is a plant-derived nonsteroidal compound that possesses estrogen-like biological activity. Daidzein has been found to have both weak estrogenic and weak anti-estrogenic effects.

Daidzein is the aglycone (aglucon) of daidzin. The isoflavone is found naturally as the glycoside daidzin and as the glycosides 6″-O-malonylgenistin and 6″-O-acetyldaidzin. Daidzein and its glycosides are mainly found in legumes, such as soybeans and chickpeas. Soybeans and soy foods are the major dietary sources of these substances. Daidzein glycosides are the second most abundant isoflavones in soybeans and soy foods; genistein glycosides are the most abundant. Nonfermented soy foods, such as tofu, contain daidzein, principally in its glycoside forms. Fermented soy foods, such as tempeh and miso, contain significant levels of the aglycone.

Daidzein and daidzin are also found in *Radix puerariae* (RP). RP is an herbal medicine prepared from the root of the legume *Pueraria lobata,* commonly known as kudzu. RP has been used for centuries in traditional Chinese medicine for the treatment of a wide range of disorders. It has also been used in traditional Chinese medicine since 600 AD for its "anti-drunkenness" effect and is still used by traditional Chinese physicians for the treatment of those who abuse alcohol. It is thought that the antidipsotropic (anti-drinking) effect of RP is due to daidzein and daidzin.

Daidzein is a solid substance that is virtually insoluble in water. Its molecular formula is $C_{15}H_{10}O_4$, and its molecular weight is 254.24 daltons. Daidzein is also known as 7-