The clinically proven, easily absorbed, low-molecular weight hyaluronic acid for youthful-looking skin.

Moisturize from the inside out



# The Rising Popularity of Nutricosmetics

Increasingly, consumers are making the link between inner health and outer beauty. As a result, the category of nutricosmetics — ingestible products taken specifically for beauty purposes — has taken off in recent years. Consider these facts:

- The global nutricosmetics market was valued at \$2 billion in 2009 and is expected to reach \$5 billion by 2015.<sup>1</sup>
- The U.S. market is under-developed compared to Europe and Japan, and therefore displays the greatest growth potential.<sup>2</sup>
- The estimated compound annual growth rate of nutricosmetics in the United States through 2017 is an impressive 14 percent.<sup>3</sup>

In other words, nutricosmetics are big business. There is just one caveat mentioned by all the top market research firms: Americans are skeptical of nutricosmetic claims. To be convinced, they need to see credible scientific validation.

Fortunately, that's exactly what DIVA Injuv<sup>®</sup> — the clinically tested, easily absorbed, low-molecular weight hyaluronic acid — provides.



By far the biggest category of nutricosmetics is skincare, with products that target wrinkle reduction being particularly appealing. Keeping the skin moist is key to diminishing the appearance of wrinkles and encouraging a healthy complexion. The ultimate internal moisturizer, hyaluronic acid is found in significant quantities throughout all layers of the skin, including the epidermis — the outermost layer that is visible to the world. Unfortunately, hyaluronic acid levels decline with age, which helps explain why skin appears dull and wrinkled over time.

The obvious solution to plummeting levels of skin hyaluronic acid is to take an oral hyaluronic acid supplement. There's just one problem...

# The Absorption Dilemma, and the DIVA Injuv<sup>®</sup> Solution

In its natural state, oral hyaluronic acid is a high molecular weight substance that is too large to be absorbed through the intestinal tract. As a result, most hyaluronic acid supplements are simply excreted, with no benefits seen.

#### DIVA Injuv<sup>®</sup> is different

Available exclusively from KWD VENTURES LLC, Inc.<sup>®</sup>, DIVA Injuv<sup>®</sup> is a proprietary low molecular weight hyaluronic acid with high oral bioavailability. It's no surprise then, that:

- Researchers have found DIVA Injuv<sup>®</sup> significantly increases the moisture content of the skin.
- Women report DIVA Injuv<sup>®</sup> improves skin moisture, softness, and smoothness.
- Animal research shows DIVA Injuv<sup>®</sup> aids wound healing.

#### Hyaluronic Acid: The Inside-Out Moisturizer

Hyaluronic acid is one of the main constituents of the extracellular matrix — the gel-like medium that houses the cells of the connective tissue, cartilage, and skin. Hyaluronic acid is also found in significant quantities throughout the skin, including the epidermis. In fact, almost 50% of the total hyaluronic acid in the body is found in the skin.

The job of the epidermis is to act as a barrier to the outside world, and the job of hyaluronic acid is to reinforce that barrier. In other words, hyaluronic acid keeps the bad elements — such as pathogens and pollutants — from penetrating the skin, while keeping the good elements — mainly moisture — from leaving.

How does it work? In layman's terms, hyaluronic acid acts as a sponge to hold onto water within the skin, keeping it fresh and youthful-looking.

#### Age, Hyaluronic Acid, and the Skin

As we age, the distribution of hyaluronic acid among the layers of the skin changes. Fetal epidermal tissues, for example, are rich in hyaluronic acid.<sup>4</sup> That's why baby skin recovers so quickly and completely from injury.

However, as we get older, hyaluronic acid migrates downward through the layers of the skin, steadily declining in the upper layers of the epidermis, while rising in the lower layers of the dermis.<sup>6</sup> That's great for the dermis, but it's terrible for the epidermis — the part of the skin that everyone sees — because that loss of moisture makes it look dull and wrinkled.

There's another problem too: the hyaluronic acid that's in the epidermis doesn't last very long. It has a half life of less than 24 hours,<sup>6</sup> which means it needs to be renewed constantly. Otherwise, the structures that it bathes in moisture, such as collagen and elastin, become brittle and lose their structural function.

Hyaluronic acid levels decline with age.



# The Moisture Loss Double Whammy

With age, the cells in the epidermis, which were once closely woven together like a water-tight basket, begin to separate from each other. As a result, the cells let more water evaporate from the skin — which makes it look prematurely old.

Thus, aging skin is hit with a double whammy: moisture loss from the lack of hyaluronic acid and moisture loss from the separation of skin cells in the epidermis.

# How Hyaluronic Acid Benefits the Skin

Hyaluronic acid has several important benefits to the skin:

- 1 It prevents transepidermal moisture loss, making skin look plump and diminishing wrinkles.
- 2 It isolates and protects skin cells, giving them "breathing space."
- 3 It allows for the easy flow of nutrients *to* the epidermis, and toxins and metabolic waste *from* it, supporting even skin tone.
- 4 It helps regulate the life cycle of skin cells, increasing their longevity, as well as the efficiency of their maintenance and repair.<sup>7</sup>
- 5 It may help the body eliminate the dead outer layer of skin cells and force skin to regenerate, acting like an internal exfoliant to reveal fresher, younger-looking skin.<sup>8</sup>



## The Problem with Oral Hyaluronic Acid

In an effort to replace the hyaluronic acid that is lost with time, several ingredient manufacturers have developed a version of hyaluronic acid for oral use. However, consumers may be wasting their hard-earned money on commodity hyaluronic acid products. That's because hyaluronic acid in its natural state is an extremely high molecular weight substance — measuring from 800,000 to 8,000,000 Daltons — that is too large for the body to absorb orally. As a result, it is simply excreted, unused.

# Introducing DIVA Injuv<sup>®</sup>

Available exclusively from KWD VENTURES LLC, DIVA Injuv<sup>®</sup> has solved the hyaluronic acid absorption dilemma.

DIVA Injuv<sup>®</sup> is manufactured through a patented enzyme-cleaving technique that dramatically reduces the molecular weight of hyaluronic acid — without altering its chemical nature. Because of its small size, Injuv<sup>®</sup> is easily absorbed through the epithelial cells of the intestinal tract, as demonstrated in human and animal research.

# DIVA Injuv<sup>®</sup> Advantages

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2

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DIVA Injuv<sup>®</sup> hyaluronic acid offers four main advantages compared to commodity hyaluronic acid:

**Easily Absorbed.** DIVA Injuv<sup>®</sup> is an easily absorbed, low molecular weight hyaluronic acid. Size exclusion high-performance liquid chromatography has verified that the low molecular weight hyaluronic acids contained in DIVA Injuv<sup>®</sup> are estimated to be between 1,500 and 5,000 Daltons — less than one percent of their original size. As a result, Injuv<sup>®</sup> is absorbed easily through the intestinal tract.

**Natural Source.** DIVA Injuv<sup>®</sup> is derived from rooster combs, which have been safely used as a source of hyaluronic acid for more than 20 years, in the form of an injectable treatment for osteoarthritis of the knee. Not only does this type of hyaluronic acid have a natural affinity for human tissues, it has been clinically shown not to cause an allergic response.

**Delivered to the Skin.** Of course, it doesn't matter if something is absorbed if it's not delivered where it's needed in the body. The absorption and delivery of Injuv ®has been demonstrated using a well-established animal model to measure wound healing capacity. The physiological activity of Injuv<sup>®</sup> — illustrated by the fact that rats treated with oral Injuv<sup>®</sup> experienced significantly improved wound healing compared to those given placebo — is a reliable indicator that Injuv<sup>®</sup> is absorbed and delivered to the target tissue: the skin.

#### Delivery Method

KWD VENTURES LLC is pleased to offer DIVA Injuv<sup>®</sup> as an off-the-shelf formulation in a soft gelatin capsule, providing 70 mg of DIVA Injuv<sup>®</sup> standardized to 9 percent hyaluronic acid.



#### DIVA Injuv<sup>®</sup> Original Research Clinical Study Finds DIVA Injuv<sup>®</sup> Improves Skin Moisture Content

A placebo-controlled human clinical study was undertaken to determine whether DIVA Injuv<sup>®</sup> could improve the moisture content of the skin. A total of 107 volunteers aged 30 to 50 years, with an average age of 45, were randomly assigned to take either DIVA Injuv<sup>®</sup> (two 70-mg soft gels twice daily) or placebo for 30 days. Skin surface moisture content was measured before and after supplementation using an SHP88 probe.

Subjects who took DIVA Injuv<sup>®</sup> showed a statistically significant increase in skin moisture content compared to both baseline and placebo. There were no adverse events reported.9



#### Pre-Clinical Trial Shows DIVA DIVA Injuv<sup>®</sup> Benefits Skin and Joints

In a pre-clinical trial conducted at Otsuma Women's University in Japan, 96 women ages 22 to 65 took DIVA Injuv<sup>®</sup> (six 70-mg tablets per day) for 45 days. Subjective interview questionnaires revealed dramatic improvements in skin moisture, smoothness, and softness.<sup>10</sup>

- 84% reported a great improvement in the moisture levels of their hands and face
- 83% reported a great improvement in the smoothness of their skin
- 78% reported a great improvement in the softness of their elbows, knees, and hands
- 50% reported a great improvement in the stiffness of their joints



Injuv<sup>®</sup> significantly increased skin moisture content compared to both baseline and placebo.

DIVA

Animal Study Indicates DIVA Injuv<sup>®</sup> Aids Wound Healing A study in mice found that oral administration of DIVA Injuv<sup>®</sup> (2000 mg/kg) significantly

DIVA Injuv<sup>®</sup> (3000 mg/kg) significantly improved wound healing compared to placebo (saline) after just three days.<sup>11</sup>

#### Toxicity Test Demonstrates Safety of DIVA Injuv<sup>®</sup>

In an acute toxicity test, rats were administered a very high single dosage of DIVA Injuv<sup>®</sup>. No observable abnormalities were observed and no mortalities occurred. The acute oral LD50 of DIVA Injuv<sup>®</sup> was determined to be greater than 5,050 mg/kg equivalent to 343,400 mg for the average human.<sup>12</sup>

## DIVA Injuv<sup>®</sup> Highlights

Available exclusively from KWD VENTURES LLC, DIVA Injuv<sup>®</sup> is a clinically proven, easily absorbed, low molecular weight hyaluronic acid.

#### Background

- **1** The ultimate internal moisturizer. Present throughout the layers of the skin, including the epidermis, hyaluronic acid acts as a sponge to hold onto water, keeping skin fresh and youthful-looking.
- 2 The moisture loss double whammy. As we get older, hyaluronic acid steadily migrates away from the epidermis, so skin loses moisture. In addition, with age, the cells in the epidermis begin to separate from each other, further exacerbating the moisture loss problem. This double whammy of moisture loss makes skin look prematurely old.
- **Commodity hyaluronic acid products are not absorbed.** Until now, oral supplements of hyaluronic acid have been useless, because hyaluronic acid is a high molecular weight substance that cannot penetrate the epithelial cells of the intestinal tract.



#### References

<sup>1</sup> A new way of delivering beauty. *Happi* magazine. http://www.happi.com/beautyio/2010/09/nutricosmetics-a-new-way-of-delivering-beauty Sept, 2010. (Accessed August 3, 2011.)

<sup>2</sup> Global Industry Analysts. Global nutricosmetics market to reach \$4.24 billion by 2017, according to a new report by Global Industry Analysts, Inc. PRweb.com. http://www.prweb.com/releases/nutricosmetics/nutritional\_supplements/prweb8262307 htm April 5, 2011. (Accessed August 3, 2011.)

<sup>3</sup> Global Industry Analysts. 2011.

<sup>\*</sup>Tammi R, Tammi M. Hyaluronan in the epidermis. *Hyaluronan Today*. Glycoforum, Mizutani Foundation for Glycoscience. http://www.glycoforum.gr.jp/science/hyaluronan/HA04/HA04E.html June 15, 1998. (Accessed Aug. 8, 2011.)

<sup>5</sup>Meyer LJM, Stern R. Age-dependent changes of hyaluronan in human skin. J Invest Dermatol. 1994 Mar;102(3):385-389.

<sup>6</sup> Tammi R, et al. Degradation of newly synthesized high molecular mass hyaluronan in the epidermal and dermal compartments of human skin in organ culture. *J Invest Dermtaol.* 1991;97:126-130.

<sup>7</sup> Tammi R, Tammi M. 1998.

<sup>8</sup> Tammi R, Tammi M. 1998.

<sup>9</sup> Wakayama S, presenter. (2009, March) *Clinical study on Injuv® demonstrates improvement of skin moisture content.* Poster session presented at the Nutracon and Supply Expo Conference, Anaheim, CA.

<sup>10</sup> Omori S. Clinical Trial on Injuv<sup>®</sup>. Otsuma Women's University, Japan. Unpublished study performed 6/1/00-7/15/00.

<sup>11</sup> Cheng FC. Effects of KBF-1 on wound healing, skin. Unpublished study performed 11/29/99-1/22/2000.

12 Cheng FC. 1999-2000.



# DIVA UNIX Moisturize from the inside out

#### Why DIVA Injuv®?

- **Easily Absorbed.** DIVA Injuv<sup>®</sup> is manufactured through a patented enzyme-cleaving technique that dramatically reduces the molecular weight of hyaluronic acid without altering its chemical nature allowing for easy absorption.
- 2 Clinically proven effective. A randomized, placebo-controlled human clinical trial found that subjects who took DIVA Injuv<sup>®</sup> showed a statistically significant increase in skin moisture content compared to both baseline and placebo.
- **3** Delivered to the Skin. The absorption and delivery of DIVA Injuv<sup>®</sup> has been demonstrated using a well-established animal model to measure wound healing capacity.
- **Safe.** An acute toxicity test on DIVA Injuv<sup>®</sup> resulted in observable abnormalities and no mortalities.
  - **Natural Source.** DIVA Injuv<sup>®</sup> is derived from rooster combs, which have been safely used as a source of hyaluronic acid for more than 20 years.

# KWD VENTURES LLC

Brookings, South Dakota, United States Phone: (605) 695-3630 Email: kwdventures@gmail.com Website: www.kwdventures.com



5



