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Pycnogenol

DESCRIPTION

The term pycnogenol refers to a specific mixture of procyanidins extracted from the bark of the French maritime pine, *Pinus maritima.* The French maritime pine grows in Bay of Biscay in the Landes de Gascogne in France. Although the term pycnogenol is now confined to procyanidins from the French maritime pine, the term was originally intended to serve as scientific name for this class of flavonoids.

Procyanidins are derivatives of the flavan-3-o1 class of flavonoids. This class includes epicatechin and catechin. Procyanidins consisting of dimers of catechin and oligomers of epicatechin and catechin are found in pycnogenol. Pycnogenol has a high amount of oligomers containing 5 to 7 units. Procyanidin oligomers are also known as oligomeric procyanidins (OPC), oligomeric proanthocyanidins (also OPCs) and procyanidolic oligomers (PCOs). In addition to OPCs, pycnogenol contains catechin, epicatechin and taxifolin, and such phenolic acids as caffeic, ferulic and para-hydroxybenzoic acids as minor constituents. It also contains glycosylation products of flavonols and phenolic acids as minute constituents. Pycnogenol is abbreviated PYC.

Procyanidins, including oligomeric procyanidins, are also found in such foods as cocoa and chocolate, grape seeds, apples, peanuts, almonds, cranberries and blueberries. They are also found in such medicinal herbs as "Sangre de drago" *(Croton lechleri).*

Procyanidins are also known as leucocyanidins. Procyanidins and prodelphinidins comprise a class of polyphenolic compounds called proanthocyanidins. Whereas procyanidins are oligomers of catechin and epicatechin and their gallic acid esters, prodelphinidins are oligomers of gallocatechin and epigallocatechin and their galloylated derivatives. Proanthocyanidins are also known as condensed tannins.

ACTIONS AND PHARMACOLOGY

ACTIONS

Pycnogenol has antioxidant activity. It may also have anti-inflammatory activity and has putative cardiovascular-protective activity.

MECHANISM OF ACTION

Pycnogenol has demonstrated a number of antioxidant activities in the laboratory. These include scavenging of the superoxide radical anion, the hydroxyl radical, the lipid peroxyl radical, the peroxynitrite radical and singlet oxygen. It has also been shown to protect low-density lipoprotein (LDL) from oxidation. The oligomeric procyanidins appear to have especially potent antioxidant activity when compared with smaller molecules, such as catechin and epicatechin. The extent of the antioxidant potential of pycnogenol in *vivo* is unclear. Some studies suggest that the antioxidant potential is at least partially available *in vivo.* Pycnogenol has been shown to have anti-inflammatory activity, again in the laboratory. This activity is thought to be due, in large part, to pycnogenol's capacity as a scavenger of reactive oxygen and reactive nitrogen species.

Pycnogenol appears to inhibit the activation of the transcription factors NF-kappa B and AP-1. NF-kappa B and AP-1 upregulate the expression of several inflammatory mediators such as intercellular adhesion molecule-1 (ICAM-1). NF-kappa B is itself activated by reactive oxygen species. Pycnogenol has been found to inhibit the inducible expression of ICAM-1. Inhibition of ICAM-1 may be accounted for by inhibition, by pycnogenol, of the activation of NF-Kappa B and AP-1. Further, the inflammatory cytokine interferon-gamma (IFN-gamma) may upregulate ICAM-1 expression in keratinocytes. This has been noted in some inflammatory skin conditions, such as lupus erythematous, atopic dermatitis and psoriasis. Pycnogenol appears to inhibit IFN-gamma activation of STAT (signal transducer and activator of transcription) 1. Inhibition of ICAM-1 expression by pycnogenol could account for possible anti-inflammatory and anti-atherogenic activities of pycnogenol.

PHARMACOKINETICS

Little is known about the pharmacokinetics of pycnogenol in humans. It appears that at least some of it is absorbed. However, the extent of absorption appears to vary widely, not only among the various components of pycnogenol, but also among subjects.

Some of the components of pycnogenol (e.g., catechin) appear to undergo extensive glucuronidation and sulfation

following and/or during absorption. The glucuronides and sulfates are excreted in the urine.

INDICATIONS AND USAGE

Claims made for pycnogenol are sweeping. It has been demonstrated to have free-radical-scavenging properties, but far from established are claims that it is useful in immune and neuro-degenerative disorders, that it is an effective anti-allergen, anticancer agent, antidiabetic agent and that it speeds healing of injuries, fights arthritis and is useful in cirrhosis of the liver and aging. Clinical trials are in short supply. Current research suggests that pycnogenol might have some cardioprotective effects and might be helpful in some vascular disorders. It is possible that some immune-modulating, anti-inflammatory and anticancer effects will emerge.

RESEARCH SUMMARY

In vitro studies have demonstrated that pycnogenol can protect some cells from lipid peroxidation and damage induced by various oxidative toxins.

In vivo, pycnogenol has shown some ability to minimize ischemic reperfusion injury in an animal model. There is some preliminary suggestion that pycnogenol may exhibit vasorelaxation activity, inhibit angiotensin-converting enzyme and enhance microcirculation by promoting increased capillary resistance. It may inhibit platelet aggregation and LDL-cholesterol oxidation. It may help maintain levels of some other antioxidants, principally vitamins C and E. Many of these effects have only been demonstrated *in vitro*.

In one of the few clinical trials of pycnogenol, the substance significantly inhibited smoking-induced platelet aggregation, more significantly with doses of 200 mg than with doses of 100 or 150 mg of pycnogenol. A single 200 mg dose of pycnogenol was reported to significantly inhibit platelet aggregation for longer than three days in smokers.

Pycnogenol has reportedly met with some success in treating certain vascular disorders, including varicose veins and chronic venous insufficiency. Pycnogenol has also inhibited some localized inflammation experimentally induced in animals.

Using doses of pycnogenol higher than could likely be administered to humans, researchers have restored some immune functions in an animal model of HIV-infection. In other animals, oral feeding of pycnogenol has resulted in significant improvement in T- and B-cell function. Natural killer cell cytotoxicity has been enhanced in animals given pycnogenol. Clinical trials are needed.

Pycnogenol has shown preliminary chemoprotective effects against NKK, a tobacco-specific nitrosamine, in rats exposed to this substance.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Pycnogenol is contraindicated in those with known hypersensitivity to any of the ingredients of a pycnogenol-containing product.

PRECAUTIONS

Pycnogenol supplementation should be avoided by pregnant women and nursing mothers.

ADVERSE REACTIONS

None reported.

INTERACTIONS

DRUGS

The use of pycnogenol and dextroamphetamine appeared superior to dextroamphetamine alone in the management of attention deficit-hyperactivity disorder, in one case report.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

Dosage ranges from 25 to 200 mg daily.

LITERATURE

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Pyruvate

DESCRIPTION

Pyruvate is the anionic form of the three-carbon organic acid, pyruvic acid. Pyruvate is a key intermediate in the glycolytic and pyruvate dehydrogenase pathways, which are involved in biological energy production. Pyruvate is widely found in living organisms. It is not an essential nutrient since