

COSMECEUTICAL CRITIQUE

Ferulic Acid

Ferulic acid (4-hydroxy-3-methoxycinnamic acid) is pervasive in the plant world. It is present in the cell walls of grains, fruits, and vegetables, where it is conjugated with mono-, di-, and polysaccharides and other compounds (Biochem. Biophys. Res. Commun. 1998;253:222-7; Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub. 2003;147:137-45; J. Sci. Food Agric. 2004;84:1261-9; Free Radic. Biol. Med. 1996;20:933-56).

Derived from the metabolism of phenylalanine and tyrosine (Biochem. Biophys. Res. Commun. 1998;253:222-7; Free Radic. Biol. Med. 1992;13:435-48), ferulic acid is prevalent in whole grains, spinach, parsley, grapes, and rhubarb. Dietary ferulic acid is now considered a significant antioxidant substance (Appl. Environ. Microbiol. 2004;70:2367-72). This potent herbal constituent also has been incorporated into cosmetic lotions and other topical products for the photoprotection it confers (Free Radic. Biol. Med. 1992;13:435-48).

Ferulic acid belongs to the polyphenolic compounds known as hydroxycinnamic acids, which also includes caffeic acid, *p*-coumaric acid, and cinnamic acid. These molecules are known to confer cutaneous benefits (J. Cosmet. Sci. 2002;53:321-35). Hydroxycinnamic acids are typically included in sunscreen formulations.

In terms of direct benefit to the skin, ferulic acid is one of the more promising botanical ingredients. It is a potent antioxidant, protecting skin from UVB-induced erythema (Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub. 2003;147:137-45). It also strongly absorbs UV, like its related compounds (Int. J. Pharm. 2000;199:39-47). And phospholipid membranes are protected by ferulic acid from UV-induced peroxidation as the lipid peroxidative chain reaction is interrupted (Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub. 2003;147:137-45; J. Sci. Food Agric. 1999;79:476-80).

Antineoplastic Action

In a study of the inhibitory effects of three phenolic compounds on benzo[*a*]pyrene-

and 7,12-dimethylbenz[*a*]anthracene-induced neoplasia in mice, ferulic acid and chlorogenic acid were active—although less so than ellagic acid—against lung carcinogenesis, but were ineffective against skin tumor formation (Carcinogenesis 1983;4:1651-3).

Since that study, the literature has added strong evidence of ferulic acid's oral and topical benefits, particularly its protective effects against cancer.



BY LESLIE S. BAUMANN, M.D.

The inhibitory effects of the topical application and oral administration of *Ixora javanica* flower extract on the growth and delayed onset of various kinds of tumors in mice were attributed, in a study nearly 15 years ago, to the active compound in the extract, namely ferulic acid (Cancer Lett. 1991;60:253-8). The phenolic nucleus and extended side chain conjugation of ferulic acid account

for the compound's facility in forming a resonance-stabilized phenoxy radical, to which its antioxidant activity is attributed (Free Radic. Biol. Med. 1992;13:435-48).

Previously, the topical application of ferulic acid was found to inhibit by 46% the induction of ornithine decarboxylase activity by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) in female CD-1 mice. Similar treatment of mice with ferulic acid together with TPA also inhibited the number of TPA-induced tumors per mouse in a dose-dependent manner (Cancer Res. 1988;48:5941-6). And in a study a decade ago, the topical application of a dehydrogenation polymer of ferulic acid inhibited TPA-induced tumor promotion, although a monomeric ferulic acid failed to exhibit the same inhibitory effect in female ICR mice (Carcinogenesis 1994;15:2069-71).

Phenolic antioxidants, including ferulic acid, fed to male F344 rats significantly lowered the incidence of tongue neoplasms (squamous cell papilloma and carcinoma) and preneoplastic lesions (hyperplasia and dysplasia). The researchers concluded these compounds show promise as chemopreventive agents in the tongue, skin, and other organs (Carcinogenesis 1993;14:1321-5).

In a study evaluating the potential of dietary polyphenols as anticarcinogenic

agents, ellagic acid, tannic acid, caffeic acid, and ferulic acid were combined with phorbol-12-myristate-13-acetate or mezerein and were topically applied to mice. The results showed significant protection against skin tumors induced by 7,12-dimethylbenz[*a*]anthracene under in vivo and in vitro conditions (Nutr. Cancer 1998;32:81-5).

Sun Protection

The vitamin E/ferulic acid compound alpha-tocopheryl ferulate (alpha-TF) has the capacity to absorb UV radiation, thereby maintaining tocopherol in a stable state. Thus, researchers investigated whether alpha-TF can act as a depigmenting agent and antioxidant to improve and prevent UV-induced facial hyperpigmentation.

The researchers studied the effects of alpha-TF on cultured human melanoma cells and normal human melanocytes in vitro, and found that alpha-TF inhibited melanization significantly better than arbutin, kojic acid, ascorbic acid, and tranexamic acid. The investigators suggested that alpha-TF has potential as a whitening agent, and hypothesized that it acted by indirectly inhibiting tyrosine hydroxylase activity (Anticancer Res. 1999;19:3769-74).

In related studies, most of the same researchers determined alpha-TF inhibits the biologic responses prompted by reactive oxygen species (Br. J. Dermatol. 1999;141:20-9) and may mitigate damage induced by active oxygen species, thus helping to suppress or decelerate skin carcinogenesis (Anticancer Res. 1999;19:3769-74).

Based on in vitro tests of the capacity of ferulic and caffeic acids to permeate excised human skin, researchers evaluated the capacity of the same organic acids to reduce UVB-induced erythema in healthy human volunteers. Dissolved in saturated aqueous solution (pH 7.2), both compounds conferred significant cutaneous protection.

Ferulic acid—which is more lipophilic and thus better able to penetrate the stratum corneum—and caffeic acid were assessed as worthy photoprotective agents in topical formulations and judged to be unaffected by the pH of the product into which they might be incorporated (Int. J. Pharm. 2000;199:39-47).

In a recent study of the free-radical scavenging abilities of ferulic acid and eugenol

that may summarize current thinking on this potent phenolic compound, ferulic acid was deemed an effective antioxidant (Anticancer Res. 2002;22:2711-7). The investigators concluded it may be useful in preventing cell damage by free radicals.

Buttressing such claims is a just-published study showing the addition of 0.5% ferulic acid to a solution of 15% L-ascorbic acid (vitamin C) and 1% alpha-tocopherol (vitamin E) stabilized the formulation and, more significantly, rendered the topically applied formulation a much better skin-protective agent, doubling photoprotection to skin from fourfold to eightfold (J. Invest. Dermatol. 2005;125:826-33).

The authors of this study found the addition of ferulic acid conferred a synergistic effect, greatly enhancing the existing synergistic effects seen in the combination of vitamins C and E, and further supporting research published by other investigators last year, which highlighted synergistic relationships between ferulic acid, vitamins C and E, and beta-carotene (J. Agric. Food Chem. 2004;52:2411-20).

Authors of the more recent study speculate that a topical antioxidant formulation combining vitamins C and E with ferulic acid in a broad-spectrum sunscreen would be an optimal way to protect skin from sun damage via a topically applied product (J. Invest. Dermatol. 2005;125:826-33).

Ferulic acid is found in SkinCeuticals C E Ferulic and in small amounts in Murad Raspberry Face Wash.

Conclusion

Significant antioxidant, photoprotective, and anticarcinogenic properties have been seen with ferulic acid. The cutaneous benefits associated with this phenolic compound continue to be borne out by research. Given advances in combining antioxidant ingredients for optimal effects, I am optimistic ferulic acid will be a significant component in the armamentarium against photoaging and skin cancer. ■

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Cross-Polarized Light Beats UV for Visualizing Asian Skin

BY PATRICE WENDLING
Chicago Bureau

PARIS — Cross-polarized light appears to be the most accurate and useful method to enhance the definition of pigmented lesions in Asian skin, Stephanie Nouveau, Ph.D., reported in a poster at the Fourth International Academy of Cosmetic Dermatology World Congress.

Ultraviolet (UV) light has been used for years to document skin disorders on patients with photo type I-III skin, but it had not been evaluated and compared with

other existing methods for Asian patients.

Cross-polarized light has been shown to be useful in white skin in published studies and at L'Oréal Recherche in Clichy, France, where Dr. Nouveau is a researcher.

In the multicenter study, a set of three standardized photographs were taken of 304 Chinese women aged 18-76 years under normal, ultraviolet, and cross-polarized light using a stereotactic face device developed by Canfield Scientific Inc., Fairfield, N.J.

Compared with normal light, UV light enhanced visualization of pigmentary dis-

orders only in women aged 30 years or younger with fair skin. UV light did not offer any significant improvement in women aged 31 years or older with wrinkles or darker skin.

Compared with normal light and UV light, cross-polarized light enhanced assessment in 95% of the studied women, independent of patient age, wrinkle grading, and skin tone.

Researchers evaluated small facial spots less than 3 mm in diameter and found that 42% of women had the highest clinical score on a scale of 0 to 5 using normal light.

A total of 76% of women achieved that score when cross-polarized light was used.

Similarly, the prevalence of large (mask-like) hyperpigmented macules was 18% when normal light pictures were assessed, and 33% at the time of cross-polarized light assessment.

The stereotactic face device, developed more than a decade ago, is in worldwide use mainly by dermatologists who participate in research trials and at research centers. That shouldn't discourage dermatologists from considering this technology for their practice, she said. ■