

- Merchant RE, Carmack CA, Wise CM. Nutritional supplementation with *Chlorella pyrenoidosa* for patients with fibromyalgia syndrome: a pilot study. *Phytother Res.* 2000; 14:167-173.
- Morita K, Matsueda T, Iida T, Hasegawa T. *Chlorella* accelerates dioxin excretion in rats. *J Nutr.* 1999; 129:1731-1736.
- Noda K, Ohno N, Tanaka K, et al. A water-soluble antitumor glycoprotein from *Chlorella vulgaris*. *Planta Med.* 1996; 62:423-426.
- Sano T, Kumanoto Y, Kamiya N, et al. Effect of lipophilic extract of *Chlorella vulgaris* on alimentary hyperlipidemia in cholesterol-fed rats. *Artery.* 1988; 15:217-224.
- Sano T, Tanaka Y. Effect of dried, powdered *Chlorella vulgaris* on experimental atherosclerosis and alimentary hypercholesterolemia in cholesterol-fed rabbits. *Artery.* 1987; 76-84.
- Tanaka K, Koga T, Konishi F, et al. Augmentation of host defense by unicellular green alga, *Chlorella vulgaris*, to *Escherichia coli* infection. *Infect Immun.* 1986; 53:267-271.
- Tanaka K, Yamada A, Noda K, et al. Oral administration of a unicellular green algae, *Chlorella vulgaris*, prevents stress-induced ulcer. *Planta Med.* 1997; 63:465-466.
- Tanaka K, Yamada A, Noda K, et al. A novel glycoprotein obtained from *Chlorella vulgaris* strain CK22 shows antimetastatic immunopotential. *Cancer Immunol Immunother.* 1998; 45:313-320.

Chlorophyll/Chlorophyllin

DESCRIPTION

Chlorophyll is the green pigment found in higher plants, as well as algae. Chlorophyll is the principal photoreceptor in photosynthesis, the light-driven process in which carbon dioxide is "fixed" to yield carbohydrates and oxygen. Chlorophyll is a cyclic tetrapyrrole, similar in structure to the heme group of globins (hemoglobin, myoglobin) and cytochromes. Chlorophyll differs from heme in a few major respects, most notably that the central metal ion in chlorophyll is magnesium while that in heme is iron.

There are a few types of chlorophyll. Higher plants and green algae, such as *Chlorella* (see *Chlorella*) contain chlorophyll a and chlorophyll b in the approximate ratio of 3:1. The molecular formula of chlorophyll a is $C_{55}H_{72}MgN_4O_5$; the molecular formula of chlorophyll b is $C_{55}H_{70}MgN_4O_6$. The difference between the two chlorophylls is that a methyl side-chain in chlorophyll a is replaced by a formyl group in chlorophyll b. Chlorophyll a is found with chlorophyll c in many types of marine algae. Red algae contain principally chlorophyll a and also chlorophyll d.

Chlorophyllin is a semi-synthetic sodium/copper derivative of chlorophyll. In contrast to chlorophyll, chlorophyllin is water-soluble. Chlorophyllin, like chlorophyll, has deodorizing activity. It is used as an aid to reduce odor from a colostomy or ileostomy and also as an aid to reduce fecal odor due to incontinence. A topical ointment of chlorophyllin is used to reduce malodors in wounds and surface ulcers.

Chlorophyll and chlorophyllin are available as nutritional supplements. Preliminary evidence from *in vitro* and animal studies suggests that these substances may have anticarcinogenic activity.

ACTIONS AND PHARMACOLOGY

ACTIONS

Chlorophyll and chlorophyllin may have antimutagenic and anticarcinogenic activities.

MECHANISM OF ACTION

Chlorophyll and its metabolites pheophytin, pyropheophytin and pheophorbide, as well as chlorophyllin, have demonstrated antimutagenic effects *in vitro* against such mutagens as 3-methylcholanthrene, N-methyl-N'-nitro-N'-nitrosoguanidine (MNNG) and aflatoxin B1. Chlorophyll and chlorophyllin have also demonstrated anticarcinogenic effects in animal models against such carcinogens as aflatoxin B1, 1,2-dimethylhydrazine and dibenzo[*a,l*]pyrene.

The mechanism of the antimutagenic and anticarcinogenic activities of chlorophyll and chlorophyllin are unknown. It is speculated that antioxidant activity of chlorophyll/chlorophyllin may play a role in these activities. Another possible mechanism is the formation of complexes between the mutagen/carcinogen with chlorophyll/chlorophyllin through strong interactions between their planar unsaturated cyclic rings. The complexes would effectively inactivate the mutagens/carcinogens.

PHARMACOKINETICS

There is little on the pharmacokinetics of chlorophyll and its derivative chlorophyllin in humans. Some older studies showed that chlorophyll, following absorption, is converted into pheophytin, pyropheophytin and pheophorbide. These three derivatives of chlorophyll are tetrapyrroles.

INDICATIONS AND USAGE

Some experimental data suggests that chlorophyll and chlorophyllin may have some antimutagenic and anticarcinogenic potential, may help protect against some toxins, and may ameliorate some drug side effects. They are useful in reducing urinary and fecal odor in some circumstances. They may help ease constipation in some. There is some preliminary indication that they could be beneficial in the treatment of calcium oxalate stone disease and that they may have some anti-atherogenic activity.

RESEARCH SUMMARY

In one *in vitro* test, chlorophyllin demonstrated significant inhibition of several mutagens, including cigarette smoke, coal dust and diesel emission particles. Its antioxidant activity may have accounted for this effect. In another assay, chlorophyllin proved a more effective antimutagen than retinol, beta-carotene, vitamin C and vitamin E. In an animal study, chlorophyllin demonstrated both antimutagenic and anticarcinogenic activity, inhibiting 1,2-dimethylhydrazine-induced nuclear damage in rat colonic epithelium.

In another animal study, chlorophyllin significantly inhibited aflatoxin B1 hepatocarcinogenesis. In a rainbow trout multi-organ tumor model, chlorophyllin markedly reduced liver, stomach and swimbladder cancer incidence.

Chlorophyllin has been used to reduce some of the side effects of cyclophosphamide. Chlorophyll consumption has been associated, in an animal study, with increased fecal excretion of polychlorinated dibenzo-p-dioxin (PCDD) congeners and polychlorinated dibenzofuran (PCDF). The researchers suggested that green vegetables rich in chlorophyll might be helpful in humans exposed to PCDD and PCDF congeners.

In a study of geriatric patients, chlorophyllin was said to be effective in helping control body and fecal odors and helped ease chronic constipation. It also reduced excessive flatus in some. In another study, this one involving incontinent geriatric patients, subjects received 100 mg of chlorophyllin daily or placebo for two weeks. A non-significant decrease in urinary odor was noted in those receiving chlorophyllin, compared with those on placebo.

One preliminary study indicated that chlorophyllin can inhibit the crystallisation and growth kinetics of calcium oxalate dihydrate in normal urine and that it might be helpful in the treatment of calcium oxalate stone disease.

Finally, chlorophyllin significantly decreased serum cholesterol and triglycerides in a study using rats with experimental atherosclerosis. Followup is needed.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**CONTRAINDICATIONS**

Chlorophyll and chlorophyllin are contraindicated in those who are hypersensitive to any component in a chlorophyll-containing or chlorophyllin-containing preparation.

PRECAUTIONS

Supplemental chlorophyll and supplemental chlorophyllin should be avoided by pregnant women and nursing mothers.

ADVERSE REACTIONS

Use of chlorophyll and chlorophyllin supplements may cause discoloration of the urine (green urine), the feces (green

stool) and the tongue (yellow to black tongue). There are occasional reports of diarrhea with use of these substances.

INTERACTIONS

In a mouse model, chlorophyllin ameliorated some of the side effects of cyclophosphamide.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

There are a few chlorophyll and chlorophyllin nutritional supplements. Chlorophyllin is available as a liquid supplement. A typical dose is 100 mg daily. Those who use chlorophyllin to reduce fecal odor due to incontinence or to reduce odor from a colostomy or ileostomy typically take 100 mg daily.

LITERATURE

- Breinholt V, Arbogast D, Loveland P, et al. Chlorophyllin chemoprevention: an evaluation of reduced bioavailability vs. target organ protective mechanisms. *Toxicol Appl Pharmacol.* 1999; 158:141-151.
- Breinholt V, Hendricks J, Pereira C, et al. Dietary chlorophyllin is a potent inhibitor of aflatoxin B1 hepatocarcinogenesis in rainbow trout. *Cancer Res.* 1995; 55:57-62.
- Chernomorsky S, Segelman A, Poretz RD. Effect of dietary chlorophyll derivatives on mutagenesis and tumor cell growth. *Teratogen Carcinogen Mutagen.* 1999; 19:313-322.
- Dashwood RH, Breinholt V, Bailey GS. Chemopreventive properties of chlorophyllin: inhibition of aflatoxin B1 (AFB1)-DNA binding *in vivo* and antimutagenic activity against AFB1 and two heterocyclic amines in the Salmonella mutagenicity assay. *Carcinogenesis.* 1991; 12:939-942.
- Nahata MC, Slencsak CA, Kamp J. Effect of chlorophyllin on urinary odor in incontinent geriatric patients. *Drug Intell Clin Pharm.* 1983; 17:732-734.
- Ong TM, Whong WZ, Stewart J, Brockman HE. Chlorophyllin: a potent antimutagen against environmental and dietary complex mixtures. *Mutat Res.* 1986; 173:111-115.
- Reddy AP, Harttig U, Barth MC, et al. Inhibition of dibenzo[*a,l*]pyrene-induced multi-organ carcinogenesis by dietary chlorophyllin in rainbow trout. *Carcinogenesis.* 1999; 20:1919-1926.
- Robins EW, Nelson RL. Inhibition of 1,2-dimethylhydrazine-induced nuclear damage in rat colonic epithelium by chlorophyllin. *Anticancer Res.* 1989; 9:981-985.
- Te C, Gentile JM, Baguley BC, et al. *In vivo* effects of chlorophyllin on the antitumor agent cyclophosphamide. *Int J Cancer.* 1997; 70:84-89.
- Vlad M, Bordas E, Caseanu E, et al. Effect of cuprofilm on experimental atherosclerosis. *Biol Trace Elem Res.* 1995; 48:99-109.
- Young RW, Beregi JS Jr. Use of chlorophyllin in the care of geriatric patients. *J Am Geriatr Soc.* 1980; 28:46-47.