

# OSTEOARTHRITIS & THE MULTI-FACETED BENEFITS OF HYALURONIC ACID

By Chris D. Meletis, ND

AS A FUNDAMENTAL COMPONENT that helps maintain cellular structure and function, Hyaluronic Acid (HA) acts as a lubricant, an antioxidant, a shock absorber during weight bearing, and a cushion to protect against physical trauma. However, HA levels often decline with advancing age.

HA is ubiquitous throughout the body, the highest amounts being found in the extracellular matrix of soft connective tissues such as synovial fluid (joint lubricant), vitreous fluid in the eyes, and in the skin. It is involved in several key processes, including cell signaling, wound repair and regeneration, morphogenesis, and matrix organization.<sup>1</sup>

HA supplementation can help make up for age-related deficiencies of this nutrient. Research has shown success with HA supplementation in inflammatory processes in areas such as rheumatology, ophthalmology, dermatology, and dentistry, as described below.

## JOINT PROTECTION

HA has been used in osteoarthritis for more than 30 years. Many studies have documented the long-lasting pain-relieving effects of intra-articular supplementation with HA in subjects with knee osteoarthritis, a procedure that was approved by the FDA in 1997.<sup>2</sup>

Oral supplementation with HA also shows promising results as seen in a recent study. This placebo-controlled trial enrolled 20 male and female subjects aged 40 years and older with knee osteoarthritis (pain for at least 15 days in the previous month and symptoms present for at least 6 months) who were randomized to oral supplementation of HA or placebo.<sup>3</sup> At the end of the study period, HA-treated participants experienced a greater decrease in total symptom scores based on a standardized osteoarthritis index, compared with placebo after just 8 weeks (-18.6 vs -15.8). There was also a greater magnitude of pain relief in the HA-treated group compared with placebo (11.1 vs. 2.2) as well as a significant improvement in physical component summary scores (6.1 vs. 3.6). The researchers also observed that the HA group needed half the amount of pain rescue medication (500 mg acetamino-



phen capsules) compared with the placebo group during the study. In addition, compared with placebo, more HA subjects perceived improvement in joint pain (75 percent vs. 50 percent) and muscle aches (75 percent vs. 38 percent). The researchers concluded that oral HA “was useful to enhance several markers of quality of life in adults with osteoarthritis of the knee.”

The results seen with oral HA supplementation may be particularly advantageous in elderly subjects in whom osteoarthritis-related pain results in a serious limitation of activities of daily living.<sup>3</sup> Oral supplementation also has obvious advantages over intra-articular HA by avoiding potential complications at the injection site and discomfort associated with repeated injections.<sup>4</sup>

Clinical studies have confirmed anti-inflammatory, anabolic, and cartilage-protective actions of HA in reducing pain and improving patient function.<sup>5</sup> HA appears to have a stimulatory effect on the metabolism of chondrocytes (cells found in the cartilage) through its interaction with CD44 receptors.<sup>6</sup>

A growing body of evidence also indicates that mitochondrial dysfunction and DNA damage play a causal role in disorders such as osteoarthritis that are linked to excessive generation of free radicals. Pretreatment of chondrocytes with HA has been shown to enhance their survival by decreasing mitochondrial damage and enhancing DNA repair capacity and cell viability, while preserving ATP levels and ameliorating apoptosis.<sup>7</sup>

Furthermore, studies have shown that the concentration and level of HA decline significantly in inflammatory arthritis,<sup>8</sup> which can be counteracted with high molecular weight HA supplementation. This measure has proved effective in promoting chondrocyte HA and proteoglycan [occurring in connective tissue] synthesis, reducing the production of substances that break down collagen such as proinflammatory mediators and enzymes called matrix metalloproteinases (MMPs), as well as maintaining healthy joints.<sup>8</sup>

### TEMPOROMANDIBULAR JOINT (TMJ) SYNDROME

As with osteoarthritis, the level of HA is significantly lower in the synovial fluid from patients with inflammation of the temporomandibular joint, which connects the jaw to the skull.<sup>9</sup> Hyaluronic acid has a natural affinity for joint tissue. In one study, the intra-articular administration of sodium hyaluronate into the temporomandibular joint in patients with Wilkes stage II disease (a classification used to define TMJ severity according to 5 stages) showed better efficacy in reducing pain and improving joint function compared with the oral administration of pain-relief tablets.<sup>10</sup>

### PROMOTING HEALTHY SKIN

In 2003, the FDA approved hyaluronic acid injections for filling soft tissue defects such as facial wrinkles. HA and collagen are both vital components of skin tissue. However, there is a progressive reduction in the number of hyaluronic acid granules in human skin, deteriorating to a complete absence in individuals over 60. It is believed these variations account for the decreased turgidity, wrinkled appearance, and altered elasticity of skin tissue.<sup>11</sup> The regulation of major skin cells known as fibroblasts is central to both healing and scarring

## Glucose, Sugar, Diabetes Increase Dementia Risk

A RECENT STUDY FROM Japan found that both diabetes and impaired glucose tolerance, or prediabetes, are associated with increased risk of developing Alzheimer’s disease and all-cause dementia. In the Hisayama Study, researchers from Kyushu University, in Fukuoka, administered an oral glucose tolerance test to 1,017 men and women age 60 and above with no baseline signs of dementia, and then tracked their dementia status over a period of fifteen years. During that time, 232 subjects developed dementia.

A study, published in the September 20, 2011, issue of *Neurology* found that diabetes patients were 74% more likely to develop dementia and more than twice as likely to develop Alzheimer’s disease than those with normal glucose tolerance. There was also some increase in vascular dementia risk among the diabetic group, but it was not statistically significant.

Lead author Tomoyuki Ohara, M.D., and colleagues reported: “Compared with those with normal glucose tolerance, the age- and sex-adjusted incidence and hazard ratio of all-cause dementia were significantly higher in

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## Glucose, Sugar, Diabetes Increase Dementia Risk

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subjects with impaired glucose tolerance as well as those with diabetes.”

“Moreover,” they found, “the risks of developing all-cause dementia and its subtypes progressively increased with elevating two-hour plasma glucose levels.” They argued that their finding indicates proper regulation of glucose levels after eating may be vital to preventing future incidence of dementia.

Hyperglycemia may impact the brain through a variety of mechanisms, including atherosclerosis, increased oxidative stress, and distorted amyloid metabolism. However, the researchers noted, more studies are needed investigating the possible ways in which hyperglycemia or diabetes might initiate dementia.

Sources: “Diabetes Linked to Alzheimer’s Risk,” *MedPage Today*, September 20, 2011, [www.medpagetoday.com](http://www.medpagetoday.com); “Diabetes May Increase Risk for Alzheimer’s Related Dementia,” *Neurology Reviews* 2011; 19(10):8, [www.neurologyreviews.com](http://www.neurologyreviews.com).

processes. Laboratory studies show that supplementing fibroblasts with HA causes a significant increase in their ability to renew skin tissue, resulting in increased proliferation within the collagen matrix.<sup>12</sup>

The anti-inflammatory effects of HA also carry important implications for collagen regeneration in maintaining healthy skin. The cutaneous benefits of HA can be seen in studies where it has been shown to block IL-1b, a cytokine that inhibits collagen biosynthesis at the transcriptional level.<sup>13</sup> IL-1 also inhibits the expression of insulin-like growth factor-1, a highly potent stimulator of collagen synthesis, while HA counteracts this process.<sup>14</sup> HA also suppresses MMP-1, which preferentially breaks down major components of collagen in

HA is a vital component of cellular structure and offers a multitude of benefits including anti-inflammatory and antioxidant effects

the skin,<sup>15</sup> and reduces levels of an inflammatory chemokine called RANTES. Both processes are mediated partly by the interaction of HA with its receptor called CD44<sup>16</sup> that is found in abundance in the oral mucosa. Using a high weight HA that is taken in a liquid or dissolving form, such as a lozenge in the mouth can help access the CD44 receptors in the mouth to support absorption and decrease the harsh acid environment of the stomach that breaks down HA into smaller molecule sizes.

The effectiveness of HA also extends to skin disorders such as oral lichen planus (OLP), a common inflammatory disease of the skin and mouth. In a study of 124 patients with oral lichen planus, HA significantly reduced soreness scores compared with placebo for up to 4 hours.<sup>17</sup> Patients treated for up to 28 days with HA showed a significant reduction in the size of the erosive/ul-

cerated area compared with baseline. The researchers concluded that HA may be a “useful addition to the treatment option for OLP.”

In the above study, HA was used in direct contact with the mucus membranes. An oral supplement, such as a lozenge of at least 30mg, provides an ideal delivery system for this type of use. Such a supplement delivers more HA for long periods of time to target tissues.

### MANAGING OCULAR HEALTH

Another important body system where HA distribution declines with aging is in human eye tissue.<sup>18</sup> Researchers have speculated that this decline may play a role in many age-related ocular disorders.<sup>18</sup>

UV light is the most common cause of radiation injury to the eye. While the cornea absorbs most UVB light to protect the inner eye, exceeded threshold levels induce corneal inflammation (photokeratitis). UVB light also triggers different signaling cascades that cause apoptosis of corneal cells. However, researchers have recently shown for the first time that high molecular weight HA protects human corneal epithelial cells against UVB-induced apoptosis as well as decreasing UVB-induced release of the proinflammatory mediators IL-6 and IL-8.<sup>19</sup> Corneal cells express CD44 receptors on their plasmic membranes, which is a specific point of interaction for HA. It is believed that this may be a key factor in understanding how HA protects against UVB radiation.<sup>19</sup> HA supplementation can also be useful to people with dry eyes as well as people suffering eye discomfort after computer use.<sup>20-22</sup>



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## Foods with Hyaluronic Acid

WHEN PROVIDED WITH the right foods, the body has the ability to produce hyaluronic acid (HA) on its own. Eating ample amounts of fruits and vegetables as well as collagen containing animal foods stimulates the body's natural production of HA.

Although there are no known fruits or vegetables that contain HA, a recent ABC report<sup>1</sup> on Japanese culture indicated that some root vegetables, similar to that of the sweet potato, may stimulate the natural production of HA in the body.

Preparing a broth made from the bones, tendons and joints of animals that contain collagen<sup>2</sup> not only supplies the body with a traditional food source of HA, but also encourage it to produce higher amounts on its own.<sup>1</sup> Bone broth also contains the amino acids glycine and proline. Glycine is important for wound healing and proline is found in connective tissue along with HA; both are important amino acids for tissues, joints and the cardiovascular system.<sup>2</sup>

1. "Secrets of Herbs Containing Hyaluronic Acid" [www.primev.com](http://www.primev.com)

2. "Bone Broth Delivers Minerals & Macro Nutrients", *Well Being Journal*, Vol. 20, No. 5; available at [www.wellbeingjournal.com](http://www.wellbeingjournal.com).

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## MAINTAINING A HEALTHY ORAL CAVITY

Another emerging benefit for the use of HA is in the treatment of plaque-induced gingivitis. HA has shown anti-inflammatory and antibacterial effects in both gingivitis and periodontitis. It is important to remember that oral disease processes contribute to cardiovascular disease and total inflammatory burden in the body, including elevated C-reactive protein, and the condition of the mouth and gums is therefore important to overall health. Due to its tissue-healing properties, HA may be a useful adjunct in diseases of the oral cavity.<sup>23-24</sup> The availability of HA in a lozenge preparation, which is well absorbed across the oral mucosa, enhances its effectiveness for optimizing dental hygiene.

HA has also been shown to be of benefit in recurrent aphthous ulcers, or canker sores, which are painful open sores inside the mouth or upper throat caused by breaks in the mucous membrane.<sup>25</sup> In addition, *in vivo* studies show that sodium hyaluronate effectively accelerates the healing process after tooth extraction by stimulating the expression of bone-forming proteins.<sup>26</sup>

Another oral condition that may cause difficulties in speech and eating as well as increasing the susceptibility of periodontal tissue to infection is known as xerostomia, or dry mouth, which is a common complaint in the elderly. Elderly patients with dry mouth, not caused by any history of connective tissue disease, have been shown to have lower HA levels in their saliva compared with age-matched controls.<sup>27</sup> Oral use of hyaluronic acid improved hyposalivation and unpleasant oral complaints associated with dry mouth.<sup>28</sup>

## CONCLUSION

HA is a vital component of cellular structure and offers a multitude of benefits including anti-inflammatory and antioxidant effects, pain-relief, joint lubrication and cartilage-protection, collagen regeneration, and enhancement of cell viability. Most of these actions are mediated via the HA-specific CD44 receptor present on endothelial, epithelial, and smooth muscle cell membranes. Since HA declines naturally with age, oral HA supplementation, especially a lozenge form, offers an efficient alternative that is well absorbed through the highly vascularized oral mucosa rich in CD44 receptors. As a result, oral HA supplementation offers an effective solution for joint protection, maintaining healthy skin and eyes, and is a useful adjunct for good dental hygiene.Δ

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