## BACKGROUND

While glucose is a vital cellular fuel, as we age and our metabolism slows, glycation causes excess glucose molecules to stick to collagen and elastin, leading to cross-linked fibers. This cross-linking forms chemical bridges between these proteins that result in advanced glycation end-products (A.G.E.). Glycated fibers become rigid, less elastic, and have reduced regenerative ability, which leads to damage such as laxity, cracking, and thinning skin. Another major contributor of intrinsic skin aging is the flattening of the dermal epidermal junction (D.E.J.). In young skin, the D.E.J. has the appearance of a mountain range that helps anchor the epidermis to the dermis, forming a network of supportive collagen fibers. As skin ages, fibers in the D.E.J., primarily responsible for the appearance and texture of skin, glycate. In addition glycosaminoglycans (GAGs), the essential molecules responsible for holding water, nutrients and modulating the extra-cellular space in the D.E.J., break down. Both glycation and GAG depletion lead to the degradation of the extra-cellular matrix and the flattening of the D.E.J., resulting in sagging, creping, and severely wrinkled skin.

# **KEY INGREDIENTS**

#### **BLUEBERRY EXTRACT**

Our advanced research group evaluated several different blueberry extracts, screening each for anti-glycation activity, selecting the particular extract in A.G.E. Interrupter for its potent anti-glycation activity, compatibility with other actives in the formula, and efficiency in skin. We currently have two patents pending with this specific ingredient, including one for anti-glycation and another for MMP inhibition. Four percent of the extract was the level found to be most effective in clinical trial.

In a clinical study using fluorescence measurements, blueberry extract in the presence of ribose as a reducing sugar had a similar dose response to positive control aminoguanidine, a potent glycation inhibitor. In addition, in reconstructed skin containing collagen modified by glycation, treatment with blueberry extract diminished CML antibodies (one of the A.G.E. found in chronologically aged skin in-vivo), and returned previously overexpressed biomarkers to a normal pattern of distribution. These results indicate a return to skin's normal morphological structure.

- Inhibits the glycation of collagen
- Normalizes MMP-1 production preventing degradation of healthy collagen types IV and VII (important to D.E.J. integrity)
- Exhibits a pro-matrix effect by stimulating procollagen I and III (important extra-cellular matrix components)

## **PROXYLANE**<sup>TM</sup>

This patented molecule is obtained from xylose produced from beechwood using an environmentally friendly, chemically simple and optimized synthesis process that characterizes this molecule as a "green chemistry product." This innovative ingredient stimulates the synthesis of glycosaminoglycans (GAGs) in the dermis, epidermis, and D.E.J. GAGs modulate the extra-cellular space and the viscosity of the skin and participate in the remodeling of the tissue structure to help repair damage that directly impacts the surface of the skin.

- Proxylane<sup>™</sup> acts like a molecular magnet, attracting GAG components to reconnect and rebuild the network of fibers, proteins, and cells in the D.E.J.
- In cultured fibroblasts, Proxylane<sup>™</sup> stimulates synthesis of collagens IV and VII. Collagen VII plays a crucial role in the structure of the D.E.J.
- Stimulates the synthesis of procollagen I and III by fibroblasts
- Considerably improves cohesion between the dermis and epidermis by increasing the number of anchoring filaments in the D.E.J. and rebuilding D.E.J. structure
- Increases expression of CD44, a hyaluronic acid receptor in the epidermis
- Proxylane<sup>™</sup> is easily biodegradable, non-bioaccumulatable, and non-eco-toxic.

## PHYTOSPHINGOSINE

#### Background

Dry skin occurs in aged skin due to reduced levels of stratum corneum natural moisturizing factor (NMF) derived from filaggrin. The barrier function also weakens due to lower levels of barrier lipids (ceramides, cholesterol, and fatty acids). In order to repair and strengthen the skin's barrier in aged skin, phytosphingosine is effective at the following:

- Reinforcing the skin's barrier by increasing the synthesis of enzymatic and cellular components
- Synthesizing the lipids necessary for barrier function (ceramides, cholesterol)
- Increasing the level of corneodesmosomal components to better structure the stratum corneum
- Facilitating orderly desquamation to maintain healthy skin by increasing the level of desquamatory enzymes
- Increasing the level of filaggrin, the precursor of the natural moisturizing factor (NMF) to make a better natural moisture barrier
- Enhancement of renewal rate of stratum corneum