

Next Generation Retinoids



The search for a more tolerable retinoid has led to study of unique delivery systems, novel retinoid molecules, and even botanicals.

BY TED LAIN, MD AND PATRICIA K. FARRIS, MD

>> Tretinoin is the gold standard topical treatment for photoaged skin. Tretinoin improves the appearance of fine lines and wrinkles, surface roughness, and discoloration. Unfortunately, poor tolerability limits the use of tretinoin in some patients, particularly those with sensitive skin. Peeling and redness are well recognized features of retinoid dermatitis, which usually occurs in the first few weeks after starting tretinoin. Those with more sensitive skin may also experience itching, burning, and stinging upon application. It is believed that retinoid dermatitis occurs due to overstimulation of the retinoic acid pathways when supraphysiologic amounts of exogenous retinoic acid (RA) are applied to the skin.

Retinyl esters, such as retinyl palmitate, retinyl acetate and retinyl propionate, retinaldehyde, and retinol have been incorporated into cosmetic formulations and are available as over the counter retinoids. These retinoids are less potent than retinoic acid but can still induce retinoid dermatitis. Retinaldehyde is the most potent, followed by retinol and then the retinyl esters. These retinoids are functionally inactive and require conversion to retinoic acid in the skin before they can activate RA pathways. The retinyl esters (REs) are hydrolyzed to retinol (ROL), which is then oxidized to retinaldehyde (RAL) that is irreversibly oxidized to retinoic acid (RA). Once this conversion occurs, retinoic acid binds to retinoic acid receptors (RAR) within the nucleus, where it modulates gene transcription responsible for epidermal growth and differentiation and collagen homeostasis.

Take Note

Drs. Farris and Lain are founding directors of the Science of Skincare Summit 2021, to be held November 6, 2021 at JW Marriott Essex House in New York.

Registration and more information are available at scienceofskincaresummit.com.



DID YOU KNOW?

The most recent innovation in retinoid delivery is the use of polarity index principles. By utilizing the polarity of specific emollients, retinoids can be delivered gradually to the skin.

The search for a more tolerable retinoid has led to study of unique delivery systems, novel retinoid molecules, and even botanicals. A novel bioengineered double conjugated retinoid touted improved tolerability has recently been introduced in the cosmeceutical market. This molecule undergoes double hydrolysis to release a retinoid and an alpha hydroxy acid (lactic acid). The delivery system is designed to maximize release of the actives and to minimize irritation. In addition to the double conjugated retinoid, also known as AlphaRet®, the finished product contains vitamin C, vitamin E, green tea extract, 10% glycolic acid, hyaluronic acid, squalene, peptides, niacinamide, ceramides and the botanicals portulaca and bisabolol. In a split face study, AlphaRet® cream was compared to tretinoin 0.025% cream and retinol 1% cream. AlphaRet proved non-inferior to prescription strength tretinoin at week 12 for most endpoints (fine lines, erythema, dyschromia and skin tone), yet was alone in its ability to improve hydration at all timepoints. The test cream also demonstrated superior tolerability compared to retinol 1% and tretinoin 0.025%.

Botanical retinoids have also been studied and may act as natural retinol alternatives. Bakuchiol, a meroterpene phenol found in the seeds of *Psoralea corylifolia*, is a functional analogue of retinol as it similarly modulates gene expression. Studies demonstrate an upregulation in type

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I and IV collagen by microarray analysis and an increase in collagen III production by fibroblasts in culture in the presence of bakuchiol. Additionally, clinical studies have confirmed bakuchiol's anti-aging benefits. In a double-blind, twelve-week randomized study, bakuchiol 0.5% cream was compared to retinol 0.5% cream. Both products decreased wrinkle surface area and hyperpigmentation equally, but the bakuchiol cream had superior tolerability. Bakuchiol has also been studied in patients with acne. A patented formulation of 0.5% bakuchiol cream reduced the number of inflammatory lesions and lightened post-inflammatory hyperpigmentation in patients with acne.

Bidens pilosa, a flowering plant in the daisy family, also has retinoid-like activity. *Bidens pilosa* extract is composed of lipids including linoleic, linolenic, oleic, palmitic, and the terpene phytol. Studies have shown that *Biden pilosa* increases extracellular matrix components, such as collagen and elastin, upregulates transcription factors TGF- β , FGF- β and EGF, and increases gene expression for retinoic acid receptor X (RXR). There are no published clinical studies on *Bidens pilosa*, although it has been incorporated into skincare products.

Unique prescription formulations, such as tretinoin lotion (Altreno®), feature a novel polymeric mesh technology with micronized tretinoin, sodium hyaluronate, soluble collagen and glycerin, ensconced in scattered oil droplets in an aqueous hydrogel. This formulation simultaneously releases tretinoin along with moisturizing and hydrating ingredients, thereby reducing dryness and irritation.

Delivery systems such as the microsphere encapsulate and slowly release tretinoin. The microsphere delivery system was used in RetinA Micro® and several over-the-counter retinol products. Nano delivery systems, including liposomes, niosomes, and solid lipid nanoparticles, have also been studied. The most recent innovation in retinoid delivery is the use of polarity index principles. By utilizing the polarity of specific emollients, retinoids can be delivered gradually to the skin. Studies on a retinol 0.5% serum delivered using the polarity index principles demonstrate less irritation under semi-occlusive patch testing compared to a prestige 0.5% retinol cream and a greater self-reported tolerability with regular daily use. ■

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