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crude shark cartilage extracts nor the ability of possible effective components to reach and irradiate cancer cells.

Cartilage is a tissue that lacks blood vessels and rarely develops malignancies. Angiogenesis, the formation of new capillaries, is now known to be important in a number of pathological conditions, including solid tumors, proliferative retinopathy, neovascular glaucoma and rheumatoid arthritis. The process is also important in other physiological events as well, such as neovascularization following coronary artery occlusion.

In 1976, Judah Folkman and his colleagues reported on the isolation of a fraction from the scapular cartilage of calves that inhibited the growth of new blood vessels supporting implanted tumors in rabbits. It also stopped the growth of the tumors. Subsequent reports demonstrated a fraction in shark cartilage that also inhibited tumor neovascularization and growth.

The study of angiogenesis inhibitors has become a new field in cancer research. Since the earliest anti-angiogenesis substances discovered were derived from cartilage, research continues looking at cartilage to try to identify and characterize novel anti-angiogenic agents. Because sharks are an abundant source of cartilage, shark cartilage is being used by several research groups.

Sharks have an endoskeleton comprised entirely of cartilage, and while cartilage comprises less than 0.6% of the body weight of calves, it comprises about 6% of the body weight of sharks. Shark cartilage, like other forms of cartilage, is mainly composed of collagen, which participates in giving cartilage its tensile strength, and proteoglycans, themselves composed of a core protein to which is attached polysaccharides known as glycosaminoglycans or mucopolysaccharides. Proteoglycans impart resilience to cartilage. The main glycosaminoglycans in shark cartilage are the chondroitin sulfates. In addition to collagen and chondroitin sulfate, shark cartilage contains about 5 to 10% water, a large percentage of calcium and phosphate, low-molecular-weight proteins and polypeptides. A few low-molecular-weight proteins and polypeptides that appear to possess antiangiogenic activity have also been identified in shark cartilage. These substances are being researched as possible therapeutic candidates.

ACTIONS AND PHARMACOLOGY

ACTIONS

Shark cartilage has putative antitumor, antioxidant, anti-inflammatory and anti-atherogenic actions, although these putative actions are so far poorly supported by credible clinical research.

Shark Cartilage

DESCRIPTION

Shark cartilage became popular as a nutritional supplement a number of years ago, based on the claim that sharks do not get cancer and that this substance must therefore be useful for the prevention and treatment of cancer. The fact is that sharks do get cancer. The claim that sharks do not, or rarely, get cancer originates from a 1992 book written by I. William Lane entitled *Sharks Don't Get Cancer*. In a 2004 review article published in *Cancer Research* and written by Gary Ostrander and his colleagues, both malignant and benign neoplasms of sharks and their relatives were described, including previously unreported cases from the Registry of Tumors in Lower Animals and two sharks with two cancers each. Although some components of cartilage, including shark cartilage, might have anticancer potential, the best scientific evidence to date supports neither the efficacy of

MECHANISM OF ACTION

The mechanism of the possible actions of shark cartilage is unclear. It appears that any possible therapeutic benefit derives mainly from low-molecular-weight protein molecules that are currently being researched. Some of these molecules possess anti-angiogenic activity and inhibit metalloproteinases and vascular endothelial growth factor (VEGF)-mediated signaling events, activities that could help explain any possible antitumor activity.

PHARMACOKINETICS

There is little known about the pharmacokinetics of shark cartilage.

INDICATIONS AND USAGE

Widespread claims are made for shark cartilage, including anticancer, anti-inflammatory, antiarthritic, antipsoriasis and antiatherosclerotic effects. At present there is no credible clinical data sufficient to support any of these claims.

RESEARCH SUMMARY

Shark cartilage has been heavily promoted as an anti-cancer agent. Some *in vitro* and animal studies show some anti-angiogenic properties. Inhibition of wound angiogenesis has recently been demonstrated in one study of human subjects given liquid shark cartilage extract, but there are no other human data related to shark cartilage's putative anti-angiogenic effects and certainly none that show this effect in cancer patients.

Shark cartilage was tested directly in human subjects with advanced cancers of various types. In this phase I/II trial of the safety and efficacy of shark cartilage in cancer treatment, the substance was found to be inactive "and had no salutary effect on quality of life." A more recent clinical trial was conducted to look at the impact of a popular shark cartilage dietary supplement in patients with advanced breast or colorectal cancer. The study was a two-arm randomized, placebo-controlled, double-blind, clinical trial. Data on a total of 83 evaluable patients were analyzed. There was no difference in overall survival between patients receiving standard care plus the shark cartilage product versus standard care plus placebo, and there was no improvement in quality of life for the patients receiving the shark cartilage compared with those receiving placebo. Some anti-inflammatory effects of shark cartilage have been demonstrated *in vitro* and in animal models, but no useful conclusion can yet be drawn from this very preliminary research.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**CONTRAINDICATIONS**

Shark cartilage is contraindicated in those who are hypersensitive to any component of a shark cartilage-containing product. It is also contraindicated in those with hypercalcemia (shark cartilage contains a high percentage of calcium).

PRECAUTIONS

Pregnant women and nursing mothers should avoid shark cartilage supplementation.

Those with renal failure or liver failure should exercise caution in the use of shark cartilage.

Those with cancer who wish to try shark cartilage must only do so under medical supervision.

ADVERSE REACTIONS

The major adverse reactions are gastrointestinal and include nausea and vomiting, bloating and constipation. Some find the taste of shark cartilage disagreeable. There is one report of hepatitis associated with the use of shark cartilage.

OVERDOSAGE

There are no reports of overdosage in the literature.

DOSAGE AND ADMINISTRATION

Shark cartilage supplements are available in powders, tablets and capsules. There are no typical doses.

LITERATURE

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Silicon

DESCRIPTION

Silicon is a non-metallic element with atomic number 14 and symbol Si. In the periodic table, it is in the same group as carbon and is carbon's closest relative. Silicon is, next to oxygen, the most abundant element in the earth's crust and is found in plants, animals and in most living organisms.

Silicon is not currently considered an essential nutrient for humans. Silicon deficiency states have been reported in chicks and rats, and silicon is an essential nutrient for some plants. Chicks fed silicon-deficient diets are found to have abnormalities in their skulls and long bones. Abnormalities include poorly formed joints, defective endochondral growth and defective articular cartilage. Bone and cartilage abnormalities have also been found in rats fed silicon-deficient diets. In these animals, silicon appears to be involved in collagen and glycosaminoglycan formation. Silicon may play such a role in other animals, including humans, but this has not yet been established. Silicon has also been reported to inhibit experimental atheromas induced by an atheromatous diet in rabbits.

Daily dietary intake of silicon in the United States ranges from approximately 20 to 50 milligrams. The richest sources of silicon are cereal products and unrefined grains of high fiber content. Significant amounts of silicon in the diet occur in the form of silicon dioxide (silica), which is poorly absorbed. Animal foods are low in silicon.

Magnesium trisilicate is frequently used as an antacid, either alone or in combination products. In the stomach, magnesium trisilicate is converted to silicon dioxide and magnesium chloride.

ACTIONS AND PHARMACOLOGY

ACTIONS

The actions of supplemental silicon are not known.

PHARMACOKINETICS

Little is known about the pharmacokinetics of supplemental and dietary silicon in humans. There is great variability in the absorption of the various forms of silicon in the diet. Most forms of dietary silicon are poorly absorbed. Most of the silicon food additives are hardly absorbed at all. Silicon dioxide or silica is more poorly absorbed than orthosilicic acid, which is formed by the hydration of silicon dioxide. The mechanisms of silicon absorption are unknown. Silicon is not bound in plasma, where it is believed to exist almost entirely as monomeric silicic acid. Most of the silicon in the body is found in connective tissues, such as in bone, tendons, the trachea, the aorta, skin, hair and nails. Absorbed silicon is mainly excreted in the urine.

INDICATIONS AND USAGE

There is, at present, insufficient evidence to support any indication for the use of supplemental silicon. A very preliminary animal study suggests that it might have some positive impact in atherosclerosis. There is very preliminary evidence suggesting that silicon supplementation might play a positive role in bone health.

RESEARCH SUMMARY

It has been hypothesized that lack of silicon may play a role in the etiology of atherosclerosis. Intravenous administration of silicon inhibited experimental atheromas in an animal model, making atheromatous plaques fewer in number and the lipid deposits more superficial. This research was conducted many years ago and needs follow-up.

Silicon deficiency has been associated with bone defects in various animals. Silicon supplementation has inhibited bone mass loss in ovariectomized rats. Little is known about the role of dietary silicon in bone health in humans. It has been reported, however, that dietary silicon correlated positively and significantly with bone mineral density at all hip sites in men and premenopausal (but not postmenopausal) women in a cross-sectional, population-based study involving 2,847 participants (Framingham Offspring cohort). This previously unrecognized association is being further explored in continuing research.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a silicon-containing product.