

THE SCIENCE SUPPORTING SILYMARIN

ABSTRACT

Exposure to ultraviolet (UV) radiation generates oxygen-free radicals and has been proven to cause photoaging and certain forms of cancer in skin. The body uses antioxidants to protect itself from free radical attack and antioxidants are depleted by sun exposure. Silymarin is an extract of the milk thistle plant that has been shown to have strong antioxidant and anti-tumor effects. This makes silymarin an excellent addition to protective skin care formulations.

UV EXPOSURE AND ANTIOXIDANTS

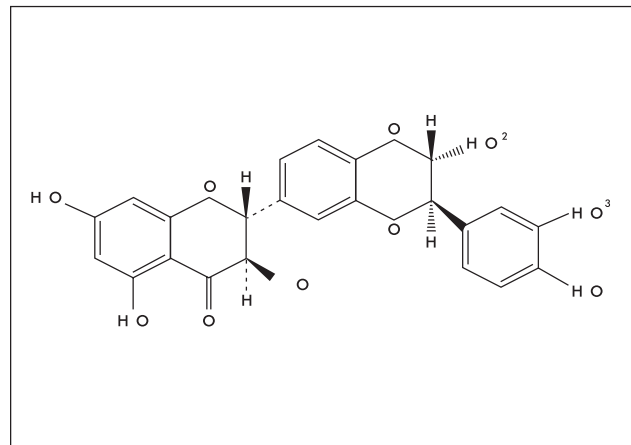
Exposure to UV radiation, smoke, and air pollution generates oxygen-free radicals that can destroy the structural components of the skin. This assault can cause visible changes in skin, including wrinkles (photoaging), solar lentigines (brown spots), actinic keratoses — and possibly even the development of skin cancer.

The body uses antioxidants to protect itself from free-radical attack, and antioxidant levels in the body are depleted significantly by sunlight and smoking. Alcohol, analgesics, antidepressants, anticoagulants, oral contraceptives, and steroids also may reduce the body's levels of key antioxidants. Oral ingestion is one way to replenish depleted antioxidant levels, but body control mechanisms tightly regulate the levels of ingested vitamins that actually get to the skin. For that reason, it is important to supplement the skin's reservoir of antioxidants with topical applications.

SILYMARIN: A STRONG ANTIOXIDANT

Silymarin is an extract of the milk thistle plant: *Silybum marianum*. Milk thistle belongs to the aster family (Asteraceae or Compositae) that includes daisies, thistles, and artichokes.^{1,2} Silymarin consists of a mixture of three bioflavonoids found in the fruit, seeds, and leaves of the milk thistle plant: silybin, silydianin, and silychristine.¹ Silybin is the main component (60-70%) and is thought to have the most biologic activity.

Figure 1. Chemical Structure of Silybin



Silymarin is extremely safe; no lethal dose exists. Oral doses of 1000 mg can be administered daily to humans without toxicity¹ and no known lethal dose exists for animals.⁷ Historically, since the 4th century BC, milk thistle extract has been used to treat disorders of the spleen, liver and gall bladder.¹

Silymarin has been shown to have utility in many liver disorders including toxin-induced liver toxicity, hepatitis, and alcoholic liver disease.^{4,5} In the animal model of cirrhosis produced by bile duct obliteration, silymarin has an anti-fibrotic effect.⁶

The mechanism of action for the beneficial effects of silymarin for liver disease is unknown. However, antioxidant activity is a leading theory. Silymarin can prevent lipid peroxidation,⁹⁻¹² inhibit LDL oxidation,¹³ and scavenge reactive oxygen species.¹⁴⁻¹⁶ Silymarin inhibited DNA synthesis,¹⁷ and fibroblast¹⁸ and epidermal cell proliferation.¹² It modulated the activation of NFkB to stimulate transcription.^{19,20}

SILYMARIN: ANTI-CARCINOGENIC EFFECTS

Because silymarin is known to have antioxidant effects, it was tested for its anti-carcinogenic effects in cancer-prone Sencar mice. First, it was tested to see if it had an effect on a group of cancer-promoting chemicals. It could be demonstrated that low doses of silymarin could essentially almost completely inhibit the effect of TPA, a tumor promoter from inducing ornithine decarboxylase activity.⁸ This suggested that silymarin might have useful tumor prevention effects.

Subsequently, topical silymarin has been shown to have a remarkable anti-tumor effect. The number of tumors induced in the skin of hairless mice by UVB light was reduced by 92%.² Silymarin reduced UV-induced sunburn cell formation and apoptosis. The result was not related to a sunscreen

effect and an antioxidant mechanism may be responsible. Figures 2 and 3 show the percentage and number of tumors in mice, treated with UVB alone compared to mice treated with UVB and silymarin.²

Figure 2. Silymarin Protects Against UVB Induced Skin Tumors (Percentage of Mice with Tumors)

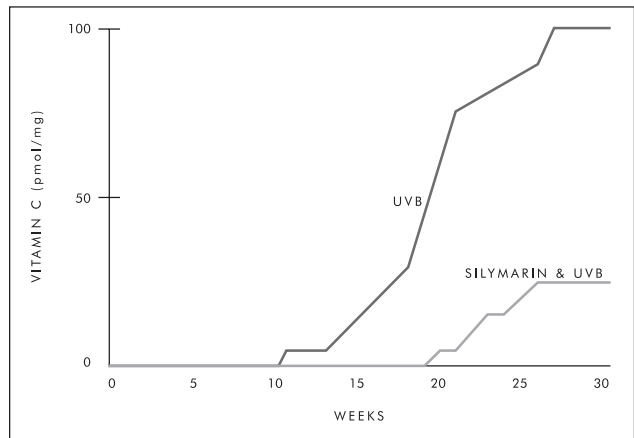
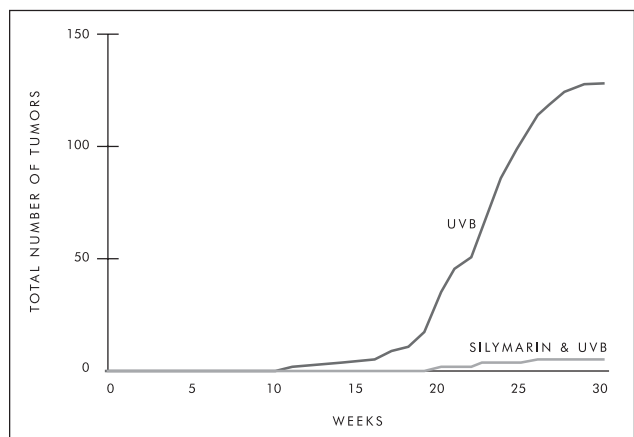


Figure 3. Silymarin Protects Against UVB Induced Skin Tumors (Total Number of Tumors per Mouse)



The mechanism of the anti-tumor effect for silymarin is unknown, although its antioxidant activity may be important.

Silymarin also prevented the formation of pyrimidine dimers following UVB exposure to hairless mouse skin.¹¹ It protected against DNA changes produced by peroxide²¹ and gamma radiation.²² Silymarin demonstrated both a potent anti-inflammatory effect²³ and anti-angiogenic action.²⁴

Silymarin has an equally protective effect against skin tumors caused by chemical carcinogenesis (i.e., no UV light).⁹ In these studies, tumors were initiated by a chemical carcinogen, DMBA and promoted by a chemical promoter, TPA.

SUMMARY

Silymarin is a strong antioxidant and has successfully been used to treat liver disorders. Silymarin scavenges reactive oxygen

species, and inhibits sunburn cells, apoptosis, and lipid peroxidation. Topical silymarin has been shown to have an anti-tumor effect although its mechanism of anti-carcinogenesis is unknown. For these reasons, it is believed that silymarin has powerful protective benefits when used in topical skin care formulations.

For more information, or for a complete bibliography of scientific research supporting SkinCeuticals products, please visit the SkinCeuticals, Inc. website at www.skinceuticals.com, or call toll free 800-811-1660.

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