



VINIFERAMINE®

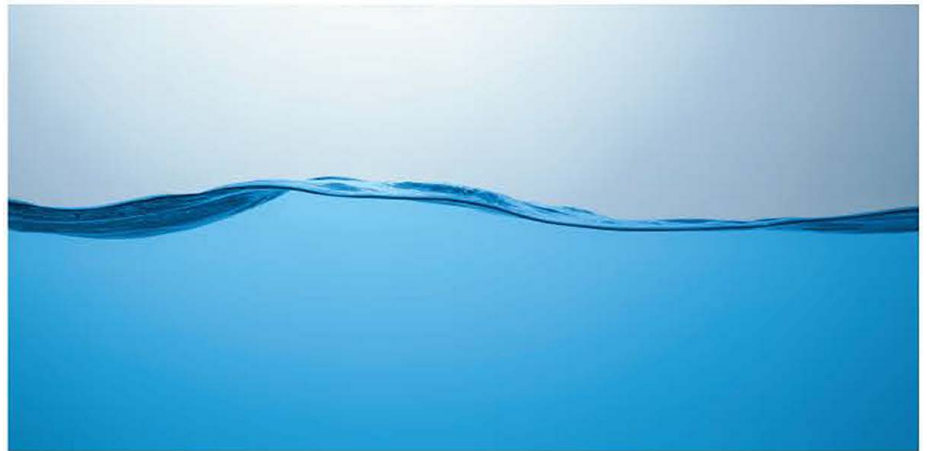
MOLECULES & HEALTH

HEALING THROUGH MODERN SCIENCE WITH SMALL MOLECULE TECHNOLOGIES

The Importance of Skin Glycans

Glycosaminoglycans (GAGs) or glycans are negatively charged molecules composed of repeating disaccharide units. GAGs are important components of the extracellular matrix (ECM), a complex interlocking meshwork found outside of skin cells (and other cells) that includes fibrous proteins such as collagens, elastin and fibronectin. The largest component of the ECM is actually water, which makes up about 80% of the ECM by weight. Connective tissues including skin and cartilage are especially rich in ECM. Two very beneficial GAGs found in skin ECM are non-sulfated hyaluronic acid (HA) and chondroitin sulfate (CS), a more typical GAG that includes a sulfate group. Viniferamine® skin and wound care products contain chondroitin sulfate (CS) and ingredients that protect HA including potent antioxidants.

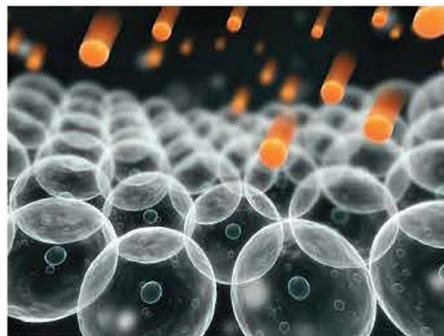
HA, also known as hyaluronan, is actually a critical component of the ECM and is one of the most ubiquitous linear polysaccharides found in nature. As an integral part of the ECM it provides a structural role, as well as many other crucial roles. HA is found in most parts of the body including in the eyes, the synovial fluid of joints and in the skin, where approximately half of the body's total HA is located. HA consists of numerous repeating disaccharide units of glucuronic



acid and N-acetylglucosamine giving it a molecular weight of up to several million daltons. Interestingly, HA is the only GAG synthesized in the cytoplasm of cells at the plasma membrane where it is secreted directly into the ECM.

Scavenging Free Radicals

Because of its negative charge, HA has a high capacity for binding water and electrolytes, which greatly enhances skin hydration and health. Its large size and charge play an important role in



HA modulation of ionic and molecular traffic through the ECM that contributes to cellular signaling. In fact, HA also excludes tissue degrading enzymes from other structural components of the ECM. In addition, HA scavenges free radicals and serves as an important antioxidant in skin, which may be particularly important for protection against solar radiation damage. Furthermore, HA is anti-inflammatory.

Dipotassium Glycyrrhizinate

Viniferamine® skin and wound care products include dipotassium glycyrrhizinate, an important ingredient derived from licorice that has anti-inflammatory activities and that has been shown to protect HA from degradation. In addition, Viniferamine® skin and wound care products include other important anti-inflammatory ingredients including the bene-



Licorice

ficial polyphenols oleuropein, resveratrol, and epigallocatechin-3-gallate (EGCG) from olives, grapes, and green tea, respectively, as well as the important small molecules, melatonin, and L-glutathione.

During inflammation that occurs with tissue injury including UV photodamage, HA levels are increased in skin tissues producing local areas of hydration that facilitate cell mobility and proliferation. In fact, in the early stages of normal wound healing, HA levels are quite elevated (up to 200 fold) promoting cell migration and granulation tissue formation, in contrast to later stages of healing when HA levels decrease as scar tissue is formed. HA regulates

many important physiological functions including cell proliferation, adhesion, migration, differentiation, and wound healing through its interaction with its signaling receptors.

Protecting Against Oxidative Stress

HA has a very high turnover and is naturally degraded by hyaluronidase. With aging, levels of HA decrease. This is partly due to the fact that HA is very sensitive to degradation by free radicals including reactive oxygen species (ROS) that occur during inflammation and with photodamage. Advanced glycation endproducts (AGEs) produced during hyperglycemia that may occur with diabetes have also been found to induce free-radical mediated degradation of HA. Low molecular weight HA degradation products generated by hyaluronidases, mechanical forces and oxidative stress promote inflammation, angiogenesis and tissue regeneration and are normally cleared within 14 days, however, chronic wounds are char-

acterized by low molecular weight HA oligomers that are associated with prolonged inflammation and fibrosis. Viniferamine® skin and wound care products include important antioxidants that counteract oxidative stress including oleuropein, resveratrol, EGCG, melatonin, and L-glutathione.

Chondroitin Sulfate

Viniferamine® skin and wound care products include chondroitin sulfate (CS), another beneficial GAG found in skin. CS consists of repeating N-acetylgalactosamine-glucuronic acid disaccharide units that are sulfated. CS is anti-inflammatory and assumes the role of the main GAG as HA levels are depleted.

It's good to know that Viniferamine® skin and wound care products include ingredients that can protect HA including dipotassium glycyrrhizinate, the ultimate protector of HA from degradation. In addition, CS can help maintain vital roles of HA in skin including wound healing activities when HA levels are low.

References

1. *Curr Med Chem* 2013; 20: 2501-2523.
2. *J Mal Med* 2012; 90: 625-635.
3. *AmJPathol* 2014; 184: 1912-1919.
4. *IntJ Mal Sci* 2014; 15: 18508-18524.
5. *Diab Vase Dis Res* 2014; 11: 92-102.
6. *Oxid Med Cell Longev* 2012; ID 560682:1-8.
7. *J Pineal Res* 2013; 55: 325-356.
8. *IntJ Gen Med* 2011; 4: 105-113.
9. *Evid Based Complement Altern Med* 2012; ID 650514:1-9.
10. *J Dermatol Sci* 2011; 62: 192-201.
11. *Wound Rep Reg* 1999; 7: 79-89.
12. *Exp Dermatol* 2009; 18: 1028-1035.
13. *Pathol Biol* 2015; 63: 32-34.
14. *AmJ Pathol* 2014; 184: 1912-1919.
15. *Ann Plast Surg* 2007; 58: 449-455.

16. *PLOS One* 2015; 10: e0115341: 1-18.
17. *Exp Dermatol* 2008; 17: 713-730.

Disclaimer: These statements have not been reviewed by the FDA. The decision to use these products should be discussed with a trusted healthcare provider. The authors and the publisher of this work have made every effort to use sources believed to be reliable to provide information that is accurate and compatible with the standards generally accepted at the time of publication. The authors and the publisher shall not be liable for any special, consequential, or exemplary damages resulting, in whole or in part, from the readers' use of, or reliance on, the information contained in this article. The publisher has no

responsibility for the persistence or accuracy of URLs for external or third party Internet websites referred to in this publication and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

About the author: Nancy Ray, PhD is the Science Officer at McCord Research. Dr. Ray received her PhD in Biochemistry and Biophysics and was a postdoctoral fellow at NIH, Harvard University and Dana-Farber Cancer Institute, and the University of Iowa. She also earned bachelor of science degrees in Chemistry and Microbiology.

Copyright 2015 McCord Research. All rights reserved
R1371AH 06.15