researchers to conclude that dietary supplementation with the lignan might result in mild estrogenic activity in humans. At this point it appears doubtful that HMR could become an alternative treatment sufficient in potency to supplant standard estrogen replacement therapy in post-menopausal women—but further investigation may be indicated.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

7-hydroxyhydroxymatairesinol (HMR) is contraindicated in those who are hypersensitive to any component of an HMR-containing product.

PRECAUTIONS

Consumption of HMR is not recommended for children.

Pregnant women and nursing mothers should avoid the use of HMR supplements.

Men with prostate cancer should discuss the advisability of the use of HMR supplements with their physicians before deciding to use them.

Women with estrogen receptor-positive tumors should exercise caution in the use of HMR supplements and should only use them if they are recommended and monitored by a physician.

ADVERSE REACTIONS

None known.

INTERACTIONS

DRUGS

Antibiotics may decrease the production of ENL from HMR.

NUTRITIONAL SUPPLEMENTS

None known.

FOODS

No known interactions.

HERBS

None known

OVERDOSAGE

There are no reports of HMR overdosage.

DOSAGE AND ADMINISTRATION

The major manufacturer of HMR recommends a daily dose of 50 mg of HMR.

LITERATURE

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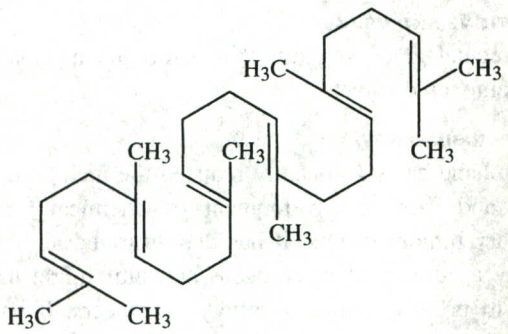
Squalene

DESCRIPTION

Squalene, a 30-carbon isoprenoid, is a lipid found in large quantities in shark liver oil and in smaller amounts (0.1 to 0.7%) in olive oil, wheat germ oil, rice bran oil and yeast. It

is a key intermediate in the biosynthesis of cholesterol. Squalene is an all-trans isoprenoid containing six isoprene units. Chemically, it is known as (all-E)-2, 6, 10, 15, 19, 23-Hexamethyl-2, 6, 10, 14, 18, 22-tetracosahexaene. It is represented structurally as:



Squalene

It is also known as spinacene and supraene. Squalene is also found in human sebum. Squalene has the ability to absorb oxygen. However, the amount of oxygen absorbed would be physiologically significant only for the shark.

ACTIONS AND PHARMACOLOGY

ACTIONS

Squalene has demonstrated proliferative activity in animal cancer studies; to date no human data are available. Squalene may have some radioprotective effects, but, again, there are no human data. Animal work suggests that squalene may also have a cholesterol-lowering effect, but this has not been tested in humans.

MECHANISM OF ACTION

Squalene is a key precursor in the biosynthesis of cholesterol. It inhibits 3-hydroxy-3-methylglutaryl coenzyme A reductase activity, thus reducing farnesyl pyrophosphate availability for prenylation of the ras oncogene, an activity that could account for its anti-proliferative effect in some animal cancer models. Apoptosis inhibition may also play a role in the anti-tumor effects of squalene in animals. The mechanism of the radioprotective effect of squalene is unknown.

PHARMACOKINETICS

Over 60% of ingested squalene is absorbed from the small intestine; from there it is carried in the lymph in the form of chylomicrons into the systemic circulation. In the blood, squalene is carried mainly in very-low-density lipoproteins and distributed to the various tissues of the body. A large percentage of squalene gets distributed to the skin. Squalene is metabolized to cholesterol.

INDICATIONS AND USAGE

Animal work suggests that indications could one day emerge for squalene in the prevention and treatment of some cancers, for immune enhancement and possibly for lowering cholesterol. It is not indicated for gastritis, joint pain and inflammation or to improve lung function.

RESEARCH SUMMARY

Squalene is being investigated as an adjunctive therapy in some cancers. In animal models, it has proved effective in inhibiting lung tumors. It has also demonstrated chemopreventive effects against colon cancer in animal models. Supplementation of squalene in mice has produced enhanced immune function and, in other animal studies, it has reduced cholesterol levels, prompting one researcher to suggest that it might be used to potentiate cholesterol-lowering drugs.

A mouse study showed squalene to confer radioprotection against lethal whole-body radiation.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a squalene-containing product.

PRECAUTIONS

Squalene supplementation should be avoided in infants, children, pregnant women and nursing mothers.

ADVERSE REACTIONS

Those taking squalene supplements may have mild gastrointestinal symptoms such as diarrhea.

INTERACTIONS

None known.

OVERDOSAGE

There have been no reports of overdosage.

DOSAGE AND ADMINISTRATION

Squalene is a liquid that is available in capsules for oral use. Doses of 500 milligrams to 4 grams are used; the higher doses are used by some cancer sufferers. The source of squalene is usually from shark liver oil and sometimes from olive oil.

Squalene should not be confused with squalamine, which is an unusual steroid found in the dogfish shark and which has antibiotic properties.

LITERATURE

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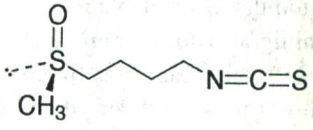
Sulforaphane

DESCRIPTION

Sulforaphane is the aglycone breakdown product of the glucosinolate glucoraphanin, also known as sulforaphane glucosinolate (SGS). Glucosinolates are beta-thioglucoside-N-hydroxysulfates and are primarily found in cruciferous vegetables (cabbage, broccoli, broccoli sprouts, brussels sprouts, cauliflower, cauliflower sprouts, bok choy, kale, collards, arugula, kohlrabi, mustard, turnip, red radish and watercress). Young broccoli sprouts and young cauliflower sprouts are especially rich in glucoraphanin.

Sulforaphane may have cancer chemopreventive activity. However, glucosinolates themselves typically have low anticancer activity. Sulforaphane is produced from sulforaphane glucosinolate via the action of the enzyme myrosinase (thioglucoside glucohydrolase), an enzyme present in cruciferous vegetables that is activated upon maceration of the vegetables.

Sulforaphane is also classified as an isothiocyanate. Its molecular formula is $C_6H_{11}NOS_2$, and its molecular weight is 177.29 daltons. It is also known as 4-methylsulfinylbutyl isothiocyanate and (-)-1-isothiocyanato-4(R)-(methylsulfinyl) butane. Sulforaphane glucosinolate (glucoraphanin) is also known as 4-methylsufinylbutyl glucosinolate. The structural formula is:



Sulforaphane

ACTIONS AND PHARMACOLOGY

ACTIONS

Sulforaphane may have anticarcinogenic activity.

MECHANISM OF ACTION

Sulforaphane's possible anticarcinogenic activity is accounted for by its ability to induce phase II detoxication enzymes, such as glutathione S-transferase and quinone reductase [NAD(P)H: (quinone-acceptor) oxidoreductase]. These enzymes may afford protection against certain carcinogens and other toxic electrophiles, including reactive oxygen species.

PHARMACOKINETICS

Little is presently known about the pharmacokinetics of sulforaphane in humans. Some preliminary studies indicate that sulforaphane is absorbed and that it is metabolized by first undergoing conjugation with reduced glutathione to form a dithiocarbamate. The dithiocarbamate is then converted sequentially to conjugates with cysteinylglycine, cysteine and N-acetylcysteine.

INDICATIONS AND USAGE

Experimental data suggest that sulforaphane may have anticarcinogenic effects.

RESEARCH SUMMARY

Sulforaphane has significantly reduced the incidence, multiplicity and rate of development of chemically induced mammary tumors in rats. It has demonstrated an ability to detoxify a number of carcinogens and thus might have the ability to protect against a variety of cancers. It has been shown that dietary supplementation with sulforaphane enhances glutathione S-transferase (GST) enzyme activity, which is known to detoxify many carcinogens.

One group of researchers has reported that three-day-old sprouts of certain broccoli and cauliflower cultivars contain 10 to 100 times higher levels of glucoraphanin, the glucosinolate of sulforaphane, than do mature broccoli and cauliflower sprouts. Thus they have concluded that "small quantities of crucifer sprouts may protect against the risk of cancer as effectively as much larger quantities of mature vegetables of the same variety." Additionally they have noted that the indole glucosinates that are prevalent in mature broccoli, for example, are present in only small quantities in the sprouts. One report suggested that the degradation products (e.g., indole-3-carbinol) of these glucosinates might themselves promote tumorigenesis, but several other investigators have not confirmed this.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Sulforaphane is contraindicated in those who are hypersensitive to any component of a sulforaphane-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid sulforaphane supplementation pending long-term safety data.

ADVERSE REACTIONS

No adverse reactions reported.

DOSAGE AND ADMINISTRATION

Sulforaphane is available in a few different formulations, usually in combination with other dietary phytochemicals. There are no typical doses.

Sulforaphane, in the form of its glucosinolate glucoraphanin, is abundant in three-day old broccoli sprouts, which are available in the marketplace. The levels of glucoraphanin in three-day old broccoli sprouts are from 10 to 100 times greater than in mature broccoli.