# Dermatology News

COSMECEUTICAL CRITIQUE

Heparan sulfate

Publish date: January 26, 2017 By: Leslie S. Baumann, MD

The discussion this month focuses on an exciting new ingredient that is showing great promise as a topical antiaging agent. For years we have known that aging skin needs more collagen, elastin, and hyaluronic acid. It is time to add a new player to the antiaging team – heparan sulfate (HS). New studies have shown that lower levels of HS are associated with aged skin. This

is what you need to know.

# Significance of HS

Endogenous HS, an essential glycosaminoglycan (GAG), contributes to skin development and homeostasis, and thus actively promotes skin health. GAGs such as HS and hyaluronic acid are well known as endogenous superhydrators that bind and retain water, thus contributing to skin hydration as well as preserving the structural integrity of collagen and elastin fibers. Specifically, HS and its protein-bound forms (HS proteoglycans such as syndecan, glypican, and perlecan) – the most common constituents on the cell surface and in the extracellular matrix (ECM) – play an important role in cutaneous cell proliferation, migration, communication, and activation as well as collagen fiber development, basement membrane regeneration, granulation tissue formation, and cell adhesion related to wound healing. This results from their capacity to bind, store, present, degrade, and amplify growth factors and cytokines.



Dr. Leslie S. Baumann

is associated with aging.

HS levels in the skin, like growth factors, diminish with age, coincident with the emergence of visible signs of aging.<sup>2</sup> While endogenous HS is too large and highly polar to penetrate the skin to be suitable for topical cosmetic products, HS analogs (also known as low-molecular-weight HS) have been developed in a stable form and appropriate size, charge, and shape to be safely and effectively delivered to the skin. It is thought that these analogs could be associated with the amplification of decreased growth factors signaling, which

Accordingly, mature skin would be potently activated by its endogenous growth factors (at lower concentration) as cell signal is amplified (lower threshold of activation) by HS analogs. When used topically, HS analogs appear to promote the formation of healthy and functional ECM, resulting in firmer, more elastic, and stronger skin. Augmenting the amount of HS in the skin may yield a rejuvenating effect by expanding the skin's ability to hold water and restore

cutaneous homeostasis. Studies with an HS analog have demonstrated that the formulation penetrates into skin, enhancing hydration, reducing transepidermal water loss, and improving the appearance of wrinkles and skin tone. The use of HS analogs or mimics, known as matrix therapy, has been shown to be effective clinically in cutaneous and corneal healing formulations, exhibiting proof of concept in humans, according to Barritault et al.

Matrix therapy also has been employed successfully in plastic and aesthetic procedures. Zakine et al. assessed the impact of using ReGeneraTing Agents (RGTA) – biodegradable polymers designed to mimic HS in the ECM of damaged tissue – in 17 patients with breast hypertrophy who underwent mammoplasty. Patients received topical treatment on one breast 1, 4, 8, and 11 days after surgery. The investigators also evaluated a different group of 50 patients after centrofacial lifting. These patients received RGTA drops bilaterally in the treatment area after surgery. Inflammation, hypertrophic scars, and pruritus were noted less frequently for the breasts treated with RGTA. Similarly, in patients receiving a centrofacial lift, scar inflammation, edema, and bruising were significantly less frequent in the treated group (10%), compared with the untreated group (90%).<sup>4</sup>

In 2015, Gallo et al. reported that 15 patients using a new HS analog formulation in an 8-week study displayed improvement in various skin metrics, including hydration, firmness, elasticity, barrier function, and the appearance of fine lines and wrinkles. The investigators concluded that photodamaged skin may benefit from the use of novel topically applied products containing low-molecular-weight HS.<sup>1</sup>

The synthetic heparan sulfate Cacipliq20 was reported in 2015 to have been used successfully to treat a chronic lower-extremity ulcer in a 22-year-old male patient with Stewart-Bluefarb syndrome,<sup>5</sup> and in 2016 to treat a refractory sickle cell ulcer, with the encouraging outcome demonstrated by complete wound coverage and significant improvement in pain score.<sup>6</sup> In 2012, Polieri et al. showed that HS 1% cream was comparable or more effective than glycosaminoglycan-polysulphate gel in alleviating the signs and symptoms of hematomas or subcutaneous hematic extravasations in a study with 96 white men and women.<sup>7</sup>

# Conclusion

Heparan sulfate does appear to be a novel viable antiaging option. Endogenous heparan sulfate

is involved in skin defense against pathogens, dehydrated/dried skin, redness, and wound healing. Theoretically, then, HS analogs should be able to modulate these processes. More research is necessary to determine if this is the case, however. In the meantime, HS analogs are extremely well tolerated by all patients and especially those with sensitive skin, which is often the case with aging skin. Further, HS analogs promote skin hydration, providing resistance to compressive forces as well as keeping skin looking healthy. Anecdotally, I can report that I have been using the Senté Dermal Repair Cream in my rosacea patients without any problems. I think HS analogs represent a good option for patients who cannot tolerate retinoids.

## Resources

- 1. J Drugs Dermatol. 2015 Jul;14(7):669-74. <a href="https://www.ncbi.nlm.nih.gov/pubmed?">https://www.ncbi.nlm.nih.gov/pubmed?</a>
  term=J+Drugs+Dermatol.%5BJour%5D+AND+14%5Bvolume%5D+AND+669%5Bpage%5D+A
  ND+2015%5Bpdat%5D&cmd=detailssearch>
- 2. Proteoglycans in Skin Aging, in "Textbook of Aging Skin" (Heidelberg, Berlin: Springer-Verlag, pp. 109-120).
- <a href="https://www.researchgate.net/publication/239619909\_Textbook\_of\_Aging\_Skin">https://www.researchgate.net/publication/239619909\_Textbook\_of\_Aging\_Skin</a>
- 3. Joint Bone Spine. 2016 Sep 20. doi: 10.1016/j.jbspin.2016.06.012. <a href="https://www.ncbi.nlm.nih.gov/pubmed/27663756">https://www.ncbi.nlm.nih.gov/pubmed/27663756</a>>
- 4. Ann Chir Plast Esthet. 2010 Oct;55(5):421-8. <a href="https://www.ncbi.nlm.nih.gov/pubmed?">https://www.ncbi.nlm.nih.gov/pubmed?</a> term=Ann+Chir+Plast+Esthet.%5BJour%5D+AND+55%5Bvolume%5D+AND+421%5Bpage%5D+AND+2010%5Bpdat%5D&cmd=detailssearch>
- 5. Int Wound J. 2015 Apr;12(2):169-72 <a href="https://www.ncbi.nlm.nih.gov/pubmed?">https://www.ncbi.nlm.nih.gov/pubmed?</a> term=Int+Wound+J.%5BJour%5D+AND+12%5Bvolume%5D+AND+169%5Bpage%5D+AND+2015%5Bpdat%5D&cmd=detailssearch>.
- 6. Int Wound J. 2016 Feb;13(1):35-8. <a href="https://www.ncbi.nlm.nih.gov/pubmed/24618185">https://www.ncbi.nlm.nih.gov/pubmed/24618185</a>
- 7. ISRN Orthop. 2012 Jan 17. doi: 10.5402/2012/504151. <a href="https://www.hindawi.com/journals/isrn/2012/504151/">https://www.hindawi.com/journals/isrn/2012/504151/</a>

Dr. Baumann is chief executive officer of the Baumann Cosmetic & Research Institute in the Design District in Miami. She founded the Cosmetic Dermatology Center at the University of Miami in 1997. Dr. Baumann wrote the textbook "Cosmetic Dermatology: Principles and Practice" (New York: McGraw-Hill, 2002), and a book for consumers, "The Skin Type Solution" (New York: Bantam Dell, 2006). Her latest book, "Cosmeceuticals and Cosmetic Ingredients," was published in November 2014. Dr. Baumann has received funding for clinical grants from Allergan, Aveeno, Avon Products, Evolus, Galderma, GlaxoSmithKline, Kythera Biopharmaceuticals, Mary Kay, Medicis Pharmaceuticals, Neutrogena, Philosophy, Topix Pharmaceuticals, and Unilever. Dr. Baumann also developed and owns the Baumann Skin Type Solution skin typing systems and related products.

### THIS PUBLICATION

About Us, Advertise, Contact Us, Editorial Advisory Board, Editorial Staff, Frontline Medical Communications

### **SPECIALTY FOCUS**

Acne, Actinic Keratosis, Atopic Dermatitis, Psoriasis

### **TOP SECTIONS**

Aesthetic Dermatology, Commentary, Make the Diagnosis, Law & Medicine

### HIGHLIGHTED FROM THIS SITE AND NETWORK

Contact ClinicalEdge Manager, Contact MD-IQ Manager, Custom Programs, MedJob Network

Advertise with MDedge

See more with MDedge! See our Other Publications

MDedge: Your Source for Clinical Advantage

<u>Copyright</u> © 2017 <u>Frontline Medical Communications Inc.</u>, Parsippany, NJ, USA. All rights reserved. Unauthorized use prohibited. The information provided is for educational purposes only. Use of this Web site is subject to the <u>medical disclaimer</u> and <u>privacy policy</u>.

