

Following a single dose of octacosanol in experimental animals, peak plasma levels are observed between 30 minutes to two hours. Following a single dose of octacosanol in human volunteers, peak plasma levels are observed at one hour and four hours later. Bile is the main route of excretion. Renal excretion is negligible.

INDICATIONS AND USAGE

Octacosanol, like policosanol (see Policosanol), may have cholesterol-lowering effects but research will have to be done to confirm this. Similarly, there is preliminary evidence suggesting that octacosanol may increase physical endurance and that it may benefit some with Parkinson's disease. Octacosanol is not indicated for use in amyotrophic lateral sclerosis despite some claims of efficacy in this disorder.

RESEARCH SUMMARY

There is limited evidence that octacosanol itself may lower cholesterol levels. This needs to be researched. (See Policosanol.) There are claims that octacosanol is useful in building strength and endurance, and these claims have made the supplement popular with some body builders and athletes. There is preliminary evidence, limited to animal experiments, that octacosanol may increase voluntary exercise in the animals.

Evidence that octacosanol may help in the treatment of Parkinson's disease is very preliminary, and the use of this substance in a well-designed study of those suffering from amyotrophic lateral sclerosis showed no benefit. Neither neurologic nor pulmonary functions were improved.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to an octacosanol-containing product.

PRECAUTIONS

Octacosanol is not recommended for children, pregnant women and nursing mothers. Parkinson's disease patients taking carbidopa-levodopa may experience side effects (see Adverse Reactions).

ADVERSE REACTIONS

Side effects of octacosanol taken up to 20 milligrams daily are infrequent. Mild position-related nonrotational dizziness, increased nervous tension and worsening of carbidopa-levodopa-related dyskinesias have been reported in a few Parkinson's disease patients taking octacosanol.

INTERACTIONS

Carbidopa-levodopa: Octacosanol has been reported to worsen dyskinesias in a few Parkinson's disease patients taking carbidopa-levodopa.

No other nutritional supplement, herb or food interactions are known.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

Typical doses used are 1 to 8 milligrams (1,000 to 8,000 micrograms) daily taken with food. A dose of 20 milligrams daily should not be exceeded. Octacosanol frequently comes in mixtures with other long-chain alcohols.

LITERATURE

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Oleocanthal

DESCRIPTION

A number of observational studies have shown that those who follow the Mediterranean diet have a lower incidence of cardiovascular disease, including heart attacks, and also a lower incidence of cancer, including breast, prostate and colorectal cancer, and other chronic degenerative diseases. The principal components of this diet are fruits, vegetables, fish, wine and olive oil. The consumption of red meat is relatively low, and olive oil is the major source of lipids in the diet. The health benefits are mainly attributed to the consumption of olive oil.

The specific substances in olive oil that appear to confer the health benefits include the monounsaturated fatty acid oleic acid and especially the polyphenolic lignans (+)-1-acetoxypinoresinol and (+)-pinoresinol and the polyphenolics hydroxytyrosol and oleuropein aglycone.

In September 2005, a short communication appeared in the international science journal *Nature* describing the anti-inflammatory effects of a recently discovered (1993) olive oil polyphenol, which the authors named oleocanthal. The press immediately picked up on the article, not only because it made for an interesting story, but also because of the possibility that the substance may be the key to understanding the health benefits of olive oil.

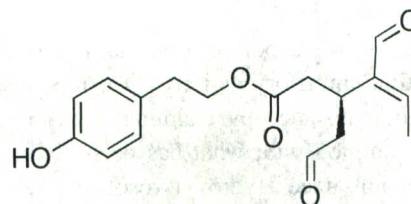
The study reported in *Nature* was directed by Paul Breslin, Ph.D. and Gary Beauchamp, Ph.D., both of the Monell Chemical Senses Center in Philadelphia. The researchers were led to the discovery by the serendipitous observation

that fresh extra-virgin olive oil irritates the back of the throat in a unique and unusual manner. To quote Dr. Beauchamp, "I had considerable experience swallowing and being stung in the throat by ibuprofen from previous studies on its sensory properties. So when I tasted newly-pressed olive oil while attending a meeting on molecular gastronomy in Sicily, I was startled to notice that the throat sensations were virtually identical."

The researchers systematically evaluated the sensory properties of a number of compounds and found one that was thought to be responsible for the irritating property of premium extra-virgin olive oil. Chemically, the molecule that conferred the throaty bite was found to be the dialdehydic form of (-) decetoxy-ligstroside aglycone, which had been isolated by another group in 1993. The Monell researchers named this compound oleocanthal, oleo for olive, canth for sting and al for aldehyde. They also proceeded to synthesize the molecule and found that the synthetic molecule produced the same throat irritant effect as did premium extra-virgin olive oil and that the effect was dependent on the dose.

The nonsteroidal anti-inflammatory drug (NSAID) ibuprofen is widely used as an analgesic and anti-inflammatory for such disorders as osteoarthritis and many more. It inhibits both cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), as does aspirin, but does not inhibit the lipoxygenases. The chemical structures of ibuprofen and oleocanthal are quite different. However, oleocanthal, like ibuprofen, was found to inhibit COX-1 and COX-2, but not 15-lipoxygenase (15-LOX).

Oleocanthal is chemically described as 2-(4-hydroxyphenyl)ethyl (3*S*,4*E*)-4-formyl-3-(2-oxorthyl)hex-4-enoate. Oleocanthal is also known as deacetoxy ligstroside aglycone. There are two enantiomers of oleocanthal. (Enantiomers are one of two stereoisomers that are nonsuperimposable, complete mirror images of each other.) (-)-Oleocanthal is the naturally occurring enantiomer. Oleocanthal's CAS Registration number is 289030-99-5, its empirical formula is C₁₇H₂₀O₅, and its molecular weight is 304.34. Oleocanthal is a member of the secoiridoid family. It was first isolated and described in 1993 by Gianfrancesco Montedoro and his co-workers. The secoiridoid family also includes the olive polyphenols oleuropein (see Oleuropein), the bitter principle of olives, and hydroxytyrosol (see Hydroxytyrosol), which is responsible for the high stability of olive oil. Chemically, the secoiridoids are monoterpene lactones. Oleocanthal is represented by the following chemical structure.



Oleocanthal

The types of phenols in extra-virgin olive oil are different from those of the olive fruit. The olives mainly contain the polar glycosides, oleuropein and ligstroside. Oleuropein is the ester of oleonic acid with 3,4'-dihydroxyphenylethanol (hydroxytyrosol), and ligstroside is the ester of oleonic acid with 4-hydroxyphenylethanol (tyrosol). Oleuropein and ligstroside are the parent compounds of the less polar oleuropein- and ligstroside-aglycones (eg, oleocanthal). Oleuropein- and ligstroside-aglycones are formed by removal of the glucose moiety from the oleuropein- and ligstroside-glycosides via beta-glucosidase during ripening. Those aglycones and their various derivatives are the most abundant phenols in olive oil.

ACTIONS AND PHARMACOLOGY

ACTIONS

Oleocanthal may have antioxidant and anti-inflammatory activities.

MECHANISM OF ACTION

Few studies have been performed on the possible antioxidant activity of oleocanthal. However, given that oleocanthal is a polyphenolic substance, it is likely to possess scavenging activity against a wide range of radicals, including hydroxyl, peroxy, and superoxide anion radicals. It might also inhibit the oxidation of LDL. Oxidized LDL is thought to be a crucial event in the pathogenesis of atherosclerosis. *In vitro* and *in vivo* studies determining if oleocanthal does indeed inhibit the oxidation of LDL should be performed.

Oleocanthal has been shown to inhibit COX-1 and COX-2, but not 15-lipoxygenase (15-LOX). Thus, it does possess ibuprofen-like anti-inflammatory activity. However, a large range of high-quality clinical studies are needed and warranted to determine if this anti-inflammatory effect has any significance regarding prevention of cardiovascular disease, cancer and cognitive disorders, such as Alzheimer's disease.

PHARMACOKINETICS

Little is known about the pharmacokinetics (PK) of oleocanthal in either experimental animals or in humans. PK studies on oleocanthal in humans are needed to fill in all the details of its ADME (absorption, distribution, metabolism and excretion).

INDICATIONS AND USAGE

Oleocanthal, an olive polyphenol, has reported antioxidative and antiinflammatory activity. One report stirred wide interest in the substance by claiming it has ibuprofen-like activity. In common with what has been claimed for other olive polyphenols (see Hydroxytyrosol and Oleuropein), it may have some cardioprotective and anticancer activity, as well, although clinical evidence for this is lacking.

RESEARCH SUMMARY

A brief communication in the journal *Nature* excited interest in oleocanthal when researchers reported that this substance, derived from newly pressed extra-virgin olive oil, has some characteristics in common with the anti-inflammatory drug ibuprofen. They noted that both induce very similar stinging sensations in the throat and thereafter determined that the two substances have structural and pharmacological similarities. They found that oleocanthal, like ibuprofen, is an inhibitor of the COX-1 and COX-2 enzymes in a dose-dependent manner. Thus they hypothesized that, through consistent long-term consumption of extra-virgin olive oil, some ibuprofen-like relief from inflammation and pain might be realized in some individuals. Others, however, have questioned whether plasma levels of the polyphenol could thus ever be high enough to have a meaningful effect. Research is needed to see whether supplements of this substance could safely and effectively be used in the same way that ibuprofen is used. If so, it might have application in a number of situations since there are data suggesting that ibuprofen, apart from providing pain relief, may, when used long-term, have some inhibiting effect on various inflammatory processes, including Alzheimer's disease.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**CONTRAINDICATIONS**

Oleocanthal is contraindicated in those hypersensitive to any component of an oleocanthal-containing product. Hypersensitivity to oleocanthal is probably very rare.

PRECAUTIONS

Those who wish to use oleocanthal for health reasons should first discuss this with his or her physician.

ADVERSE REACTIONS

No reports.

INTERACTIONS

No reports.

OVERDOSAGE

There are no reports of overdose.

DOSAGE AND ADMINISTRATION

The concentration of oleocanthal in extra-virgin olive oil is variable. Premium extra-virgin olive oil contains up to 200 micrograms of oleocanthal per milliliter. Fifty grams of

premium extra-virgin olive oil contains about nine milligrams of oleocanthal. The potency of oleocanthal and ibuprofen is approximately the same. Therefore, nine milligrams of oleocanthal is approximately equal to nine milligrams of ibuprofen, which is about 10% percent of a low dose (100 milligrams) of ibuprofen.

Dietary supplements of oleocanthal are currently unavailable.

LITERATURE

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Oleuropein and Oleuropein Aglycone

DESCRIPTION

Olive oil is the principal fat component in the Mediterranean diet, and the consumption of olive oil by those who live in the Mediterranean basin has been associated with a lower incidence of coronary heart disease (CHD), some cancers, including prostate, breast and colorectal cancer, and other chronic degenerative diseases. A large number of phenolic compounds are found in olive oil, and it is thought that some