

Medesthetics

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Update on
Cosmetic
Dermal Fillers

Skin
Lightening
And Hydroquinone

David P. Van Dam, MD

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fading

CONTROVERSY

By Stacey A. Burns

The aging of America has resulted in increased requests for a solution to “age spots” or solar lentigines. Sun-induced brown spots combined with those caused by inflammatory disorders, hormones (as with melasma), and drug side effects have created a huge demand for effective treatments. Although approaches include chemical peels, laser therapy and other modalities, this update will focus on the topical products currently available and explore the controversy now surrounding the use of hydroquinone. Experts will address the pros and cons of this drug and we will present some of the available alternatives.

There is no argument that the best way to prevent hyperpigmentation problems is to minimize sun exposure, but treating this common skin condition is now more controversial than ever. The large numbers of aging baby boomers, indications that sunscreens are failing to meet expectations and the U.S. Food and Drug Administration is proposed restrictions on hydro-

Hydroquinone is currently banned in many countries including Japan, the European Union, South Africa and Australia. In August of 2006, the FDA issued a proposal to "establish that over-the-counter skin bleaching drug products are not generally recognized as safe and effective and are misbranded...FDA is issuing this proposed rule after considering

AAD response was, "Evidence of carcinogenicity related to high oral doses of hydroquinone in the mouse and rat species cannot necessarily be extrapolated to the human species."

The FDA also claimed, "Hydroquinone has been shown to cause disfiguring effects (ochronosis, darkening and thickening of the skin) after use of concentrations

SYSTEMS

SERAPHIM SKIN CARE
Rx Whitening Cream, a prescription-only 4% hydroquinone bleach for the skin, and Rx Peel & Bleach Cream for the face with 5% hydroquinone, 1% tretinoin, 1% hydrocortisone. 800.884.8408, www.seraphimskincare.com

DONNELL
Lightening Cleanser formulated with a GABA amino-acid complex to suppress melanin production; Lightening Gel designed to exfoliate hyperpigmented cells; and Brightening Cream with tyrosinase inhibitors. 800.324.7455, www.donnelskin.com

ENVIRON
Evenescence Clarifying Lotion combines niacinamide and sepiwhite-MSH as tyrosinase inhibitors; Evenescence Clarifying Patch combines niacinamide and sepiwhite-MSH in a transdermal patch. 877.337.6227, www.dermaconcepts.com.

YOUNG PHARMACEUTICALS
Kojilac-CHO Skin Lightening Pads & TouchStick combine either 2% or 4% hydroquinone with vitamin C, kojic and salicylic acids plus green tea in a convenient pad and stick form. 800.874.9686, www.youngpharm.com

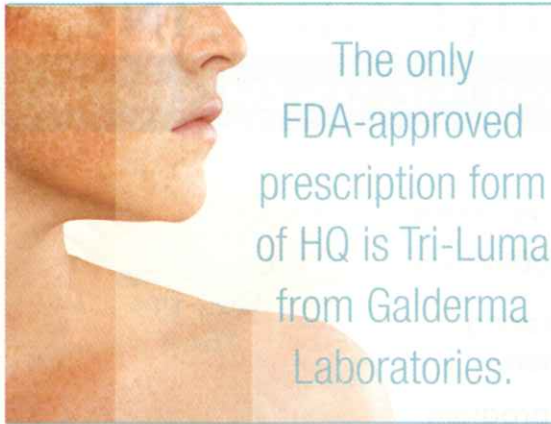
quinone have made hyperpigmentation treatments, especially topical formulations, a hot topic.

Historically, the most effective bleaching creams have contained hydroquinone (HQ). John Kulesza, president of Young Pharmaceuticals states, "[HQ] is the best pharmaceutical for short term treatment of hyperpigmentation. However, it has never been approved for long-term use, nor for use in treating photoaging. A combination of sunscreens and retinoids are best for overall skin health."

new data and information on the safety of hydroquinone."

Response from the dermatological community included a nine-page letter dated December 27, 2006, from Stephen P. Stone, MD, FAAD, president of the American Academy of Dermatology (AAD). The letter addressed the concerns outlined in the FDA proposal in detail. The FDA stated, "Based on evidence of carcinogenicity in animals, FDA cannot rule out the potential carcinogenic risk from topically applied hydroquinone in humans." An excerpt of the

as low as 1% to 2%." The AAD response to this claim was lengthy, first offering a hypothesis to explain why ochronosis was so prevalent in the black, South African populous then continuing with, "in the United States, exogenous ochronosis has been and remains a remarkably uncommon cutaneous disorder...Industry estimates are of at least 10 million users of hydroquinone containing products in the past 40 years. Fifteen case reports of exogenous ochronosis supports the fact that this disease entity occurs infrequently in the



The only
FDA-approved
prescription form
of HQ is Tri-Luma
from Galderma
Laboratories.

United States." As a side note, a 2004 paper published by R.M. Halder, MD and G.M. Richards, MD, reports 30 ochronosis cases in North America.

In a letter dated December 19, 2006, from AGI Dermatics president Daniel Yarosh, several of the

arguments stated by the AAD were reiterated along with the comment that, "Restricting access to hydroquinone, or eliminating it from the marketplace, will not reduce the demand for over-the-counter skin lightening products. The effect of such action, as has been seen in Japan, will be to drive consumers to purchase less effective and much less characterized botanical and chemical lighteners...making scientific study and responsible regulation...very difficult."

Point, Counterpoint

Kulesza, who began his 30-plus year career as a formulating chemist, states a more centrist view: "Based on the history of hydroquinone that I know, this drug is safe for use as directed.

What I mean by 'as directed,' is for short-term use, roughly 12 weeks' duration, specifically for hyperpigmentation."

Kulesza continues, "The FDA does have a valid concern based on the chemistry of HQ, because its structure is only one oxygen atom away from the chemical structure of phenol. Phenol is used in antiseptics to kill living cells. In addition, phenol is chemically related to benzene, a known carcinogen. Therefore with the chemical relationships being so close, the FDA is saying, 'Wait, we should look more closely at how hydroquinone is being used.'"

Ken Smiles, research director at AGI Dermatics believes that HQ will remain the standard for treating hyperpigmentation. "There is a

a theoretical concern regarding metabolites generated when hydroquinone is metabolized by the body, but I've never seen evidence of problems in people. Hydroquinone is much more effective in treating hyperpigmentation than any other therapy and has an excellent, long-term, safety record."

The June 2007 edition of the *Journal of Cosmetic Dermatology* included an abstract of a study introducing the formulation of a less irritating hydroquinone (HQ) cream. Smiles directed the study and explained that the formulation and testing of the new formulation preceded the FDA investigation of HQ, and was conceived to improve patient compliance. The new formulation combines an antioxidant for stability and a biomi-

metic of an herbal extract for skin calming. The study showed overall less irritation than three commercially available HQ products and faster onset of the bleaching effect. The formulation will be marketed as Remergent HQ.

As of publication, the FDA had not issued a final ruling regarding hydroquinone. Should they decide to proceed with the proposed removal of HQ from the market, there may remain a single legal source for the treatment. The only FDA-approved prescription form of HQ is Tri-Luma from Galderma Laboratories.

For those seeking an alternative, there are a number of other ingredients being used in a wide array of products (see photos and descriptions) designed to help

fade brown spots. Most of these, like hydroquinone, act to inhibit the enzyme tyrosinase, which in turn reduces the conversion of DOPA to melanin. They include azelaic acid, which was shown in one South American study to be as effective in treating melasma as 2% HQ; kojic acid; arbutin; and licorice extract (glabridin). Other ingredients such as L-ergothioneine, niacinamide and GABA amino acid complex have also been shown to play a part in inhibiting melanin production. Although many are new, they may prove to be excellent additions to the arsenal against hyperpigmentation. ✦

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