Apigenin

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**Cosmeceutical Critique**

**Apigenin**

Apigenin (3,5,7-trihydroxyflavone) is a low-toxic, nonmutagenic plant flavonoid that is widely found in herbs (endive, clove, and German chamomile), fruit (apples, cherries, and grapes), beverages (tea and wine), vegetables (broccoli, celery, lettuce, onions, parsley, and tomatoes), and propolis (Skin Pharmacol. Appl. Skin Physiol. 2002;15:297-306; Eur. J. Cancer 1996;32A:146-51; J. Cell Biochem. [Suppl.] 1997;28-9; 39-48).

Apigenin shows promising chemopreventive activity against skin cancer (J. Pharm. Sci. 1997;86:721-9) and has demonstrated antioxidant and anti-inflammatory properties (Skin Pharmacol. Appl. Skin Physiol. 2001;14:373-85). It is also believed to be partly responsible for the soothing, antispasmodic, anxiolytic activity that has been attributed to chamomile (Planta Medica 1995;61:213-6).

**Antitumor Actions in Animals**

In a series of studies conducted almost 2 decades ago, the topical application of apigenin to Senecio mice inhibited, in a dose-dependent manner, skin tumorigenesis initiated by 7,12-dimethylbenz[a]anthracene (DMBA) and promoted by 12-O-tetradecanoylphorbol-13-acetate (TPA). In the first study, 48% of DMBA/TPA-treated mice developed carcinomas by 33 weeks after DMBA initiation, but no carcinomas occurred in the DMBA/apigenin/TPA-treated groups. In the second study, apigenin-prolonged the latency period of papilloma formation by 3 weeks and dose dependently reduced papilloma incidence. Apigenin also significantly inhibited carcinoma incidence and reduced the number of tumors. In addition, the researchers concluded that apigenin inhibited the tendency to reduce conversion of papillomas to carcinomas (Carcinogenesis 1996;17:2367-75).

In another study of apigenin’s inhibitory influence on skin tumorigenesis, investigators found, using DNA flow cytometric analysis, interruptions in the cell cycle. Keratinocytes cultured for 24 hours in apigenin-containing medium induced a G2/M arrest in two mouse skin-derived cell lines, C50 and 308, and in human HL-60 cells. This effect was fully reversible after an additional 24 hours in apigenin-free medium (Carcinogenesis 1996;17:2367-75).

Subsequent research from the same laboratory provided evidence that apigenin can induce G1 arrest in human diploid fibroblasts by inhibiting cyclin-dependent kinase 2 (cdk2) activity and phosphorylation of retinoblastoma protein, and by inducing the cdk inhibitor p21/waf1.

These activities, the researchers wrote, may mediate the flavonoid’s in vivo chemopreventive activities (Mol. Carcinog. 1997;19:74-82).

The presence of research on this botanical antioxidant points toward anti-carcinogenic activity. In a study evaluating 15 flavonoids for their effects on morphologic changes in soft agar and cellular growth in vitro, flavonol-transformed NIH3T3 cells, only apigenin, kaempferol, and genistein had a reversing effect on the transformed morphology of these cells. The researchers concluded that the suppression of protein kinase C activity and nuclear oncogene expression might contribute to the molecular mechanism of activity exhibited by apigenin (as well as curcumin) in its inhibition of TPA-induced tumor promotion (J. Cell Biochem. [Suppl.] 1997;28:9-93-48).

Other authors have expressed optimism that apigenin will show a broad spectrum of chemopreventive effects by influencing various molecular targets that affect pathways in the cell (J. Nutr. 2003;133:1800S-45).

**Alternative Sunscreen?**

In a study aimed at ascertaining the efficacy of apigenin as a chemopreventive agent against UV-induced skin cancer as well as DNA damage in a cell-free system, investigators found that apigenin treatment for 12 hours before and after 1 hour of UVB exposure inhibited 25%-45% of ornithine decarboxylase activity. Further, apigenin treatment of SKH-1 mouse skin before each UVB exposure lowered cancer incidence (52%-65%) and increased tumor-free survival, compared with control mice (Anti-cancer Res. 1997;17:85-91).

Of particular interest related to several promising studies is the speculation among some authors that apigenin may represent an alternative sunscreen agent for humans (Mol. Carcinog. 1997;19:74-82; Carcinogenesis 1996;17:2367-75).

For an apigenin formulation to prevent skin cancer, though, it has been determined that the apigenin must be delivered into viable epidermis (Pharm. Res. 1996;13:1710-5). In vivo skin penetration studies of the flavonoids apigenin, luteolin, and apigenin-7-O-beta-glucoside demonstrated several years ago that the compounds were adsorbed at the skin surface, but also penetrated into deeper layers (Pharmazie 1994;49:509-11).

**Down the Road**

The stage may be set for apigenin to be included in formulations, because, in addition to the expanding body of evidence indicating its anticarcinogenic properties, recent work has shown apigenin’s potential as an antiaging treatment.

Researchers focusing on identifying anti-titphotogening assays compared the antioxidant activity and inhibitory effects on matrix metalloproteinase-1 (MMP-1) of the extracts of a marine plant, Zostera marina L. These extracts contained apigenin-7-O-beta-glucoside, chrysoeriol, and luteolin. All of the compounds were found to scavenge the 1,1-diphenyl-2-picrylhydrazyl radical and the superoxide radical. These botanical constituents are deemed to have antioxidative activity and inhibitory effects on MMP-1 expression, and are considered promising targets for inclusion in antiaging formulations (Arch. Pharm. Res. 2004;27:177-83).

**Conclusions**

The great upsurge in research and interest in plant polyphenols in recent years has already been characterized by greater understanding of these compounds’ potential health benefits. The body of research on the phenolic flavonoid apigenin is relatively small, with the preponderance of data accumulating in the past 15 years. Apigenin is found in German chamomile and is most likely to be included in dermatologic products featuring chamomile. It is also an active ingredient in propolis. With its promising research profile indicating anticarcinogenic and anti-photaging effects, in vitro and in vivo, which more research regarding this potent antioxidant is likely warranted.

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**Expert Favors Proven Agents Over Peptide Cosmeceuticals**

**By Timothy F. Kirn**

Sacramento Bureau

LAS VEGAS — Dermatologists should tell their patients to be skeptical of “peptide” cosmeceuticals and to stick with proven agents, Dr. Kathy A. Fields, a dermatologist in San Francisco who is a co-winner of the American Society of Cosmetic Dermatology and Aesthetic Surgery’s 2004 award for most promising new agent of the year, said at the American Academy of Dermatology annual meeting.

“Peptides may or may not penetrate the stratum corneum to any great degree, and they need to reach the dermis to be taken up by cells to have their effects,” she said.

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**Dr. Baumann is director of cosmetic dermatology at the University of Miami. To respond to this column, or to suggest topics for future columns, write to Dr. Baumann at our editorial offices via e-mail at sknews@elsevier.com.**