COSMECEUTICAL CRITIQUE

Saffron

Saffron (*Crocus sativus*), a member of the Iridaceae family, is native to Southwest Asia, particularly Iran, but was first cultivated in Greece. It has been used as a spice or food flavoring agent, as well as a fragrance, clothing dye, and medicine, for 3,000 years. Saffron also was used for various medical indications by the ancient Persians and Egyptians, and later by the medieval Europeans (Exp. Biol. Med. 2002;227:20-5).

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The traditional uses of saffron are borne out in modern medicine, as this botanical product continues to be known for its antispasmodic, carminative, diaphoretic, emmenagogic, and sedative properties (Acta Histochem. 2009 Mar 26 [doi:10.1016/j.acthis.2009.02.003]). Significantly, pharmacologic studies have shown that saffron has other salubrious benefits, including antioxidant, antimutagenic, and immunomodulatory activities (Asian Pac. J. Cancer Prev. 2004;5:70-6). Much recent research has focused on these properties, as well as on evidence that the spice exhibits anticarcinogenic activity (Exp. Biol. Med. 2002;227:20-5). This column will briefly review the primary investigations of saffron that may potentially lay the groundwork for dermatologic applications.

Anticarcinogenic Actions

In 2004, Das et al. assessed the effects of an aqueous infusion of saffron on a two-stage skin papillogenesis/carcinogenesis mouse model, using 7,12-dimethyl benz[*a*]anthracin (DMBA) to initiate, and croton oil to promote, tumor formation. Saffron application was found to significantly decrease papilloma development during the pre- and postinitiation periods, especially when the saffron was administered during both periods. The authors attributed the inhibitory effects of saffron, at least in part, to the modulatory effects of *C. sativus* on phase II detoxifying enzymes, such as glutathione *S*-transferase, glutathione peroxidase, and superoxide dismutase (Asian Pac. J. Cancer Prev. 2004;5:70-6).

Early in 2009, Das et al. utilized a histopathologic approach to evaluate the chemopreventive effect of aqueous saffron on chemically induced skin carcinogenesis in mice. Animals were divided into five groups: three saffron-treated groups, a carcinogen control group, and a normal control group. Twice a week for 8 weeks, the carcinogen control and saffron groups were administered three topical applications of DMBA followed by croton oil on shaven dorsal skin. Only topical applications of the vehicle (acetone) were given to normal controls. The three saffron groups were orally fed with saffron infusions either before (group A), after (group C), or both before and after (group B) the application of DMBA.

Standard histologic examination revealed that the skin benefited from saffron treatments administered both before and after chemically induced skin carcinogenesis. Specifically, the saffron-fed groups exhibited inhibition of papilloma formation, as well as reductions in the size of papillomas that did form, compared with the control groups. The authors concluded that early treatment with saffron suppresses DMBA-induced skin carcinoma in mice, at least partly because of activation of cellular defense systems, namely cellular antioxidant enzymes (Acta Histochem. 2009 Mar 26 [doi:10.1016/j.acthis.2009.02.003]).

The anticarcinogenic properties of saffron were also demonstrated in much earlier studies. In 1991, Salomi et al. found that topical application of extracts of the common food spices *Nigella sativa* and *C. sativus* suppressed skin carcinogenesis initiation and promotion in a mouse model also using DMBA and croton oil. Specifically, they observed a delay in the formation of papillomas and a lower mean number of papillomas per mouse with application of a 100-mg/kg body weight dose of the extracts. They also evaluated the effects of the extracts on 20-methylcholanthrene (MCA)–induced soft tissue sarcomas in albino mice. Whereas tumor incidence was 100% in MCA-treated control mice, intraperitoneal administration of *N. sativa* and oral administration of *C. sativus* (both at 100 mg/kg body weight) 30 days after subcutaneous administration of MCA (745 nmol/day for 2 days) yielded tumor incidences of 33.3% and 10%, respectively (Nutr. Cancer 1991;16:67-72).

That same year, some of the same researchers, led by Nair, studied the antitumor activity of saffron extract against intraperitoneally transplanted sarcoma-180 (S-180), Ehrlich ascites carcinoma (EAC), and Dalton's lymphoma ascites (DLA) tumors in mice. The life spans of S-180, EAC, and DLA mice were increased respectively by 110.0%, 83.5%, and 112.5%, respectively, compared with baseline life spans, as a result of the oral administration of 200 mg/kg body weight of the saffron extract. In vitro, the extract was cytotoxic to S-180, EAC, DLA, and P38B tumor cells. The authors concluded that these results suggest the potential for saffron as an anticancer agent (Cancer Lett. 1991;57:109-14).

Speed Burn Healing

In a recent study of the potential role of saffron in wound healing, investigators compared the treatment of heat-induced burn wounds in rats using saffron pollen extract and silver sulfadiazine. Hot water was used to generate the wound. Rats were divided into four groups and treated with a topical cream control, base, saffron (20%), or silver sulfadiazine (1%) 24 hours after the induced injury.

Researchers measured wound size on day 25 and determined the average wound area to be 5.5, 4.1, 4, and 0.9 cm^2, respectively, in the control, silver, base, and saffron groups. They also found, through histologic comparison, that reepithelialization was significantly augmented by saffron use, compared with wounds treated with other creams. The authors speculated that such wound healing may result from the anti-inflammatory and antioxidant effects of saffron. They concluded that their study indicates the potential efficacy of saffron in enhancing burn wound healing (Keio J. Med. 2008;57:190-5).

Bioactive Components

In 2004, Giaccio evaluated the known constituents of saffron as well as its characteristics (e.g., antitoxic effects, hormonelike effects, and anticarcinogenic properties). Crocetin (8,8'-diapo-8,8'-carotenoic acid), a carotenoid and one of the main active ingredients in saffron, was of particular focus. This carotenoid is known to enhance oxygen's capacity to diffuse through liquids, including plasma, and has been shown to increase alveolar transport and cerebral and pulmonary oxygenation. Notably, crocetin also suppresses skin tumor promotion in mice and exhibits other anticarcinogenic properties, which are typically ascribed to its antioxidant activity. Although Giaccio highlighted the significant properties of a key constituent of saffron, the author acknowledged that the promising results associated with crocetin have been identified in vitro or in laboratory animals, but not in humans (Crit. Rev. Food Sci. Nutr. 2004;44:155-72).

In 2005, Assimopoulou et al. reported on a *C. sativus* extract (including crocin and safranal, two bioactive components). They found that a methanol extract of saffron demonstrated significant antioxidant activity against the 1,1-diphenyl-2-picrylhydrazyl radical. Crocin exhibited greater radical scavenging activity than safranal, but the scavenging capacity of the latter compound was still noted to be high. The investigators concluded that saffron has the potential for functional uses in foods, beverages touted for antioxidant activity, and medical purposes, namely in pharmaceutic and cosmetic formulations intended to confer antioxidant and antiaging activity (Phytother. Res. 2005;19:997-1000).

Conclusion

Although saffron has a long history of traditional uses, it is no turmeric in terms of the body of modern research and evidence. Nevertheless, current scientific investigations appear to be promising, suggesting a significant potential for the contemporary uses of this spice in medical practice. The data supporting saffron's antioxidant properties and successful topical use in animal models are encouraging. That said, while saffron is used as an oral supplement and in Ayurvedic medicine, much more research is necessary to determine its efficacy and effectiveness in topical skin care. ■

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Sclerotherapy Microfoam for Varicose Veins on the Horizon

AUSTIN, TEX. — A new microfoam in trials in the United States holds promise for sclerotherapy, said Dr. Girish Munavalli, who also discussed other techniques currently available for addressing varicose veins.

It is important to address these veins, as they are indicative of venous insufficiency and saphenous reflux, Dr. Munavalli of Charlotte, N.C., said at the annual meeting of the American College of Mohs Surgery.

Some 60% of the U.S. population has varicose veins, and the frequency increases with age. Approximately 6 million workdays are lost annually because of complications from varicose veins, which can include venous leg ulcers, he said. Current treatment options include surgery (ligation and stripping); endovenous heat ablation; sclerotherapy; and a newer device, called ClosureFAST (VNUS Medical Technologies), which ablates the veins with a radiofrequency catheter. He said that he tends not to use lasers for sclerotherapy.

Dr. Munavalli is currently investigating the new microfoam, which is being used in Europe. It "is a really interesting technique. Hopefully, we'll get [Food and Drug Administration] approval soon," he said.

The product is contained in a can that holds air, but with less nitrogen than room air. When the sclerosant is pumped through the can, it creates much smaller bubbles, which increases the surface area of contact. The microfoam is thicker, compared with a sclerosant that's mixed with room air, said Dr. Munavalli. It still should be administered with ultrasound guidance.

In addition to being an investigator for the microfoam, Dr. Munavalli disclosed that he is on the speakers bureau and is a consultant for DUSA Pharmaceuticals.

—Alicia Ault