

Wheat grass supplements may contain high amounts of vitamin K. Those on warfarin should exercise caution in the use of wheat grass supplements.

#### ADVERSE REACTIONS

No reports of adverse reactions.

#### INTERACTIONS

Some wheat grass supplements may be rich in vitamin K and may affect the INR of those on warfarin.

#### DOSAGE AND ADMINISTRATION

There are various forms of wheat grass and barley grass supplements. Both are available as a powder, in tablets and as a juice. It is also available as a juice. Wheat grass and barley grass are also found in combination "green food" products with spirulina, chlorella, oat grass and alfalfa. Those who use wheat grass typically take 3.5 grams daily. The typical dose of barley grass is also about 3.5 grams daily.

#### LITERATURE

Lai C-N. Chlorophyll: the active factor in wheat sprout extract inhibiting the metabolic activation of carcinogens in vitro. *Nutr Cancer*. 1979; 1:19-21.

Lai C-N, Dabney BJ, Shaw CR. Inhibition of in vitro metabolic activation of carcinogens by wheat sprout extracts. *Nutr Cancer*. 1978; 1:27-30.

Peryt B, Miloszewska J, Tudek B, et al. Antimutagenic effects of several subfractions of extract from wheat sprout toward benzo[a]pyrene-induced mutagenicity in strain TA98 of *Salmonella typhimurium*. *Mutat Res*. 1988; 206:221-225.

Peryt B, Szymczyk T, Lesca P. Mechanism of antimutagenicity of wheat sprout extracts. *Mutat Res*. 1992; 269:201-215.

Tudek B, Peryt B, Miloszewska J, et al. The effect of wheat sprout extract on benzo(a)pyrene and 7,2-dimethylbenz(a)anthracene activity. *Neoplasma*. 1998; 35:515-523.

## Whey Proteins

#### DESCRIPTION

Whey proteins comprise one of the two major protein groups of bovine milk, the other group being the caseins. Caseins account for about 80% of the total protein in bovine milk, while whey proteins account for the remaining approximately 20%. Whey is derived as a natural byproduct of the cheese-making process. In addition to proteins, the raw form contains fat, lactose and other substances. The raw form is processed to produce protein-rich whey protein concentrates (WPC) and whey protein isolates (WPI), among other things.

Whey proteins are comprised of high-biological-value proteins and proteins that have different functions. The main

whey proteins are beta-lactoglobulin and alpha-lactoglobulin, two small globular proteins that account for about 70 to 80% of total whey protein. Proteins present in lesser amounts include the immunoglobulins IgG, IgA and IgM, but especially IgG, glycomacropptides, bovine serum albumin, lactoferrin, lactoperoxidase and lysozyme. Whey proteins also contain smaller peptides derived from various proteins which are called biopeptides.

A few different types of whey proteins are marketed. Whey protein concentrates are rich in whey proteins and also contain fat and lactose. Some whey protein concentrates contain higher amounts of immunoglobulins than others. Whey protein isolates are low in fat and lactose.

There are various processes for preparing whey protein isolates. Ion-exchange whey protein isolates are high in protein but low in glycomacropptides, lactoferrin, lactoperoxidase and some bioactive peptides. Microfiltration/ultrafiltration whey protein isolates have higher amounts of glycomacropptides, lactoferrin, lactoperoxidase and the bioactive peptides, but are lower in bovine serum albumin. Interestingly, bovine serum albumin, along with beta-lactoglobulin and IgG1, are proteins with abundant glutamylcysteine sequences. Glutamylcysteine is the precursor to glutathione. Cross-flow microfiltration gives a whey protein isolate which is greater than 90% in protein that is undenatured and that retains all important sub-fractions in natural ratios, with no fat or lactose.

#### ACTIONS AND PHARMACOLOGY

##### ACTIONS

Whey proteins may have antimicrobial and immunomodulatory actions. They may also have antioxidant activity.

##### MECHANISM OF ACTION

The mechanism of the possible antimicrobial actions of whey proteins may be accounted for by examining the activities of some of the whey proteins. Lactoferrin binds iron very tightly. Iron is a nutrient essential to support microbial growth, especially the growth of pathogenic bacteria. Lactoferrin may also inhibit the adsorption and/or penetration of bacteria and viruses in the intestinal wall. Lactoperoxidase may inactivate or kill microorganisms via an enzymatic activity producing reactive oxygen species. The immunoglobulins may also play a passive immunity role.

The possible immunomodulatory activity of whey proteins may also be due, in part, to the immunoglobulins playing a role in passive immunity. Whey proteins are rich in L-cysteine and L-glutamate, two amino acids that are precursors to the tripeptide glutathione. Some are also abundant in the dipeptide sequence of glutamylcysteine. This dipeptide is also a precursor to glutathione. There is some indication that

intake of whey proteins enhance monocyte glutathione levels. Enhanced glutathione levels may also contribute to a possible immunomodulatory role of whey proteins, as well as to the possible antioxidant activity of these proteins. In addition, lactoferrin may modulate immune function.

#### PHARMACOKINETICS

The pharmacokinetics of whey proteins should be similar to those for dietary proteins. There is indication that lactoferrin and some of the immunoglobulins in whey proteins may be more resistant to proteolytic degradation than are other types of proteins. Some proteins may be digested to peptides that may be absorbed and may have various activities (bioactive peptides). Some (e.g., bovine serum albumin, beta-lactoglobulin) may yield glutamylcysteine during their digestion, which may be absorbed and serve as a precursor to glutathione in some tissues.

#### INDICATIONS AND USAGE

Whey proteins may be useful in the nutrition of some infants and others, and there is some very preliminary evidence that they may have some immune-modulating and anticancer effects. There is no credible evidence that they build muscle faster than other protein sources.

#### RESEARCH SUMMARY

Whey proteins have been used as the sole proteins in some infant formulas, and this has reportedly resulted in fewer allergies in these infants. In one study, the use of a whey protein formula in the first six months of life significantly reduced atopic disease up to one year of age. In another study, infants receiving a whey protein-hydrolysate formula during the first six months of life had a lower incidence of cow's milk protein sensitivity at age six months, less eczema during the first year of life and less diarrhea of non-infectitious origin during the first half-year of life.

There are several animal studies in which whey and whey factors are said to exert some positive effects on immunity and cancer. Observed immuno-enhancing properties are believed by some researchers to be related only partially to whey's nutritional effects. Enhancement of host humoral immune response has been associated, in some of these studies, with whey's role in increasing glutathione levels in the body.

In animal studies, whey proteins were found to be protective against colon cancer, relative to red meat and some other protein sources. A whey protein diet significantly decreased tumor burden and extended life in mice with colon cancer, compared to mice with colon cancer fed-standard diet.

Whey protein concentrate was administered to five patients with metastatic cancers (30 grams daily for six months). Two of these patients exhibited some evidence of tumor regres-

sion, normalization of hemoglobin and peripheral lymphocyte counts. In two other patients, there was stabilization of tumor growth and increased hemoglobin levels. More research is needed.

#### CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

##### CONTRAINDICATIONS

Whey proteins are contraindicated in those who are hypersensitive to milk proteins.

##### PRECAUTIONS

See Contraindications.

##### ADVERSE REACTIONS

No reports. However, those who are hypersensitive to milk products are expected to experience allergy symptoms, including possible serious ones, if they use whey protein products.

##### INTERACTIONS

No known interactions with drugs, nutritional supplements, food or herbs.

##### DOSAGE AND ADMINISTRATION

There are several types of whey protein supplements available, including whey protein concentrates, ion exchange whey protein isolates, microfiltration/ultrafiltration whey protein isolates and whey protein hydrolysates. Some preparations contain mixtures of these various forms, and some are enriched with other substances, including branched-chain amino acids and L-glutamine. Dosages are variable. Some (athletes, for example) use whey proteins as a protein supplement and take 10 to 25 grams daily and, in some cases, higher doses.

##### LITERATURE

- Barth CA, Behnke U. [Nutritional physiology of whey and whey components.] [Article in German.] *Nahrung*. 1997; 41:2-12.
- Bell S J. Whey protein concentrates with and without immunoglobulins: a review. *J med Food*. 2000; 3:1-13.
- Bounous G, Batist G, Gold P. Immunoenhancing property of a dietary whey protein in mice: role of glutathione. *Clin Invest Med*. 1989; 12:154-161.
- Bounous G, Batist G, Gold P. Whey proteins in cancer prevention. *Cancer Lett*. 1991; 57:91-94.
- Bounous G, Gervais F, Amer V, et al. The influence of dietary whey protein on tissue glutathione and the diseases of aging. *Clin Invest Med*. 1989; 12:343-349.
- Kennedy RS, Konok GP, Bounous G, et al. The use of a whey protein concentrate in the treatment of patients with metastatic carcinoma: a phase I-II clinical study. *Anticancer Res*. 1995; 15(6B):2643-2649.
- Kinsella JE, Whitehead DM. Proteins in whey: chemical, physical, and functional properties. *Adv Food Nutr Res*. 1989; 33:343-438.

Papenburg R, Bounous G, Fleiszner D, Gold P. Dietary milk proteins inhibit the development of dimethylhydrazine-induced malignancy. *Tumor Biol.* 1990; 11:129-136.

Tong LM, Sasaki S, McClements DJ, Decker EA. Mechanisms of the antioxidant activity of a high molecular weight fraction of whey. *J Agric Food Chem.* 2000; 48:1473-1478.

Vandenplas Y, Hauser B, Van den Borre C, et al. Effect of a whey hydrolysate prophylaxis of atopic disease. *Ann Allergy.* 1992; 68:419-424.

Wong CW, Watson DL. Immunomodulatory effects of dietary whey proteins in mice. *J Dairy Res.* 1995; 62:359-368.

## Xanthohumol

### DESCRIPTION

Beer is a fermented aqueous drink based on starch and flavored with hops. Hops provide the characteristic bitterness of the beer and contribute to its aroma and foam stability.

The hop plant (*Humulus lupulus* L.) is a dioecious plant, meaning that there are separate male and female hop plants. Only the female hop plant produces the flowers, or, more specifically, the strobiles that are used for brewing or possible medicinal purposes. Male plants have no commercial value but are used to pollinate the female plants. Pollination stimulates higher yields by increasing cone size and seed set, but because brewers prefer seedless hops, males are only grown with otherwise poor-yielding female varieties. Hop seed from a pollinated female is only planted when a cross between the male and female is desired to obtain a new variety.

The term 'hop' in a strict sense refers to the hop plant, and the term 'hops' refers to the flower cones ("hop cones" or "hops"). However, both terms are commonly used interchangeably. The flowers in a female hop plant are arranged in characteristic clusters on stems. The flower cluster is called an inflorescence. The female inflorescences are rich in polyphenolic compounds and acyl phloroglucides that are widely used to preserve beer and give beer its characteristic flavor and aroma.

The hop cones are green, built like pine cones and vary in size. At the base of the leaves (bracts, also called scales) of the cones, are collections of small, yellow spheres called the lupulin glands. The lupulin glands are little sacs of bitter and aromatic acids and oils. In the lupulin glands can be found the alpha-acids and their derivatives, including the iso-alpha-acids and the rho-iso-alpha acids, the beta acids and xanthohumol, among several other compounds. The iso-alpha-acids, including isohumulone, account for the bitter

taste of beer. The oils in the hops are mainly responsible for the aroma of beer.

In addition to their role in beer, hops extracts have been used for medicinal reasons. The traditional use of hops as a mild sedative has its origin in the observation that the transfer of hop resin from the hands of hop-pickers to their mouths appeared to cause sleepiness and fatigue in the workers. In Germany, the use of hops is approved for the treatment of restlessness, anxiety and sleep disorders. However, high-quality clinical studies supporting the use of hops as a sedative are few and far between. Thus, the effectiveness of the use of hops for the treatment of sleep disorders is uncertain.

Recently, there has been great interest in studying certain phytochemicals found in hops for their possible anti-inflammatory, anticancer, chemopreventive and estrogenic activities. Two of the phytochemicals found in hops that have been receiving a great deal of attention are xanthohumol for its possible anticancer activity and 8-prenylnaringenin for its phytoestrogenic activity (see 8-Prenylnaringenin).

Xanthohumol is a prenylated chalcone derived from hops. In hops, the yellow compound is found in high amounts in the lupulin glands of the female inflorescence.

Xanthohumol is secreted as part of the hop resin (lupulin) by glandular trichomes found on the adaxial surfaces of cone bracts. It is also found in the trichomes on the underside of young leaves. The chalcone is found in small amounts in the Chinese traditional medicine plant, *Sophora flavescens*, extracts of which are used in the treatment a number of diseases, including certain cancers and viral diseases. A chalcone is an aromatic ketone that forms the central core for a variety of biological compounds. Chalcones are the immediate precursors in the biosynthesis of flavonoids, and their structures differ from that of other flavonoids by the inclusion of an open C-ring. (Chalcones are sometimes referred to as open C-ring flavonoids.) Xanthohumol is usually referred to as a prenylflavonoid. It is the precursor of the flavonoid, isoxanthohumol, which belongs to the flavanone subclass of flavonoids. Xanthohumol possesses a free 2'-hydroxy group and can therefore readily isomerize to isoxanthohumol.

Xanthohumol has been found to have broad-spectrum anticancer activity.

However, in contrast to some other phytochemicals in hops, especially 8-prenylnaringenin, xanthohumol per se does not possess phytoestrogenic activity.

Xanthohumol's empirical formula is C<sub>21</sub>H<sub>22</sub>O<sub>5</sub>, its molecular weight is 354.396, and its CAS Registry Number is 6754-58-1. Xanthohumol is described chemically as (*E*)-1-[2,4-dihy-