SYNERGIE SKIN
CLEAN SCIENCE

CLINICAL DATA – Sodium Hyaluronate (Hyaluronic acid)

Sodium Hyaluronate (Hyaluronic acid) plays a major role in the way your skins looks, feels and functions. Sodium Hyaluronate provides volume, helping to contribute to a plumped, youthful appearance.

A natural complex sugar found in humans, Sodium Hyaluronate is a vital component of the connective tissue matrix in the skin's dermis the dense, inner layer of skin beneath the epidermis). This matrix is made up of natural Hyaluronic acid as well as two connective fibres - collagen and elastin.

Sodium Hyaluronate retains water like a sponge, absorbing more than 1000 times its weight. This helps to attract and maintain water within the extracellular space, hydrating your skin and increasing its volume and density. Sodium Hyaluronate is also involved with the transport of essential nutrients to the skin's viable cells.

Studies show that ageing begins at around 18-20 years. After the age of 40 this process accelerates and skin start to lose its elasticity and lines and wrinkles appear. Middle-aged adults are estimated to have less than half the Sodium Hyaluronate they had in youth. As we age our skin is exposed to environmental pollutants and the sun's harmful ultraviolet rays. As this occurs, skin slowly loses the ability to produce Sodium Hyaluronate. Studies have shown that older skin has lower levels of Sodium Hyaluronate than younger skin. As you age, skin tissue becomes dehydrated and the collagen and elastin fibres lose their structure. This results in a loss of skin volume and the formation of the facial wrinkles and folds that are common characteristics of aged skin.

Sodium Hyaluronate also supports the formation and maintenance of collage and elastic, an important connective tissue. Collagen and elastin degradation is believed to cause loss of skin elasticity.

Sodium Hyaluronate: Skin matrix health is not just about proteins
The skin matrix is what would remain if you took the dermis (the fibrous middle layer of the skin) and removed all cells from it.

The skin matrix is responsible for:

- Structural integrity
- Mechanical resilience
- Stability

The degradation of the skin matrix plays an important role in the development of wrinkles and other signs of skin ageing. The best-known components of the skin matrix are structural proteins (notably collagen and elastin), which are vital to skin health and youthfulness. Structural proteins are necessary but insufficient for a healthy skin matrix. In addition to the framework of structural proteins, the skin matrix also needs

appropriate fillers, which provide mechanical cushioning, hold moisture, enhance barrier function, and so forth.

The principal skin matrix fillers are glycans, a class of glucose-based polymers that includes:

- Glycosoaminoglycans
- Proteoglycans

As far as skin rejuvenation is concerned, the most important glycan may be Sodium Hyaluronate.

Chemistry of Sodium Hyaluronate

Sodium Hyaluronate is a polymer whose unit consists of D-Glucuronic acid and N-Acetyl Glucosamine. Sodium Hyaluronate chains can be up to 25,000 units long or even longer; their molecular weight ranging from about 5,000 to 20,000,000 Da.

Sodium Hyaluronate is synthesised by the enzymes called hyaluronan synthases. Humans have at least three types of Sodium Hyaluronate synthases: HAS1, HAS2, and HAS3. HAS1 and HAS2 synthases produce high molecular weight Sodium Hyaluronate whereas HAS3 produces low molecular weight Sodium Hyaluronate. Sodium Hyaluronate is degraded by the enzymes called hyaluronidases, of which there also appear to be several types.

Sodium Hyaluronate and skin physiology

Sodium Hyaluronate has many functions throughout the body, especially in the connective tissue. In the skin, some of its known roles are the following:

- Holding moisture
- Increasing viscosity and reducing permeability of extracellular fluid
- Contributing to mechanical resilience and suppleness of the skin
- Regulation of tissues repair
- Regulation of movement and proliferation of cells
- Regulation of immune and inflammatory responses

It is important to note that physiological effects of Sodium Hyaluronate depend to a large degree on the size (molecular weight) of its chains. In particular, relatively small Sodium Hyaluronate molecules (weight less than about 20,000 Da) appear to trigger the early phases of wound healing, including activation of various types of immune cells and inflammatory responses. This is understandable considering that tissue injury would typically result in increased degradation of extra cellular matrix (and Sodium Hyaluronate in particular), it makes sense that the degradation fragments (I.e. small size Sodium Hyaluronate fragments) would act as indicators of injury and trigger wound healing. On the other hand, large Sodium Hyaluronate molecules appear to suppress local immune response and inflammation. By similar logic, the predominance of large Sodium Hyaluronate molecules sends a signal that the skin is intact and defense and/or repair are not required.

Sodium Hyaluronate and ageing

The skin content of Sodium Hyaluronate decreases with age (after peaking in adolescence or early adulthood). This contributes to the loss of moisture; the skin becomes thinner and less supple. The loss of Sodium Hyaluronate may also impair the skin's ability to repair itself and possibly affects the synthesis and deposition pattern of other skin matrix components.

Can you boost Sodium Hyaluronate in your skin?

Reversing the age-related decline in the skin content of Sodium Hyaluronate is an increasingly visible topic in skin care. It would complement other steps to preserve the health of the skin matrix (such as replenishing collagen and elastin). Unfortunately, as of the time of this writing, there is no simple, inexpensive and broadly effective way to preserve/restore Sodium Hyaluronate levels in the skin. Below, we discuss what options are currently available or hold promise for the future.

Topical Sodium Hyaluronate

Topical Sodium Hyaluronate in the form of gels, serums and so forth is widely available but its usefulness is limited.

Sodium Hyaluronate can provide effective skin surface moisturising, either alone or in combination with other moisturising ingredients. However, there is controversy about whether concentrated Sodium Hyaluronate formulas should be used as a moisturiser in dry climate. When air humidity is very low, Sodium Hyaluronate may preferentially pull water from the skin rather than from the air, thus producing the opposite effect. The optimal use of Sodium Hyaluronate as a moisturiser needs further research.

But can topical Sodium Hyaluronate go beyond moisturising? Can it penetrate into the dermis and help rebuild the skin matrix? Generally, large molecules do not penetrate the skin or do so in very small amounts. Most likely, medium-to-large size Sodium Hyaluronate molecules (perhaps with molecular weight above 20,000 Da) won't penetrate sufficiently to have an impact on the skin matrix. However, small size Sodium Hyaluronate (5,000 – 20,000 Da) may penetrate into the dermis in significant amounts. However, this may not necessarily be a good thing. Assuming the small size Sodium Hyaluronate molecules penetrate into the dermis, they are likely to trigger some elements of the wound healing response (as we discussed above), such as immune activation, inflammation, cell division, blood vessel growth, new skin matrix synthesis and so further. The net effect might be either matrix degradation and accelerated skin ageing or matrix remodelling and improved skin texture. Studies are required to answer this question.

Sodium Hyaluronate based fillers

Considering that medium and large Sodium Hyaluronate molecules cannot penetrate the skin in significant amounts, one alternative is to deliver Sodium Hyaluronate via injection. This approach may improve localised imperfections (e.g. wrinkles, furrows, depressed scars) but cannot revitalise the skin overall. For details, see our article on Sodium Hyaluronate based fillers.

Stimulating synthesis of Sodium Hyaluronate

One way to increase the skin content of Sodium Hyaluronate would be to stimulate its synthesis in the skin. Unfortunately, there is little data on practically useful ways to do it. One approach to explore would be to provide the body with more building blocks for Sodium Hyaluronate, such as glucosamine and N-acetyl-glucosamine. Research is needed to determine with oral or topical administration of the Sodium Hyaluronate building blocks increases its synthesis in the skin – particularly the synthesis of medium-to-large size molecules. (This approach has been shown to work for cartilage but each tissue is different.) Another approach is to find agents that stimulate the activity of hyaluronan synthases, the enzymes producing Sodium Hyaluronate. Presumably, the ideal agent should preferentially activate HAS1 and HAS2, the enzymes producing high molecular weight Sodium Hyaluronate.

Inhibiting the degradation of Sodium Hyaluronate

If stimulating Sodium Hyaluronate synthesis is problematic or insufficient, an alternative could be to inhibit its degradation. Plugging the drain instead of pouring more, so to speak. One way to do it would be to inhibit the Sodium Hyaluronate-degrading enzyme hyaluronidases. Unfortunately, practically useful hyaluronidases inhibitors appear as hard to come by as hyaluronan synthase activators. These are a few leads, however. One candidate is escin, a saponin extracted from horse chestnut. In a few clinical trials, it was shown to strengthen veins and improve venous insufficiency, presumably via inhibiting hyaluronidases and elastase in vein walls. It may (or may not) be able to inhibit these matrix-degrading enzymes in the skin. The other candidate, surprisingly, is a variant of a well-known skin care ingredient ascorbyl palmitate. Ascorbyl palmitate is often considered inferior (as a skincare ingredient) to other common vitamin C derivatives because it is a poor activator of collagen synthesis. A variant (isomer) of ascorbyl palmitate called L-Ascorbic Acid 6-Hexadecanoate was shown to inhibit hyaluronidases in some species, including mammals. Whether this effect can be reproduced in the human skin remains to be seen. If it is, the skin care reputation of ascorbyl palmitate may get a boost.