

This issue reviews skin barrier changes with oral isotretinoin and a rationale for skin barrier therapy

Welcome to SkinTopics™—an ongoing review of selected articles of importance to you.

This issue of SkinTopics™ features a recent review article that appeared in *The Journal of Drugs in Dermatology (JDD)* by James Q. Del Rosso, DO, a practicing dermatologist, clinical researcher, published author of numerous articles and textbook chapters, and Past President of the American Acne & Rosacea Society. In his article entitled “Clinical Relevance of Skin Barrier Changes Associated With the Use of Oral Isotretinoin: The Importance of Barrier Repair Therapy in Patient Management,” Dr. Del Rosso explores the importance of barrier repair therapy in patient management—a topic of growing importance in dermatology today.

The importance of the skin barrier

The epidermal skin barrier performs multiple functions that, collectively, contribute to the maintenance of healthy skin. The central function of the epidermal skin barrier is to maintain physiologic control of water content and flux—known as the permeability barrier—as well as to provide antimicrobial, immunologic, antioxidant, and photoprotective barrier defenses.

The processes that create the permeability barrier occur mainly in the stratum corneum (SC), the uppermost epidermal layer composed of flattened corneocytes embedded in a lipid-enriched intercellular matrix. This matrix is not randomly formed. Rather it is composed of a lipid bilayer that is made up of an equimolar ratio of three predominant physiologic lipids, ceramides, cholesterol, and essential free fatty acids.

When the SC barrier is compromised by exogenous factors, such as use of poorly formulated skin cleansers, topical agents (ie benzoyl peroxide, retinoids, certain vehicles), oral retinoids, or ultraviolet radiation, transepidermal water loss (TEWL) increases and water content declines. The ability of several water-dependent SC enzymes involved in barrier integrity, function, and normal desquamation to

function efficiently is diminished when water content is inadequate, leading to scaling, roughness, fine fissuring, and decreased elasticity of the skin. Scaling occurs as the enzymatic separation of individual corneocytes that allows for visibly imperceptible desquamation is impaired, resulting in clumping of corneocytes, which are visible as flakes or scales on the skin surface. Without correction, signal amplification—induced by cytokines that are produced as a self-repair response—promotes cellular cascades that lead to clinically evident cutaneous abnormalities—some of which include xerosis, desquamative changes, and hyperkeratosis.

“Almost all patients treated with oral isotretinoin develop dose-dependent mucocutaneous side effects. Epidermal barrier damage...is a predictable consequence of oral isotretinoin use.”

— James Q. Del Rosso, DO

Skin barrier integrity and cohesion: effects of oral isotretinoin

Oral isotretinoin, a retinoid used to treat severe recalcitrant cystic acne, predictably alters the structure and function of the epidermal barrier. The use of oral isotretinoin is typically marked by superficial desquamative changes due to decreased corneocyte cohesiveness. Oral isotretinoin also increases TEWL, progressively decreases sebum production, and alters the relative concentrations of sebaceous lipids. Isotretinoin does not appear to alter the composition or relative concentration of physiologic lipids integrated into the lipid bilayer of the SC. Corneocyte dyscohesion—induced by isotretinoin—produces dose-dependent increases in TEWL, which leads to desquamative and xerotic skin changes that are clinically evident in most patients. Repair and maintenance of the SC permeability barrier can inhibit retinoid-induced increases in TEWL, thus reducing clinically visible skin surface changes, such as roughness and dryness.

The effects of oral isotretinoin on the epidermis as reviewed in this article are useful in helping to better understand the alterations involved in the structure and function of the SC, and the consequences that may occur in the absence of adequate repair of the epidermal permeability barrier.

Rationale for the use of barrier repair

Barrier repair therapy (BRT) is shown to reduce TEWL and replenish SC lipids. As a result, permeability barrier integrity and function can be restored. In addition to decreasing roughness and dryness, BRT also repairs microfissures in the SC. This is important as microfissures compromise the natural protection of the skin against bacterial penetration and colonization.

Factors that support BRT selection

Ideally, BRT formulations should provide an optimized balance of occlusivity, humectancy, and lipid restoration. Without occlusive ingredients to retard TEWL, humectants may increase water loss. Lipid replenishment without a humectant to sustain SC water content is less efficient at optimizing the function of the permeability barrier. High humectant concentrations in the absence of agents that provide occlusivity and/or lipid replenishment do not optimize and adequately sustain SC permeability barrier function. Incorporation of the proper combination of components in the BRT formulation is vital. Inclusion of physiologic SC lipids, cholesterol, ceramides, and free fatty acids in the correct concentrations will help to optimize incorporation of these components into the SC as opposed to merely remaining inert on the skin surface, which serves to provide only a short-lived occlusive effect.

"The inclusion of core components in a topical formulation, and in the proper range of concentrations, is fundamental to the creation of a product that helps to restore and sustain stratum corneum structural and functional integrity."

— James Q. Del Rosso, DO

Suggested Reading

Del Rosso JQ, Levin J. The clinical relevance of maintaining the functional integrity of the stratum corneum in both healthy and diseased skin. *J Clin Aesthet Dermatol.* 2011;4(9):22-42.

Loden M. Effect of moisturizers on epidermal barrier function. *Clinics in Dermatology* 2012;30:286-296

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Reference: Del Rosso JQ. Clinical relevance of skin barrier changes associated with the use of oral isotretinoin: the importance of barrier repair therapy in patient management. *J Drug Dermatol.* 2013;12(6):626-631.

What was the clinical relevance of this review article?

The findings in this review article are relevant clinically, as they suggest that newer BRT formulations that incorporate physiologic lipids and other essential components may offer important advantages over traditional moisturizers. These advantages include return of the SC to a more physiologic state and greater substantivity of repair of the permeability barrier. Furthermore, it is recommended that a quality BRT, which reduces TEWL and incorporates physiologic lipids in appropriate concentrations, be used adjunctively from the outset of oral isotretinoin therapy.

Review at a glance

- The epidermal skin barrier performs multiple functions that, collectively, contribute to the maintenance of healthy skin structure, function, and appearance.
- When the permeability barrier becomes compromised by exogenous factors, such as topical or oral retinoid use; or ultraviolet radiation, TEWL increases and the enzymes involved in barrier structure and function are impaired, leading to decreased SC cohesiveness and integrity
- Without correction, signal amplification can produce cascades that lead to clinically evident cutaneous abnormalities – some of which include xerosis, desquamative changes, and hyperkeratosis
- BRT is shown to reduce TEWL and replenish skin surface lipids
- Newer BRT formulations that incorporate physiologic lipids and other essential components at the proper concentrations may offer clinically relevant advantages over traditional moisturizers

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