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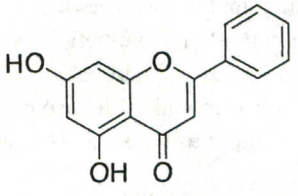
Chrysin

DESCRIPTION

Chrysin belongs to the flavone class of flavonoids. Chrysin is found naturally in various plants including the *Pelargonium* species, which are germanium-like plants; the *Passiflora* or passion flower species, which include tropical passion fruit; and the *Pinaceae* species, including pine trees.

Chrysin, principally obtained from the plant *Passiflora coerulea*, is marketed as a nutritional supplement and is especially popular among male body builders and other athletes because of its possible action in inhibiting the conversions of androgens to estrogens.

Chrysin is a solid substance with the molecular formula $C_{15}H_{10}O_4$. Its molecular weight is 254.24 daltons. It is practically insoluble in water. Chrysin is also known as 5,7-dihydroxyflavone and 5,7-dihydroxy-2-phenyl-4*H*-1-benzopyran-4-one. Chrysin is found in plants as such but is mainly found naturally in the form of a glucoside. Chrysin has the following chemical structure:



Chrysin

ACTIONS AND PHARMACOLOGY

ACTIONS

Chrysin may have aromatase-inhibitory action. It may also have phytoestrogenic, antioxidant and anxiolytic activities.

MECHANISM OF ACTION

Aromatase is a cytochrome P-450 enzyme that catalyzes the rate-limiting step in estrogen synthesis, the conversion of androgens to estrogens. Androstenedione and testosterone serve as substrates for aromatase. Aromatase, also known as estrogen synthase or synthetase, is inhibited by chrysin *in vitro*.

Chrysin has been demonstrated to bind weakly to estrogen receptors alpha and beta, again *in vitro*.

Chrysin's antioxidant potential has been shown by its ability to inhibit xanthine oxidase and consequently suppress the formation of uric acid and certain reactive oxygen species. It may also, under some conditions, inhibit lipid peroxidation.

Other *in vitro* studies have shown that chrysin binds to an area of the $GABA_A$ receptor known as the benzodiazepine receptor.

PHARMACOKINETICS

Little is known of the pharmacokinetics of chrysin in humans. Intestinal and hepatic cell cultures indicate that chrysin can get into cells but that it undergoes extensive glucuronidation and sulfation within the cells. If oral chrysin were to be extensively metabolized following absorption, one would expect that it would be essentially inactivated. Human pharmacokinetic studies are needed to clarify this. Chrysin does appear to be absorbed and to have activity in certain animal models.

INDICATIONS AND USAGE

Chrysin's aromatase-inhibiting effects have made it popular among some body builders and athletes who use androgens. Very preliminary research suggests that chrysin may emerge as a useful anxiolytic agent, that it might aid in the control of morphine withdrawal and that it might have some chemopreventive properties in cardiovascular disease and cancer.

RESEARCH SUMMARY

Chrysin's ability to inhibit the aromatization of androstenedione and testosterone to estrogens has been demonstrated in the laboratory. Chrysin has been shown to be among the most potent of the natural and synthetic flavone inhibitors of human estrogen aromatase. There are no studies directly demonstrating that chrysin makes the use of testosterone and related steroids less likely to produce estrogenic side effects.

A study using rats has shown that various flavonoids, including chrysin, can selectively bind to the central benzodiazepine receptor and thus exert potent anxiolytic and other benzodiazepine effects. More research is warranted.

Another study, this one *in vitro*, has suggested that chrysin might be helpful in controlling morphine withdrawal. Still other *in vitro* studies have found some chrysin-related chemopreventive effects in cardiovascular disease and cancer. No conclusions can yet be drawn from these very early studies.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Chrysin is contraindicated in those with prostate cancer. It is also contraindicated in those hypersensitive to any component of a chrysin-containing product.

PRECAUTIONS

Pregnant women, nursing mothers, children and adolescents should avoid using chrysin. Women generally should avoid its use.

Hormonal manipulation may have unforeseen consequences. Those interested in chrysin supplementation should exercise caution in its use.

Women with hormone dependent malignancies (breast, uterine, ovarian) should only use chrysin if they are in a clinical study or if chrysin is prescribed and monitored by their physicians.

ADVERSE REACTIONS

No reported adverse reactions.

INTERACTIONS

Aromatase inhibitors: Chrysin may be addictive to the effects of such aromatase inhibitors as aminoglutethimide, anastrozole, exemestane and letrozole.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

Body builders and athletes—typically male—who use chrysin take about one gram daily during training.

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Cocoa Flavonoids

DESCRIPTION

Cocoa and chocolate are products derived from cacao beans, the seeds of the *Theobroma cacao* tree. Polyphenols comprise about 12 to 18% of the dry weight of cacao beans. About 60% of the polyphenols are in the form of procyanidins (also known as leucocyanidins).

Procyanidins in cocoa and chocolate are mainly homodimers and homotrimers of (-)-epicatechin or heterodimers of (-)-epicatechin and (+)-catechin. (-)-Epicatechin and (+)-catechin belong to the flavan-3-ol class of flavonoids. Procyanidins containing up to 10 subunits (decamers) are found in fresh cacao beans and in dark chocolate. These are also called oligomeric procyanidins.

In addition to containing (-)-epicatechin, (+)-catechin and procyanidins, cocoa and chocolate contain other flavonoids, including other catechins and the flavanol quercetin and its glycosides. Collectively, these flavonoids are known as cocoa flavonoids or cocoa polyphenols.

Interestingly, the Mayans and Aztecs used cacao beans for the preparation of various remedies. The cocoa flavonoids appear to have potent antioxidant activity and may eventually turn out to have health-promoting benefits.

ACTIONS AND PHARMACOLOGY

ACTIONS

Cocoa flavonoids have antioxidant activity. They also may have anti-inflammatory and immunomodulatory activities.

MECHANISM OF ACTION

Cocoa flavonoids have been demonstrated to scavenge reactive oxygen and reactive nitrogen species. They may also chelate metals, such as ferrous cations, which participate in reactive oxygen species-generating reactions. Further, there is some evidence that the larger procyanidin oligomers have greater antioxidant potential.

Cocoa flavonoids have been shown to inhibit the oxidation of LDL. The oxidation of LDL is thought to be a crucial event in the pathogenesis of atherosclerosis.

Some of the cocoa flavonoids appear to reduce the expression of phytohemagglutinin-induced interleukin 2 (IL-2) mRNA, as well as the expression of interleukin 1beta (IL-1B), in peripheral blood mononuclear cells (PBMC).

Reduction of IL-2 and IL-1beta in PBMC could account, in part, for possible anti-inflammatory and immunomodulatory activities of cocoa flavonoids. The mechanism of these actions could again be due to the antioxidant action of cocoa flavonoids. Reactive oxygen species can activate nuclear transcription factor-Kappa B (NF-Kappa B). NF-Kappa B, in turn, may stimulate the production of such pro-inflammatory factors as IL-2 and IL-1 beta.

PHARMACOKINETICS

Little is known about the pharmacokinetics of cocoa polyphenols in humans. It appears that they do, at least partially, get absorbed. However, the extent of absorption appears to vary widely, not only among the different cocoa flavonoids, but also among subjects.

It also appears that the cocoa flavonoids undergo extensive glucuronidation, sulfation and methylation following and/or during absorption.

INDICATIONS AND USAGE

Cocoa flavonoids have been shown, in some mostly small, preliminary studies, to have possible benefit in blood pressure and in heart health generally.

RESEARCH SUMMARY

The cocoa bean is a rich source of polyphenols that exhibit significant antioxidant activity *in vitro.* These polyphenols are found in cocoa, baking chocolate and milk chocolate, among other foods. In one *in vitro* study, all three of these showed some ability to inhibit oxidation of LDL-cholesterol. Cocoa was the most potent of the three in this respect. In the decade since cocoa polyphenols have been investigated, some further small studies have demonstrated some benefits in humans, including lower platelet aggregation in one study and increased HDL-cholesterol in another.

In a few studies, improved insulin sensitivity was noted and blood pressure was improved. In a recent review of studies conducted over the past decade, the authors questioned the value of many of these studies since so many of them were small, poorly controlled and utilized healthy, well-nourished subjects. They also questioned whether observed effects were from cocoa polyphenols or from some other components in the agents used, such as caffeine or magnesium, or from synergistic effects of several components with cocoa. They noted that the majority of the studies were industry-