Cosmeceutical Critique

Angelica: Part II

Besides *Angelica sinensis*, discussed last month, other species of *Angelica* have been studied for their medicinal potential, and, gradually, these species have been introduced into topical formulations.

Antitumor Activity

In a 2005 study, mice with highly metastatic drug-resistant tumors were used to test the effects of various herbal compounds on tumor growth and metastasis. Although the focus of the study was stilbene compounds, investigators found that two chalcone derivatives from *Angelica keiskei* roots inhibited tumor growth and metastasis. The chalcone derivatives worked by suppressing tumor-induced neovascularization and/or reducing the immune suppression brought on by tumors (In Vivo 2005;19:37-60).

BY LESLIE S. BAUMANN, M.D.

Chalcone extracts of *A. keiskei* root, also known as ashitaba, which is consumed as a vegetable in Japan, also exhibited antitumorigenic activity in the two-phase mouse skin cancer model, in which carcinogenesis is induced by 7,12-dimethylbenz[*a*]anthracene (DMBA) and promoted by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) (Planta Med. 1991;57:242-6).

In another study, xanthoangelol, a major chalcone constituent of *A. keiskei*, was found to dose-dependently decrease the survival rates of human neuroblastoma (IMR-32) and leukemia (Jurkat) cell lines. The findings indicated that the angelica component induced apoptosis by activating caspase-3 in neuroblastoma and leukemia cells without involving Bax/Bcl-2 proteins. The investigators concluded that xanthoangelol has potential as an agent against these cancers (Biol. Pharm. Bull. 2005;28:1404-7).

Other *Angelica* species besides keiskei and sinensis have shown antitumorigenic activity. Constituents of the Japanese drug shi-un-kou, which contains *A. acutiloba*, have been evaluated in assays. *A. acutiloba* alone and in combination with another constituent, *Macrotomia euchroma*, exhibited inhibitory effects, including reduced cytotoxicity, on Epstein-Barr virus activation induced by the tumor promoter TPA. The authors reported that a subsequent in vivo study in mice showed that shi-un-kou significantly inhibited skin tumor formation induced by TPA (Yakugaku Zasshi 1989;109:843-6).

In other research, investigators isolated the coumarin compound decursin from Korean angelica (*A. gigantis*, also known as *A. gigas*) root. They observed that decursin treatment for 24-96 hours strongly inhibited growth and dose-dependently induced apoptosis in human prostate carcinoma cells (Urol. Oncol. 2005;23:379-80).

In addition, another *Angelica* species, *A. archangelica*, exhibits antitumorigenic properties. Investigators evaluated the in vitro and in vivo effects of *A. archangelica* leaf extract on the growth of Crl mouse breast cancer cells. In vitro, the extract was found to be mildly antiproliferative. In the in vivo segment of the study, 11 of 20 mice were injected with *A. archangelica* leaf extract, and 9 of them developed no or small tumors, whereas control mice developed tumors that were significantly larger. The antitumor properties of *A. archangelica* extract could not be attributed to the antiproliferative characteristics of the furanocoumarins in the extract (In Vivo 2005;19:191-4).

Significant antiproliferative activity has also been identified in the tincture of *A. archangelica*, using the human pancreas cancer cell line PANC-1 as a model. Investigators ascribed most of the antiproliferative activity to imperatorin and xanthotoxin, the two furanocoumarins most prevalent in the *A. archangelica* tincture (Z. Naturforsch. [C] 2004;59:523-7).

Dermatologic Potential

In addition to antitumorigenic activity, several *Angelica* species have exhibited properties pertinent to clinical dermatology. Hwaotang, a traditional Korean formulation that combines seven herbs, including *A. gigas*, exerts anti-inflammatory effects related to the inhibition of human neutrophil functions and of nitric oxide and prostaglandin E2 production (Immunopharmacol. Immunotoxicol. 2004;26:53-73).

In a study of the anti-inflammatory activity of a new formulation containing *Synurus deltoides* and *A. gigas* extracts, along with glucosamine sulfate, the medication (SAG) dose dependently inhibited ear edema in mice induced by arachidonic acid and TPA. Prostaglandin E2 production associated with mouse skin lesions was also significantly reduced by SAG, as well as by treatment with *S. deltoides* extract alone. The authors acknowledged that although SAG is not as potent as anti-inflammatory products in widespread use, this *A. gigas*–containing preparation has potential benefits as a neutraceutical therapy for inflammatory conditions (Arch. Pharm. Res. 2005;28:848-53).

A study of herbs used in traditional Chinese and Japanese medicine to treat acne revealed that the ethanol extract (0.01%) of *Angelica dahurica* substantially inhibited neutrophil chemotaxis, at a level comparable to that of erythromycin (0.01%). In the same study, *Rhizoma coptidis* displayed a stronger antilipogenic effect than did retinoic acid (0.01%), and *Glycyrrhiza glabra* (licorice) showed significant antibacterial activity against *P. acnes*. These results led the researchers to conclude that a formulation containing all three herbs would have potential in the prevention and treatment of acne (Skin Pharmacol. Appl. Skin Physiol. 2003;16:84-90). *A. dahurica*, which also contains lactones and psoralen, and has been used traditionally to treat psoriasis and for its reputed antihistamine effects.

In a study evaluating extracts from 15 plants used in traditional Chinese medicine to treat topical inflammations, investigators focused on the inhibitory effects on enzymes that are therapeutic targets in cutaneous conditions, specifically 5-lipoxygenase, cyclooxygenase, and elastase. Four plant species, including *A. dahurica* and *A. pubescens*, inhibited elastase in intact leukocytes and platelets (J. Pharm. Pharmacol. 2003;55:1275-82; Planta Med. 1998;64:525-9). In addition, *A. pubescens* has been found to confer analgesic and anti-inflammatory effects (Planta Med. 1995;61:2-8). One of the main active components isolated from *A. pubescens*, osthole, a coumarin compound, has also been shown to exert a nonspecific relaxant effect on the trachea of guinea pigs (Naunyn Schmiedebergs Arch. Pharmacol. 1994;349:202-8).

At the Store

Zestra Feminine Arousal Fluid (Zestra Laboratories Inc.) is a topical botanical formulation containing *A. archangelica* along with borage seed oil, evening primrose oil, ascorbyl palmitate, and alpha tocopherol. The product is intended to enhance female sexual pleasure and arousal.

Investigators conducted a randomized, double-blind, crossover study to assess the efficacy and safety of Zestra in 10 women with and 10 women without female sexual arousal disorder. Using questionnaires, participants reported on a range of sexual functions pertaining to home use of the formulation. The results indicated statistically significant overall improvements in sexual function in both test groups, compared with placebo (J. Sex Marital Ther. 2003;29 [Suppl 1]:33-44).

Conclusions

A wide range of *Angelica* species possess properties found to be of medical, including dermatologic, benefit. In addition to *A. sinensis* (discussed in this column in August), *A. archangelica*, *A. dahurica*, and *A. gigas* have been used successfully in traditional herbal medicines, and research is ongoing on these and other species, including *A. keiskei*, *A. pubescens*, and *A. acutiloba*.

While the overall body of research is slim on the efficacy of these herbs, the extant evidence supports further investigation and provides reasons for optimism. In the meantime, as is typical in the case of myriad botanic ingredients, there are several unproven formulations available to consumers that contain botanical cocktails including the biologically active *Angelica* species. ■

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Experience May Be Dispelling the 'Old Wives' Tales of Botox

BY BETSY BATES
Los Angeles Bureau

Santa Monica, Calif. — In the early days of cosmetic botulinum toxin type A therapy, rumors greatly outnumbered scientific facts about its safety, storage, and storied effect on furrowed brows and deep crow's feet.

The faculty at a recent cosmetic dermatology seminar sponsored by Skin Disease Education Foundation helped to put some of these myths to rest.

► **Botox is deadly.** Among 28 deaths reported to the Food and Drug Administration from December 1989 to May 2003, none involved cosmetic use of Botox (J. Am. Acad. Dermatol. 2005;53:407-15). Indeed, of 16 deaths recently highlighted by citizens' groups, all involved serious disorders treated with huge volumes of Botox, said Dr. Allan Wirtzer, a dermatologist in private practice in Sherman Oaks, Calif.

Among the potentially deadly uses of Botox is treatment of severe cervical dystonia, which can lead to spread of the toxin to the esophagus, prompting dysphagia or aspiration pneumonia.

► **Book prewedding Botox sessions on Friday afternoons.** Disappointed brides and furious mothers-in-law will blame you for the wedding pictures if you schedule cosmetic procedures too close to the ceremony, said Dr. Mitchell Goldman, a dermatologist in private practice in La Jolla, Calif. Botox's full effect takes 5-6 days, and unexpected bruising may need time to heal.

► **Avoid freezing.** The refrigerator is the place for Botox, but Dr. Richard Glogau, a dermatologist in San Francisco, may have chipped away at the myth that freezing "will degrade the molecule," when Botox that was frozen by mistake worked just fine on his patients, Dr. Goldman said.

► **Save the paralysis for the muscles.** There was a day when patients were told to sit perfectly upright, avoid exercise, and cancel air travel plans for hours after Botox injections. These precautions are "just old wives' tales—such ridiculous stuff," said Dr. Goldman.

Dr. Wirtzer has served as a consultant for Medicis, distributor of Reloxin (botulinum toxin type A, not approved in the United States). Dr. Goldman has received grant support from, and served as a consultant and speaker for, Allergan Inc., maker of Botox.