

taking melatonin. Melatonin supplements derived from animals should be avoided.

#### LITERATURE

- Antunes F, Barclay LRC, Ingold KU. On the antioxidant activity of melatonin. *Free Rad Bio Med.* 1999; 26:117-128.
- Barni S, Lissoni P, Cazzaniga M, et al. A randomized study of low-dose subcutaneous interleukin-2 plus melatonin versus supportive care alone in metastatic colorectal cancer patients progressing under 5-fluorouracil and folates. *Oncology.* 1995; 52:243-245.
- Brzezinski A. Melatonin in humans. *N Engl J Med.* 1997; 336:186-195.
- Bursztajn HJ. Melatonin therapy: from benzodiazepine-dependent insomnia to authenticity and autonomy. *Arch Intern Med.* 1999; 159:2393-2395.
- Cupp MJ. Melatonin. *Am Fam Physician.* 1997; 56:1421-1425.
- Dolberg OT, Hirschmann S, Grunhaus L. Melatonin for the treatment of sleep disturbances in major depressive disorder. *Am J Psychiat.* 1998; 155:1119-1121.
- Force RW, Hansen L, Bedell M. Psychotic episode after melatonin [letter]. *Ann Pharmacother.* 1997; 31:1408.
- Garfinkel D, Zisapel N, Wainstein J, Laudon M. Facilitation of benzodiazepine discontinuation by melatonin. *Arch Intern Med.* 1999; 159:2456-2460.
- Hartert S, Grozinger M, Weigmann H, et al. Increased bioavailability of oral melatonin after fluvoxamine administration. *Clin Pharmacol Therap.* 2000; 67:1-6.
- Middleton BA, Stone BM, Arendt J. Melatonin and fragmented sleep patterns. *Lancet.* 1996; 348:551-552.
- Murphy PJ, Myers BL, Badia P. Nonsteroidal anti-inflammatory drugs alter body temperature and suppress melatonin in humans. *Physiol Behav.* 1996; 59:133-139.
- Reiter RJ. Melatonin, active oxygen species and neurological damage. *Drug News Perspect.* 1998; 11:291-296.
- Reppert SM, Weaver DR. Melatonin madness. *Cell.* 1995; 83:1059-1062.
- Sainz RM, Mayo JC, Reiter RJ, et al. Melatonin regulates glucocorticoid receptor: an answer to its antiapoptotic action in thymus. *FASEB J.* 1999; 13:1547-1556.
- Turjanski AG, Rosenstein RE, Estrin DA. Reactions of melatonin and related indoles with free radicals: a computational study. *J Med Chem.* 1998; 44:3684-3689.
- Voorduow BC, Euser R, Verdonk RE, et al. Melatonin and melatonin-progestin combinations alter pituitary-ovarian function in women and can inhibit ovulation. *J Clin Endocrinol Metab.* 1992; 74:108-117.
- Wiid I, Hoal-van Helden E, Hon D, et al. Potentiation of isoniazid activity against *Myobacterium tuberculosis* by melatonin. *Antimicrob Agents Chemother.* 1999; 43:975-977.

## Methylsulfonylmethane (MSM)

#### DESCRIPTION

Methylsulfonylmethane, abbreviated MSM, is an organic sulfur-containing compound that occurs naturally in a variety of fruits, vegetables, grains and in animals, including humans in at least trace amounts. MSM has also been found in such plants as *Equisetum arvense*, also known as horsetail. The biological role of MSM, if any, is not known. MSM is a metabolite of dimethyl sulfoxide or DMSO (see Dimethyl Sulfoxide). It is believed that some of the possible effects of DMSO could be attributed to MSM.

MSM is a water-soluble, solid compound. It is also known as dimethyl sulfone, DMSO<sub>2</sub>, sulfonylbismethane and methyl sulfone.

#### ACTIONS AND PHARMACOLOGY

##### ACTIONS

Known hypersensitivity to an MSM-containing product.

##### PHARMACOKINETICS

Little is known about the pharmacokinetics of MSM in humans. Sulfur from MSM was found to be incorporated into protein methionine and cysteine when fed to guinea pigs. MSM was also detected in the brain of a normal 62-year old male, following its ingestion, using *in vivo* proton magnetic resonance spectroscopy. Thus, it appears that MSM gets absorbed and can cross the blood-brain barrier.

#### INDICATIONS AND USAGE

Claims for MSM include pain relief, particularly in arthritis, immune modulation in autoimmune disorders, muscle repair, sleep aid and diabetes therapy. There is no credible evidence to support any of these claims. There is very preliminary research suggesting some possible MSM anti-cancer effects.

#### RESEARCH SUMMARY

Two animal studies showed that MSM and other bipolar solvents can prolong latency period to time of tumor appearance in chemically induced animal model cancers. In one of these studies, there was no effect on tumor incidence; in the other, MSM seemed to reduce the incidence of poorly differentiated tumors. More research is indicated.

There is no research to support other claims made for MSM.

#### CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

##### CONTRAINDICATIONS

Known hypersensitivity to an MSM-containing product.

##### PRECAUTIONS

MSM should be avoided by pregnant women and nursing mothers.

**ADVERSE REACTIONS**

Reported adverse reactions include nausea, diarrhea and headache.

**OVERDOSAGE**

There are no reports of overdosage.

**DOSAGE AND ADMINISTRATION**

Doses used are typically 1 to 3 grams daily.

**LITERATURE**

Childs SJ. Dimethyl sulfone (DMSO) in the treatment of interstitial cystitis. *Urol Clin North Am.* 1994; 21:85-98.

Kandorf H, Chirra AR, De Gruccio A, Girman DJ. Dimethyl sulfoxide modulation of diabetes onset in NOD mice. *Diabetes.* 1989; 38:194-197.

Kocsis JJ, Harkaway S, Snyder R. Biological effects of the metabolites of dimethyl sulfoxide. *Ann NY Acad Sci.* 1975; 243:104-109.

Layman DL. Growth inhibitory effects of dimethyl sulfoxide and dimethyl sulfone on vascular smooth muscle and endothelial cells in vitro. *In Vitro Cell Dev Biol.* 1987; 23:422-428.

Morton JI, Siegel BV. Effects of oral dimethyl sulfoxide and dimethyl sulfone on murine autoimmune lymphoproliferative disease. *Proc Soc Exp Biol Med.* 1986; 183; 227-230.

O'Dwyer PJ, McCabe DP, Sickle-Santanello BJ, et al. Use of polar solvents in chemoprevention of 1, 2-dimethylhydrazine-induced colon cancer. *Cancer.* 1988; 62:944-948.

Pearson TW, Dawson HJ, Lackey HB. Natural occurring levels of dimethyl sulfoxide in selected fruits, vegetables, grains and beverages. *J Agric Food Chem.* 1989; 29:1089-1091.

Richmond VL. Incorporation of methylsulfonylmethane sulfur into guinea pig serum proteins. *Life Sci.* 1986; 39:263-268.

Rose SE, Chalk JB, Galloway GJ, Doddrell DM. Detection of dimethyl sulfone in the human brain by in vivo proton magnetic resonance spectroscopy. *Magn Reson Imaging.* 2000; 18:95-98.

---

## Modified Citrus Pectin

**DESCRIPTION**

Modified citrus pectin refers to citrus pectin which has been hydrolyzed to yield smaller molecular weight molecules which appears to render it more absorbable. Unmodified citrus pectin is not absorbable. Pectin (see Pectin) is a soluble fiber that is found in citrus fruits (oranges, lemons, grapefruits) and apples. Pectin obtained from orange or lemon rinds, both rich sources of pectin, is referred to as citrus pectin. Citrus pectin is a linear polysaccharide containing from about 300 to 1,000 monosaccharide units. D-galacturonic acid, an acid form of the sugar D-galactose, is the principal monosaccharide unit of citrus pectin. The D-

galacturonic acid residues are bonded together by alpha-1,4 glycosidic linkages in linear chains. Neutral sugars, present in side chains on the pectin molecule, include D-galactose, L-arabinose, D-xylose and L-fructose. L-Rhamnose is also found in pectin. Some of the galacturonic acid residues in pectin are in the form of methyl esters. The molecular weight of citrus pectin ranges from 20,000 to 400,000 daltons, with the majority of the molecules having molecular weights ranging from 50,000 to 150,000 daltons.

Modified citrus pectin is formed from citrus pectin via a depolymerization process in which citrus pectin is first treated with sodium hydroxide at a pH of 10 for a short time, and then hydrochloric acid at a pH of 3 for a much longer period of time. The pectin fragments that are formed are principally comprised of D-polygalacturonates, absent the methoxyl groups. The molecular weight of modified citrus pectin ranges from 1,000 to 15,000 daltons, with an average weight of about 10,000 daltons. Modified citrus pectin is comprised of linear polygalacturonate chains containing from 5 to 90 galacturonic acid residues, with an average of approximately 55 residues. Also present, are D-galactose residues in side chains. Modified citrus pectin is also known as modified pectin, depolymerized pectin and pH-modified pectin. It is abbreviated as MCP. It is water soluble.

**ACTIONS AND PHARMACOLOGY****ACTIONS**

Modified citrus pectin has putative anticarcinogenic activity.

**MECHANISM OF ACTION**

Modified citrus pectin, when administered orally to rats, was found to inhibit spontaneous prostate carcinoma metastasis. It had no effect on the growth of the primary tumor. Injected modified citrus pectin was found to inhibit metastasis of melanoma cells in mice. The mechanism of these anticarcinogenic effects is not clear.

Galectins comprise a family of galactoside-binding mammalian lectins. Lectins themselves comprise a group of hemagglutinating proteins found in plant seeds, which bind the branching carbohydrate molecules of glycoproteins and glycolipids on cell surfaces, resulting in agglutination or proliferation, among other things. Galectins are proteins that can bind to carbohydrates via carbohydrate recognition domains (CRDs). At present, the galectin family includes 10 members. Apparently, galectins are secreted from cells via nonclassical secretory pathways. Galectin-3, one of the members of the family, is thought to be involved in mitosis and proliferation. On the cell surface, galectin-3 mediates cell-cell adhesion and cell-matrix interaction via binding to its complementary glycoconjugates, such as laminin and fibronectin, and thereby is thought to play an important role in the pathogenesis of cancer metastasis.

---