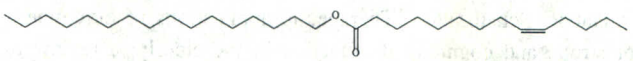
carbon monounsaturated fatty acid *cis*-9 tetradecenoic acid, or myristoleic acid. It was originally isolated from a NIH Swiss albino mouse strain that was resistant to adjuvant-induced arthritis. Cetyl myristoleate is known to exist naturally in sperm whale oil and in a small gland in the male beaver. It is marketed and used as an anti-osteoarthritis supplement. A waxy, lipid substance, it has the following chemical structure:



Cetyl myristoleate

ACTIONS AND PHARMACOLOGY

ACTIONS

Cetyl myristoleate has supposed anti-osteoarthritic activity.

PHARMACOKINETICS

No studies have been done on the pharmacokinetics of cetyl myristoleate. It is likely to be absorbed in the small intestine and transported from the lymph to the blood in lipid particles. Upon metabolism in the cells, it is likely that cetyl myristoleate undergoes enzymatic hydrolysis and that the component molecules, cetyl alcohol and myristoleic acid, are catabolized by normal cellular oxidative processes.

INDICATIONS AND USAGE

There is little credible support for claims that cetyl myristoleate is effective in arthritis, fibromyalgia, chronic fatigue syndrome and immune disorders.

RESEARCH SUMMARY

Claims for this substance have been sweeping, based upon an isolated finding that it provides protection against adjuvant-induced arthritis in a mouse strain (see above). In one animal study, high doses of cetyl myristoleate given parenterally were found to reduce the severity of arthritis in a rat adjuvant arthritis model. Another animal study found that cetyl myristoleate given in high doses orally had a modest antiarthritis effect in the mouse collagen-induced arthritis model. There are hardly any credible human clinical studies. A 68-day human placebo-controlled, single-blind, randomized controlled trial (RCT) of subjects having severe knee osteoarthritis reported an increase in knee flexibility in those receiving the study test article compared with those who received placebo. However, the study test article contained a number of substances, including olive oil, fish oil, lecithin and various cetylated fatty acids. Therefore, this was a low-quality RCT providing limited scientific evidence of efficacy for cetyl myristoleate. Until further positive research results are obtained from well-designed and well-executed clinical trials, the human use of cetyl myristoleate supplements has little scientific rationale. Claims that it is helpful in fibromyalgia, chronic fatigue syndrome and immune disorders have not been substantiated by credible research.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a Cetyl myristoleate-containing product.

PRECAUTIONS

Children, pregnant women and nursing mothers should avoid cetyl myristoleate supplements.

ADVERSE REACTIONS

May cause mild gastrointestinal symptoms.

DOSAGE AND ADMINISTRATION

There are no typical doses.

LITERATURE

Diehl HW, May EL. Cetyl myristoleate isolated from Swiss albino mice: an apparent protective agent against adjuvant arthritis in rats. *J Pharm Sci.* 1994;83:296-299.

Hesslink R Jr, Armstrong D 3rd, Nagendran MV, et al. Cetylated fatty acids improve knee function in patients with osteoarthritis. *J Rheumatol.* 2002;29(8):1708-1712.

Hunter KW Jr, Gault RA, Stehouwer JS, et al. Synthesis of cetyl myristoleate and evaluation of its therapeutic efficacy in a murine model of collagen-induced arthritis. *Pharmacol Res.* 2003;47(1):43-47.

Kraemer WJ, Ratamess NA, Anderson JM, et al. Effect of a cetylated fatty acid topical cream on functional mobility and quality of life of patients with osteoarthritis. *J Rheumatol.* 2004;31(4):767-774.

Whitehouse MW, McGeary RP. Concerning the anti-arthritic action of cetyl myristoleate in rats: An interim report. *Inflammopharmacology.* 1999;7(3):303-310.

Chelated Minerals

DESCRIPTION

Chelated minerals are minerals complexed with various amino acids, oligopeptides or other organic molecules that can bind with minerals to form a molecular complex.

It is believed by some that chelated minerals are better absorbed than non-chelated minerals. There may be certain minerals, e.g., trivalent chromium and zinc, where this is possibly the case. However, in most cases chelated and non-chelated minerals are absorbed with equivalent efficiency.

ACTIONS AND PHARMACOLOGY

ACTIONS

Chelated minerals are delivery forms of minerals.

MECHANISM OF ACTION

See monographs on individual minerals. Chelated chromium forms appear to be better absorbed than non-chelated forms. The mechanism of this is not entirely clear.

PHARMACOKINETICS

See monographs on individual minerals.

INDICATIONS AND USAGE

See individual mineral monographs to determine whether chelated forms confer any advantage. The mere claim of "chelation" does not necessarily mean a superior product.

RESEARCH SUMMARY

The issue of mineral chelation is a complex one. See monographs on individual minerals.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

See monographs on individual minerals.

OVERDOSAGE

The only mineral in which overdosage is a significant problem is iron. See monograph on Iron.

DOSAGE AND ADMINISTRATION

See monographs on individual minerals.

LITERATURE

See monographs on individual minerals.

Chicken Collagen II

DESCRIPTION

Chicken collagen II is type II collagen derived from the sternum of chickens. Type II collagen is the most abundant collagen found in hyaline cartilage (in synovial joints, sternum, respiratory tract), comprising 80 to 90% of the total collagen content. Chicken collagen II is also known as type II chicken collagen and is abbreviated as CCII.

Type II chicken collagen shares some similar antigenic regions with type II human collagen. Autoimmune response to type II collagen is thought to be a significant factor in the pathogenesis of rheumatoid arthritis. A few studies suggest that oral type II chicken collagen may be beneficial to some with rheumatoid arthritis, acting by a process known as oral tolerance.

ACTIONS AND PHARMACOLOGY

ACTIONS

Chicken collagen type II may have anti-rheumatoid arthritis activity in some.

MECHANISM OF ACTION

The mechanism of the possible anti-rheumatoid arthritis activity of chicken collagen type II may be through oral tolerance. Oral tolerance refers to the observation that if a protein is orally administered, subsequent immunization with the protein leads to a state of systemic hyporesponsiveness to it. Autoantibodies to type II collagen are thought to play a role in the pathogenesis of rheumatoid arthritis. Therefore, feeding antigenic type II collagen may be predicted to lead to the induction of immune tolerance to type II collagen, especially in the context of elevated autoantibodies to this substance.

The mechanism for oral tolerance appears to depend on the dose of the fed antigen. Low doses appear to induce active suppression, while high doses result in clonal anergy. Suppressive cytokines, such as interleukin-4 and transforming growth factor beta, appear to mediate active suppression. Studies in animals demonstrate the generation of regulatory lymphocytes in Peyer's patches, which subsequently migrate to mesenteric lymph nodes and spleen. Secretion of suppressive cytokines by these cells is believed to depend on antigen-specific stimulation with the fed antigen. Further, it is believed that active suppression of the inflammatory process by the regulatory lymphocytes requires their migration to the location where the fed antigen is present. Since the clinical studies to date indicate that low doses, but not high doses, have possible mild efficacy in rheumatoid arthritis, the mechanism responsible for oral tolerance would appear to be induction of active suppression, rather than clonal anergy.

PHARMACOKINETICS

There are no reports on the pharmacokinetics of chicken collagen type II. The pharmacokinetics of the substance should be similar to those of dietary proteins.

INDICATIONS AND USAGE

Chicken collagen II may offer some mild benefit for some with rheumatoid arthritis.

RESEARCH SUMMARY

A multicenter, randomized, controlled trial of oral type II collagen derived from chicken cartilage tested the substance in four different daily doses versus placebo in 273 rheumatoid arthritis patients. Various criteria were used to evaluate the results. The daily dose levels were 20 micrograms, 100 micrograms, 500 micrograms and 2,500 micrograms.

Results were negative at all dose levels except the lowest dose (20 micrograms daily). The difference in response between this dose level and placebo was significant only with respect to what was described as the weakest of the evaluative criteria. A *post hoc* analysis revealed that those who had antibodies reactive with type II collagen in their serum (at the baseline exam) were more likely to respond to collagen administration.

More research is needed, in part to investigate whether still lower doses might further improve efficacy of this antigenic substance.