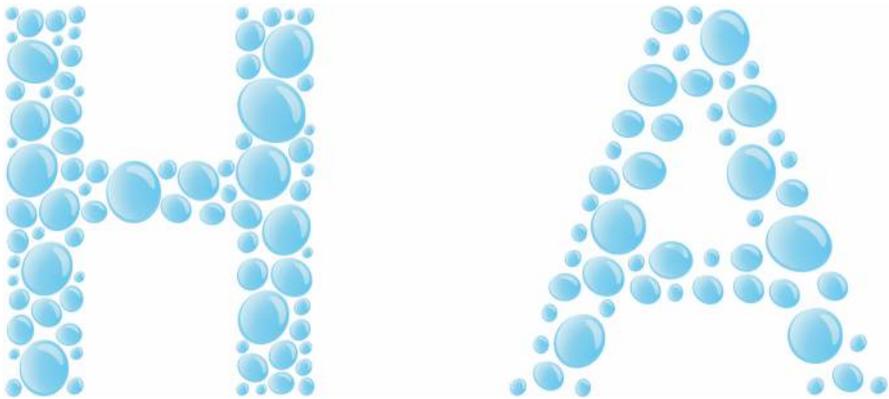


A Text Book on HYALURONIC ACID

For
professional
use only



USING HYALURONIC ACID FOR
FLEXIBLE JOINTS, VIBRANT SKIN,
AND HEALTHY EYES

Syno-Vital[®]
Hyaluronan

Manufacturer of Premium Hyaluronic Acid Products

1. The Village of Long Life

In late 2002, the ABC News show Primetime sent correspondent Connie Chung to the small farming village of Yuzuri Hara, located in a hilly region just two hours outside of Tokyo, Japan. Curiously, the townspeople of Yuzuri Hara were living well into their 90s without the usual signs of aging. When Chung introduced the world to this small town and the remarkable longevity and health its people were experiencing, of course, the world wanted to know the town's age-defying secret.



In Yuzuri Hara, roughly ten percent of the villagers are aged 85 or older. That figure might not sound like much, but if you compare it to the national average here in the United States, where it is one percent, it is indeed curiously high.

Even more remarkable, the elderly population of Yuzuri Hara enjoys unusually good health compared to what one observes elsewhere in the world. Even those who have a lifetime of unhealthy habits, such as smoking or unprotected sun exposure, are in good health. Men and women well into their 80s and 90s still have smooth, beautiful skin. They are active, oftentimes able to perform physically demanding work in the fields that requires strength and flexibility. They also demonstrate excellent eye-sight and seldom get sick. Doctors, farmers, innkeepers, all routinely practice their professions into their 80s.



Japanese researchers believe that one major factor in the health and longevity of the villagers is their diet. Because the village is in a particularly hilly region, they rely on a variety of starchy root vegetables rather than rice cultivation. Staple foods include satsumaimo, a type of sweet potato; satoimo a sticky white potato; konyaku, a gelatinous root vegetable concoction; and imoji, a potato root.



These particular vegetables contain nutrients that stimulate Hyaluronic Acid (HA) production in the body, which normally slows as the body ages. Comparatively, the people of Yuzuri Hara have higher levels of HA in their body than most. The increased levels of HA may ward off the aging process by helping the cells of the body thrive and retain moisture, keeping joints lubricated, protecting the retina in eyes, and keeping skin smooth and elastic.

Dr. Toyosuke Komori, the town doctor who has studied and written books on longevity in Yuzuri Hara, is interviewed in the Primetime segment and attributes the diet and increased HA production in the body as a probable factor. Komori, 80, who himself follows the local diet of very little meat and a lot of homegrown sticky starches, tells Chung, "I feel very strongly that if I had not come here to Yuzuri Hara, I would not have lived this long and healthy of a life.

I probably would have died from some adult disease' Sadly, Komori also mentions statistics showing that since Western-style processed food infiltrated the village, heart disease doubled. With the younger generation falling prey to unhealthy foods, an upside-down death pyramid has emerged in which adults die before their elderly parents.

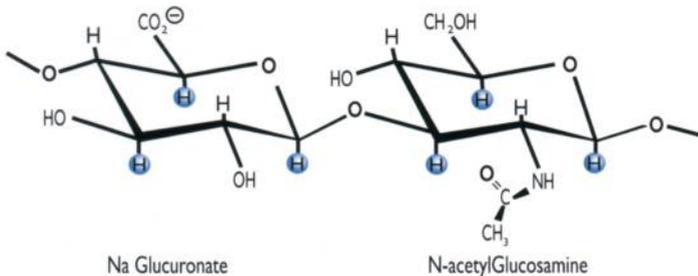
Regardless of the more recent statistical changes in Yuzuri Hara, the story of the Village of Long Life triggered widespread interest in hyaluronic acid and its age-defying effects.

2. What Is Hyaluronic Acid?

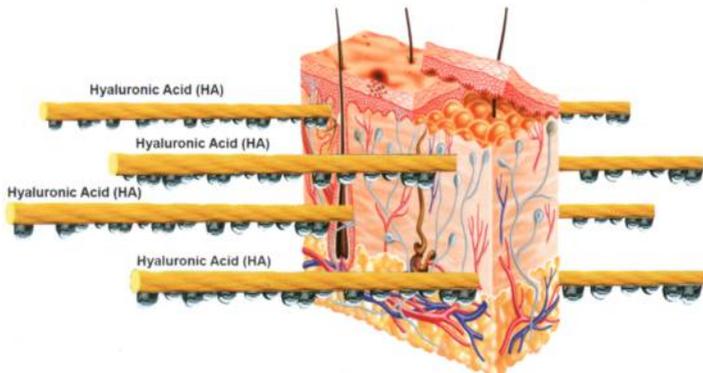
Hyaluronic Acid (HA), also known as hyaluronan or hyaluronate, is a hydrophilic (waterloving) carbohydrate found naturally throughout the human body. First isolated by Karl Meyer in 1934, HA is comprised of the molecules N-acetyl glucosamine and glucuronic acid. Its linear, rope-like structure allows it to bind up to 1,000 times its weight in water. As HA seeks out and binds to water, it becomes a viscous, Jell-O-like substance that serves as the body's natural lubricant and provider of cushioning and elasticity. HA is found in our bodies' connective tissues (ten-dons, ligaments, cartilage, skin, ground substance/matrix or extra cellular matrix fluid) and synovial fluid between the joints and eyes.



Hyaluronic Acid's Molecular Structure



Hyaluronic Acid's Rope Structure



HA was first used commercially in 1942 when Endre Balazs applied for a patent to use it as a substitute for egg whites in baked goods. Its discovery was very unique. No other molecule had ever been examined with such unusual properties in the human body. Balazs went on to become the leading expert on HA, and made the majority of findings concerning hyaluronic acid benefits. However, HA was not commonly used medically until the 1990s.

Where is Hyaluronic Acid In The Body?

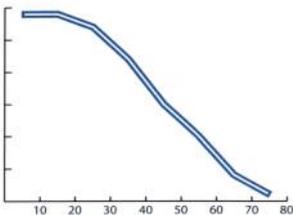


Today, thousands of clinical trials exist that examine the use of HA mostly in the fields of eye surgery and orthopedics. Orthopedic injections are now commonly used to support healthy joint movement. HA oral supplementation is used for eye and joint health support. HA is often used to support the eye during eye surgery. Since the airing of *Primetime's* segment on Yuzuri Hara in 2002, HA has been widely studied for its age-defying properties for beautiful, youthful-looking skin. Cosmetic injections under the skin have become increasingly popular for smoothing wrinkles. HA is also applied topically to hydrate, moisturize and enliven aging skin.

HA and Aging

The human body degrades about one-third of its HA stores each day. Normally, this HA is simply replaced with new HA that the body synthesizes, but beginning as early as young adulthood, our production of HA begins to decrease, and this decrease accelerates with age. By middle age, our bodies can no longer make up the amount of HA they lose, and the telltale signs of aging become apparent. Joints lose their ability to maintain proper cushion, and there is a need to support healthy movement. The collagen in our skin loses its moisture, and the skin sags and wrinkles. Around age 50, it's estimated that we can have as little as half the amount of HA in our skin that we did in our 20s. Put simply: without enough HA, we look and feel old!

Age and the amount of HA in the skin



3. Hyaluronic Acid and Healthy Mobility



HA plays a critical role in healthy movement throughout our lifetime. As we grow older, discomfort begins and the joints experience limitations in movement. **Maintaining healthy levels of HA in our joints and bodies is one way to ensure healthy joints and flexibility as we age.**

Our joints are surrounded by a synovial membrane, which forms a capsule around the ends of two articulating bones, and HA is a major component of the synovial fluid that lubricates this joint capsule and provides cushion.

HA is to our joints what motor oil is to a car's engine: it provides lubrication to keep the parts running smoothly without grinding against each other. Similarly, as we age, the viscosity of synovial joint fluid lessens. We need to maintain healthy levels of HA in the body, just as we might top off our car's oil pan.

HA's long complex molecule forms a ball shape, which resists compression and provides cushion. However, with inflammation or other conditions the complex hyaluronic acid molecule breaks down to smaller pieces and is unable to maintain a ball shape. In this broken down state, HA can no longer provide cushioning in the joint. The fluid becomes water like and unable to cushion the joints.

In addition to HA-rich synovial fluid's elastic, shock-absorbing and lubricating properties, it carries nutrients to the cartilage and removes waste from the joint capsule. As cartilage is without blood flow, the synovial fluid's HA helps perform these functions in the body.

Since we lose HA as we age, it's not surprising that research has shown that the joint fluid of consumers with joint health issues have reduced levels of HA. Stimulating the body's production of HA or increasing the presence of HA through injection or supplementation appears to be a logical means to support joint health. Multiple studies show that those with joint health concerns benefit from HA as it supports proper joint cushioning. Fortunately HA is available to everyone who wishes to support joint health.



Individuals wishing to maintain healthy joints can do so easily, conveniently and affordably by supplementing with HA. Findings have shown that after a single oral dose of HA, ample HA may find its way to the joints.

Glucosamine and HA

Glucosamine is a well-known joint health supplement. Interestingly, studies have found that the effectiveness of glucosamine supplementation may be largely due to its ability to boost synthesis of HA in the joint fluid. Glucosamine is actually only a piece of the joint-health puzzle, and in fact, a molecular component in HA. Glucosamine is a modified sugar, whereas HA is a complex molecule that, when broken down, releases a glucosamine molecule. There are properties related to HA's complexity that aren't present in glucosamine—mainly that HA is the key ingredient in joint fluid lubrication.



Supplementing with HA and glucosamine together is a great strategy for overall joint health support.

Healthy Tendons and Ligaments—HA and the Connective Tissue Connection

Connective tissue is found everywhere in the body. It does much more than connect body parts; it has many forms and functions. Its major functions include binding, support, protection, and insulation. One such example of connective tissue is the cordlike structures that connect muscle to bone (tendons) and bone to bone (ligaments). In all connective tissue there are three structural elements. They are ground substance (HA), stretchy fibers (collagen and elastin) and a fundamental cell type.

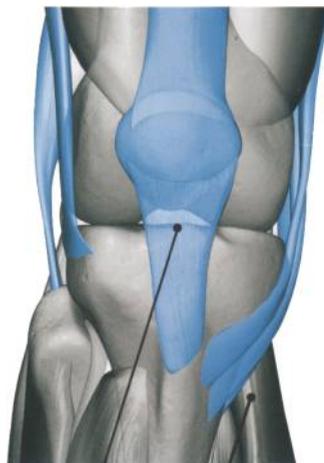
Whereas all other primary tissues in the body are composed mainly of living cells, connective tissues are composed largely of a nonliving ground substance (HA), which separates and cushions the living cells of the connective tissue. The separation and cushioning allow the tissue to bear weight, withstand great tension and endure abuses that no other body tissue could. All of this is made possible because of the presence of the HA and its ability to form the gelatinous ground substance fluid.

Ultimately, HA serves to keep tendons and ligaments hydrated and nourished—and the presence of HA helps lessen friction and is an important component in maintaining healthy mobility.

Methods of Increasing HA in the Body

To promote healthy aging, it makes perfect sense to do all we can to maintain adequate amounts of HA in the body. There are nutritional ways of supporting the body's production of HA. While our western diet may not resemble that of the people of Yuzuri Hara, we can incorporate foods that are rich in magnesium, zinc, copper and silicon into our diet. These minerals are helpers in the preparation of HA.

Knee Diagram



Tendons Ligaments

Another nutritional strategy is to favor foods and herbs such as grape seed extract, horse chestnut and resveratrol may help the body prevent hyaluronidase, the enzyme that breaks down HA, from getting out of control and attacking our own increasingly scarce supplies.

HA skin injections to improve skin appearance and knee injections for joint health are common procedures provided by medical doctors.

One of the easiest and most affordable ways to increase the amount of HA in our bodies is to supplement with HA orally or used topically in shampoos, conditioners, skin serums, scrubs, moisturizers, and other preparations. High molecular weight (HMW) HA is roughly the size of the body's naturally formed HA, which may make it more beneficial as a supplement.

4. Hyaluronic Acid and Healthy Skin

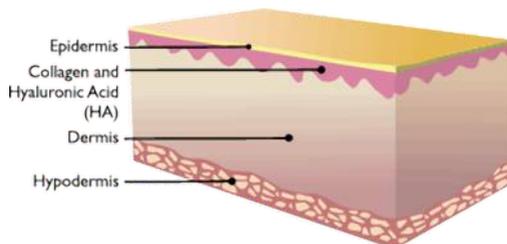
When you understand how integral HA is to healthy, youthful skin, you'll wonder why HA's age-defying effects were not discovered sooner! Although HA can be found naturally in most every cell in the body, it is found in the greatest concentrations in the skin tissue and collagen. Roughly half our body's HA is found in the skin, which is the largest organ in the body comprising about 15 percent of our body weight. While the half-life of HA in the body is estimated to be less than three days, it can be as little as one day in the skin.

Smooth, elastic young skin is naturally loaded with HA—as our young bodies produce HA abundantly and easily replace the HA that is lost. The HA provides continuous moisture to the skin by binding up to 1,000 times its weight in water. Unfortunately, the ability of our skin to produce HA decreases as we age and consequently, the amount of HA in our skin drops significantly. In addition to our body producing less water-loving HA as we age, over time free radicals, produced mostly through exposure to pollutants and sunlight, destroy the HA in the skin. Without enough HA in the skin, the skin loses its ability to hold water leaving a drier, thinner and wrinkled appearance. It's similar to what happens to drying plums and grapes—as they lose moisture, they become dried and wrinkled.



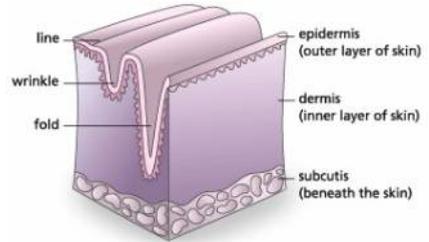
The skin consists of three main layers: the epidermis, dermis and hypodermic.

Less than a millimeter thick, the epidermis protects our bodies from heat and cold. The condition of the epidermis determines how the skin looks and also how well the skin absorbs and holds moisture.



The dermis is the middle layer of the skin and the skin's support structure. It is the thickest layer and comprises a network of collagen and elastin fibers. The dermis represents the majority of the thickness of the skin (the epidermis above it makes up only a small percentage of the skin). The dermis gives the skin its elasticity and resilience.

At the very bottom layer of our skin is the subcutaneous tissue or hypodermis. This tissue consists mainly of fat that keeps the body warm, stores energy, and protects inner organs. The subcutaneous tissue houses sweat glands as well as a system of tiny muscles connected to our hair follicles. As we age and the subcutaneous tissue thins, our skin begins to sag and the epidermis contracts, causing wrinkles to appear.



HA and the Dermis

HA of the skin is found in both the deep underlying dermal areas as well as the visible epidermal top layers. The dermal layer of the skin and lips is composed of collagen and HA, which contribute to the structure and shape. While collagen makes up the majority of the dry weight of the dermis, HA provides the moisture. It hydrates the dermis, which is roughly 70 percent water.



HA's affinity to water is akin to a sponge. HA binds to water creating a viscous fluid that hydrates the surrounding tissue and keeps the collagen nourished and healthy. HA allows the skin to retain its supple and firm tone and youthful appearance.

HA and the Lips

The lips are a core of skeletal muscle covered by skin tissue. The dermal layer of the lips is composed primarily of connective tissue (made up of HA and collagen), which gives the lips structure (shape) and plumpness. The HA binds to water creating a gelatinous fluid that hydrates the

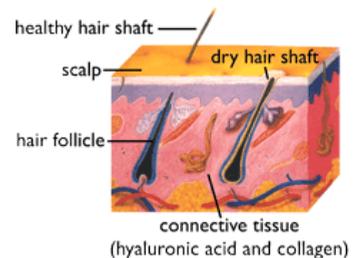


surrounding tissue and keeps the collagen (the rubber bands responsible for keeping the skin tight) nourished and healthy. The result is healthy, well-hydrated and plump lips that are protected from the environment.



HA and the Scalp

Structurally the scalp is identical to the skin tissue located throughout the body except it also contains about 100,000 hair follicles that give rise to hair. The hair and the hair follicle are a derivative of skin tissue. The dermis is where the hair follicle is located. The dermal layer is composed of connective tissue and is rich with HA. It nourishes and hydrates as well as supports the deep layers of the scalp. The result is healthy lustrous hair and a moisturized scalp. Again, all of this is made possible because of the presence of HA in the scalp.





HA for Gorgeous Skin

Today, HA injections are a common cosmetic procedure to safely enliven, plump and smooth wrinkles and improve elasticity of aging skin. HA is also used topically to hydrate and smooth skin in serums and moisturizers. Additionally, its used in shampoos and conditions for lustrous hair and lip balms for shapely, smooth lips.

Topical HA provides a great convenient and affordable way to provide HA to the skin.

Findings shows that topical HA makes its way to the dermis where it hydrates and nourishes the collagen and helps to smooth and plump the skin. In a study published in 1999 in the Journal of Investigative Dermatology, HA made its way to the dermis of test subjects within a relatively short period after application.

The best news about HA is that it really can work. In a study published in the May 2008 issue of Dermatologic Surgery, researchers made note of HA's ability to rejuvenate facial skin.

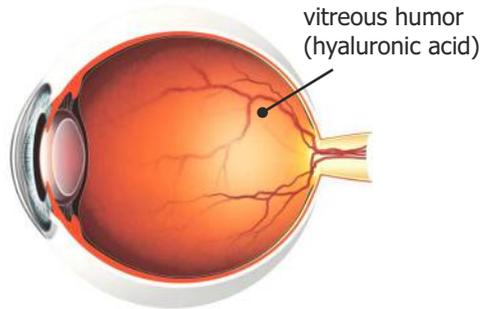
5. Hyaluronic Acid and Eyesight

The very substance that nourishes the collagen in our skin and provides the cushion in our joints, also makes up a large percentage of our eyes' vitreous humor gel fluid. We need an abundance of HA for healthy eye function.

The vitreous humor is the clear substrate that light shines through until hitting the back of the eye to form an image on the retina. The HA in the vitreous humor cushions the structures of the eye and helps maintain its shape as we play contact sports, run, or just move about

throughout the day. Think of how different it feels to walk or run barefoot on a hard surface—you can feel the shock in your legs and hips—versus walking with soft shoes or cushioned insoles. Most of this skeletal shock from our movement is transferred up the vertebral column to the skull and the eyes and brain. In its infinite wisdom, the body supplies an abundance of HA to act as a shock absorber within the eyes to stabilize vision and protect delicate eye tissues. It has become a common practice for eye surgeons to inject HA directly into the eye in order to maintain the shape of the eye during surgery. The hydrating, viscous properties of HA support not only eye shape and resilience, but also transport nutrients into the eye. Thus, HA helps play a major role in maintaining the health of other ocular tissues like the cornea and retina. It is believed that after the fifth decade of life, our eyes may stop producing HA which may result in various eye problems such as poor vision, dry eyes and floaters. Healthy levels of HA in the eyes is important to their proper functioning and longevity.

Eye Diagram



6. Hyaluronic Acid and Gum Health

Our bodies' connective tissue is composed of fibrous tissue surrounded by HA. HA is also known as the extra-cellular matrix, acting much like mortar between the bricks.



The gums (gingivae) are composed of dense fibrous connective tissue (ligaments), which secure the teeth to the alveolar bone (jaw bone). Without enough hyaluronic acid, the gums connective tissue becomes unhealthy. When an abundance of HA is present, it helps to provide the tensile strength of the ligaments that secure the tooth in place by providing hydration and nourishment. **Having adequate amounts of HA in the connective tissue is integral to maintaining the health and longevity of your gums.**

Of course, as we age and our bodies are not able to produce enough HA to replace what is broken down. Our gum health is at risk too.

An overall HA supplement or toothpaste may help bring needed HA to the gums as well as to the joints, skin, eyes and other areas of the body.

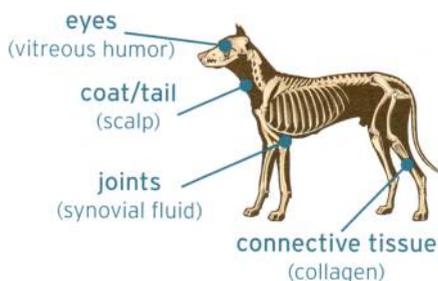
7. Hyaluronic Acid for Animals



What's good for a human may be good for animals too.

Anyone who has owned a dog, cat or horse knows that with age, pets' joint health and flexibility need support. This is, in part, due to the fact that they also gradually lose their bodies' supplies of HA just like us. A healthy presence of viscous HA in your pet's joints acts as a necessary lubricant and provider of cushioning and elasticity for long-term mobility health. Specifically, your pet needs a healthy amount of HA in its joint structure to cover and protect the ends of its long bones, and in its synovial fluid, to lubricate the joints and keeps them moving smoothly.

A 2003 study published in Veterinary Record showed promising results using joint fluid injections on canines with joint issues. This study appears to show the benefits of not only HA, but also of HMW HA. In another study published in the September, 2012 issue of Arthritis and Rheumatism, researchers found that the addition of HA to deficient equine joint fluid restored lubrication function to joints.



Also similar to humans, HA supports the health of your pet's skin and fur coat, gums and eyes.

When pets are healthy, it makes life easier for owners too. Today, HA supplements for pets are available at health foods stores, pet stores and veterinarians.

8. Types of Hyaluronic Acid

It's important for consumers and health care professionals to know that there are three major types of HA materials used in dietary supplements and skin care products—each with varying results.

The three major source materials of HA are natural microbial fermentation, rooster combs and hydrolyzed chicken sternal cartilage. Natural microbial fermentation creates HA that is vegan-friendly and closely similar to that of the HA naturally produced by the body. This HA has a long residual life in the anatomy. It has high viscosity for buffering and lubrication. And best of all, usually only a small amount is needed to receive benefits.

Rooster combs and hydrolyzed chicken sternal cartilage yield smaller pieces of the HA molecule, which the body must reassemble. Aging reduces healthy HA into smaller pieces as HA deteriorates. Hence, these sources may not produce the most efficient or beneficial HA.

Low Molecular Weight HA vs. High Molecular Weight HA

We all know that a human joint lacking proper lubrication or with minimal joint fluid will invariably allow articulating (joint) bones to rub directly on top of each other causing long-term damage to the cartilage. In the body, HA most commonly presents itself as a large, high molecular weight molecule. It is critical to its function to be a large molecule. As we discussed earlier, the molecule is made up of a repetitive sequence of two modified simple sugars—glucuronic acid and N acetyl glucosamine. When these compounds come together, they are both negatively charged and repel, causing the long molecule to stretch out naturally. A long, rope-like molecule has far more water binding capacity. Molecules that are long and stretched out often give a high viscosity, which can resist compression of the joint. HMW HA is a common type of HA used in research as it closely resembles the majority of naturally occurring HA in the joint structure. When the HA molecule breaks into small pieces, the short rope like pieces lose their ability to bind to water and create the cushiony joint fluid.



High Molecular Weight HA

LMW HA does not typically have the surface area for binding to water and thus proper lubrication is harder to achieve. HMW HA typically weighs up to 5 times that of LMW HA—a significant difference. LMW HA in the body is generally compromised and is not as successful at providing cushion, hydrations and transfer of nutrients.

The difference can be seen in these clear tube images below. The first tube is filled with a liquid form of low molecular weight (LMW) HA. When the tube is turned upside down, the blue marble located inside quickly moves from one end of the tube to the other. It takes approximately 5 seconds for this to occur. The LMW HA solution does not have enough viscosity to cushion the fall of the blue marble.



Less body cushioning



More body cushioning

The second clear tube is filled with solution of high molecular weight (HMW) HA. The orange marble inside is well protected and cushioned. The long and highly viscous HA molecule creates a very thick gel like solution which cushions and provides shock absorption for the orange marble at the bottom of the tube. When this tube is turned upside down, the orange marble slowly moves from one end of the tube to the other and takes approximately 30 to 45 seconds to drop all the way. The marble is gently laid at the bottom of the fall.

When shopping for HA either as a dietary supplement or a topical, be sure to choose animal-free, HMW HA. Natural Fermentation is the most common non-animal source of hyaluronic acid. It's non-GMO and vegan friendly. It's most commonly used for medically administered joint and skin HA injections.



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