

# Expanding Treatment Options for Photoaging with Botanical Agents

From kinetin to botanical antioxidants, what can dermatologists expect from plant-derived wrinkle-fighters?

By Dee Anna Glaser, MD

To produce appreciable improvement in the signs and symptoms of photodamage using an at-home topical regimen, prescription retinoids are the treatment of choice. As noted last month, OTC topical retinol and related compounds show some promise, but they do not match the efficacy of tretinoin, adapalene, or tazarotene. But patients and physicians wonder if there are any topical OTC options that might provide notable improvement in the signs of photoaging for patients who cannot tolerate or will not undergo retinoid therapy.

## Furfuryladenine

Though results of treatment are not as dramatic as with topical retinoids, furfuryladenine (Kinerase, Valeant) has been shown to provide benefit in the treatment of photoaging and is an option in my practice for patients who cannot tolerate topical retinoids. To date, only a rare patient has been unable to tolerate this product due to irritation.

Furfuryladenine or kinetin is a synthetic cytokinin plant growth hormone that has demonstrated age-retarding properties in plants, although the mechanism of action is not fully understood.<sup>1,2</sup> In vitro studies on human fibroblasts showed that the addition of kinetin delayed the onset and decreased the severity of age-related cell changes.<sup>2</sup> These included alteration in cell size and shape, growth

rates, cytoskeletal structure, macromolecular synthesis, and quantity of lipofuscin. Of note, studies uncovered no potential harmful effects, such as altered normal cell lifespan, increased cell proliferation, or promotion of carcinogenesis.

Studies suggest that optimal effects would result from continuous application of kinetin. The studies showed that in cultures in which kinetin was continuously present, the delay of age-related cellular characteristics was most pronounced; some of these characteristics began to reappear upon removal of kinetin. The same studies suggest kinetin may be a suitable option for patients with the earliest signs of photodamage. Kinetin was more effective at maintaining the youthful characteristics of younger cells than reversing the age-related characteristics of older cells.

Despite these promising in vitro findings and favorable clinical experi-

ence, the literature currently contains no studies to document in vivo efficacy of furfuryladenine. Proprietary data on file with Valeant (McCullough and Weinstein) demonstrates improvement in the categories of skin texture, color,

blotchiness and fine wrinkles after 24 weeks of twice-daily application of 0.01%, 0.05%, or 0.10% furfuryladenine among virtually all 96 study participants. Average improvements ranged from 17 to 63 percent over baseline. A demonstrated mean decrease of 26 percent in transepidermal water loss (TEWL) after 24 weeks of use suggests that furfuryladenine improves barrier

function. Fewer than one percent of patients reported erythema, edema, dryness, peeling, burning/stinging, or pruritus.

## Botanical Antioxidants

Kinerase has become a popular OTC anti-aging treatment. Other plant-based agents—primarily botanical antioxi-

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dants—are also available. They are worth reviewing because they show promise, though they are not first-line anti-wrinkle treatments. As described below, some of these agents are already incorporated into skin care products not only for potential effects on the skin, but as preservatives and coloring agents.

Like other antioxidants, botanical antioxidants scavenge reactive oxygen species. The many botanical antioxidants available are generally classified into one of three categories: carotenoids—related to vitamin A, flavonoids, and polyphenols. The flavonoids have a polyphenolic struc-

ture and are reported to provide UV protection and metal chelation in addition to antioxidant properties. The large class of polyphenols contains rosmarinic acid (rosemary), hypericin (Saint John's wort), and oleuropein (olive leaf).

**Curcumin.** This polyphenol is found in the turmeric root, which is used as a yellow coloring for natural foods and skin care products. Because yellow coloring in cosmetics is generally undesirable, off-white tetrahydrocurcumin is usually added. Tetrahydrocurcumin is a hydrogenated form of curcumin that offers antioxi-

dant properties and helps preserve lipids in moisturizers.<sup>3</sup>

**Genistein.** The cutaneous effects of several soybean-derived flavonoids, called isoflavones, may be linked to estrogenic effects, especially for postmenopausal women. Genistein, one specific isoflavone, was found to increase collagen gene expression in cell culture.<sup>3</sup>

**Pycnogenol.** An extract of French marine pine bark, pycnogenol can reduce the vitamin C radical to the active form of vitamin C, which in turn helps to regenerate vitamin E to its active form.<sup>3</sup> The water-soluble liquid has demonstrated no allergenicity or chronic toxicity.<sup>3</sup> It is sold as an oral supplement touted to improve the appearance of photoaged skin; topical application of the product purportedly augments this effect.

**Silymarin.** An extract of the milk thistle plant, which belongs to the aster family, silymarin contains three separate flavonoids: silybin, silydianin, and silychristine. Together, these strong antioxidants studied topically in hairless mice demonstrated 92 percent reduction of skin tumors following UVB exposure.<sup>3</sup>

## Planting the Seeds

Data so far suggest that botanical antioxidants may play a role in anti-aging therapies, either for their potential effects on skin or their stabilizing and coloring action in skincare formulations. Among plant-derived ingredients, kinetin has shown the greatest promise in the clinic and may be a suitable topical intervention for retinoid-sensitive patients with signs of mild-to-moderate signs of photoaging. 

1. Olsen A, Siboska GA, Clark BF et al: N(6)-furfuryladenine, kinetin, protects against Fenton reaction mediated oxidative damage to DNA. *Biochem Biophys Res Commun* 265:499-502, 1999.

2. Rattan SI, Clark BF: Kinetin delays the onset of ageing characteristics in human fibroblasts. *Biochem Biophys Res Commun* 201:665-672, 1994.

3. Draelos ZD. Botanical Antioxidants. *Cosmetic Dermatology* September 2003, 16(9) 46-49.

## New in Your Practice

**Going Once...** If Allergan has its way, the Botox manufacturer may soon add a line of dermal fillers to its product offerings. In a recent move, Allergan proposed to acquire Inamed Corporation with a package whose value totals \$1.45 billion in cash and 17.9 million shares of Allergan. The offer, according to Allergan, is superior to a previous bid by Medicis, which had offered its proposal this summer.

According to a statement from Allergan, the company anticipates cross-marketing and cross-selling opportunities resulting from the acquisition. Many dermatologic cosmetic specialists experienced in the use of dermal fillers already recommend combining Botox therapy with the filling agents in order to enhance results of rejuvenation procedures. In addition to a range of dermal fillers, including Captique, Inamed's products include a minimally invasive surgical device used to treat obesity (the BioEnterics LAP-BAND System).

Inamed has announced that it will consider Allergan's proposal.

**Time-Saving Tip.** The Thermage procedure just became easier and potentially more convenient for both patients and doctors. The company recently introduced the 3.0cm<sup>2</sup> ThermoTip, which clinical studies show enables time savings, reduced costs, and improvement in patient comfort. The 3.0cm<sup>2</sup> tip was available to customers in the US starting last month and globally in January at the same price as the 1.5cm<sup>2</sup> tip.

**Saving Face.** Patients with atopic dermatitis on the face who are allergic to or intolerant of topical corticosteroids may have a new alternative for topical therapy. According to data presented last month at the congress of the European Academy of Dermatology and Venereology and reported by Novartis, 46.5 percent of patients treated with Elidel (pimecrolimus) for six weeks were clear or almost clear of facial eczema compared to just 16.2 percent of patients in the group treated with placebo.