HYACTIVE
very low molecular weight sodium salt of hyaluronic acid
An active ingredient of biotechnological origin for the cosmetic industry

PRODUCT DESCRIPTION

Hyaluronic acid (HA) is a linear polysaccharide built from regularly alternating units of glucuronic acid and N-acetylglucosamine. The degree of polymerisation is in the order of $10^2$ to $10^3$ units. This implies that molecular weight is in the range from tens of thousand up to several hundred thousand Daltons. HA is the most hydrated biopolymer known (see booklet - SMW Hyaluronic Acid). In living tissue it serves as a water reservoir. In water solutions, HA molecules give rise to spherically coiled structures nesting about 99% of immobilised water. Due to the polyanionic nature of HA, its properties are very sensitive to pH and to the ionic strength of the solution. Since HA is normally found in the body, it is free of immunogenic activity. HA forms cellular coats and it is a normal component of blood lymph and connective tissue.

Trade name: HyActive
Chemical name: poly(sodium-β-D-glucuronate-[1-3]-β-N-acetyl-D-glucosamine-[1-4])
Other names: sodium hyaluronate, hyaluronan, hyaluronic acid
CAS No: 9067-32-7
INCI name: Sodium Hyaluronate
EINECS/ELINCS: 232-678-0

Source: HyActive is produced by fermentation. As a starting material we use Hyaluronic acid with low molecular weight, which is split by a controlled combination of different physical methods to desired molecular weight. As the combination of biotechnological and physical methods is used to produce HyActive, the product is free of contaminants such as glycosaminoglycans and proteins of animal origin. GMO’s are not used during the production process.

Solubility:
- dissolves rapidly in water.
- soluble in mixtures of water with ethylalcohol, isopropylalcohol, propylene glycol and butylene glycol at the concentration of organic solvent up to 70%
- insoluble in non-water miscible solvents

Compatibility and processing: HyActive solution is
- relatively stable. Only small changes in molecular weight occur while heating at extreme pH values.
- very sensitive to free radicals
- incompatible with cationic substances, e.g. quaternized polymers or proteins (Quaterniums, Polyquaterniums, etc.)

Toxicological data:
- non-irritating
- non-cytotoxic
- non-phototoxic
- non-mutagenic

Supplied forms: powder
Specification:

**HyActive**, powder

Appearance: white to slightly yellow powder or granules

Clarity of 1% aqueous solution (660 nm, 1cm): clear to slightly opalescent, colourless solution

pH of 1% aqueous solution: 5.0-8.0

Residue on drying: > 90.0 %

Ash: < 10.0 % calc. on dry basis

Uronic acid (UA): > 45.0 % calc. on dry basis

Sodium hyaluronate: > 93.0 % calc. on dry basis

Protein: < 0.2 % calc. on dry basis

Preservatives: none

Total microbial count: < 100 CFU/g

Molecular weight: 10-20 kDa *

* most commonly used range of molecular weight

**HyActive can be supplied with any molecular weight in the range of 10-150 kDa.**

**USE IN COSMETICS**

Daily skin care 0.01 - 0.20%

Night and reparative preparations 0.02 - 0.20%

After sun 0.02 - 0.50%

Pre-shaves/After shaves 0.005 - 0.05%

**EFFICACY DATA**

**ANTI-AGEING**

A 24 hours-treatment of HaCaT cultures with 24 kDa **HyActive** (500 µg/ml) stimulates gene expression of epidermal growth factor and hyaluronan synthase-2. At the same time, gene expression of matrix metalloproteinases 1 and 3 is decreased.

A 48 hours-treatment of keratinocyte cultures with 12.7 kDa **HyActive** (1000 µg/ml) stimulates gene expression of tissue metalloproteinase inhibitor 1 in addition to hyaluronan synthase-2.

Due to its relatively small molecule, **HyActive** is able to penetrate stratum corneum. A 14 day-treatment of skin in vivo with 12 kDa **HyActive** showed reduced gene expression of hyaluronidase-1 and increased expression of serine protease inhibitor (Kazal-type 5), which protects desmosome junctions in deeper epidermal layers from proteolysis and premature desquamation.
On the molecular level, HyActive stimulates β-glucocerebrosidase activity within the stratum corneum in vivo, even after skin irradiation with UBV/UVA light. Ceramides released from their glucosylated precursors are incorporated into lipidic bilayers between corneocytes and strengthen the epidermal barrier function. After 21 days of pretreatment (1% HyActive, 37 kDa), skin areas were irradiated with 1.5 MED (UVA+UVB). Next day, β-glucocerebrosidase activities were determined by the tape stripping method. Pretreatment by HyActive prior to the skin UV-irradiation stimulated the enzyme activity in contrast to untreated skin.

Elasticity improvement after a long-term application of HyActive

When the skin is submitted to a sudden and sustained strain under conditions of elasticity measurement (Corneometer SEM 575), three successive phases of skin deformation are found: purely elastic phase I, phase II with variable creep and phase III with constant creep. Elderly skin shows low elastic phase (low parameters R5 and R7) and considerable creep phases (high parameters R6 and R8).

A long-term application of HyActive shows a decrease of elasticity parameter R8, thus, the skin is more flexible in comparison to control preparation without HyActive.

EPIDERMAL RENEWAL AND INTEGRITY SUPPORT

A long-term application of HyActive in vivo results in accelerated stratum corneum turnover, which was estimated by the measurement of decreased colour intensity of dihydroxyacetone-stained skin surface. HyActive significantly accelerated corneocyte shedding even after several days of treatment.

After a 20-day treatment period, sizes of corneocyte aggregates collected from skin surfaces of volunteers were estimated by direct laser measurement (Ankersmid CIS-100). Their aggregation is displayed in distribution curves, where percentages of total corneocyte area are calculated for separated ranges of corneocyte sizes. The lower area under the curve, the less of large aggregates were present in stripped stratum cornenum samples. Data collected from volunteers show lower areas under curves corresponding to skin sites treated with HyActive in comparison to their controls, which confirms lesser corneocyte sizes and lowered aggregation in the skin treated with HyActive.

Such effect can only be obtained by stimulation of proteolytic reactions in superficial layer of stratum corneum, which leads to the disruption of corneocyte bindings. In conclusion, long-term application of HyActive results in accelerated desquamation. In contrast to AHA, which causes invasive desquamation or even peeling, the effect of HyActive is gentle, and dermally safe. Final cosmetics preparations containing HyActive can be used in daily cosmetics without any risk of skin irritation.
HyActive stimulates desquamation only in superficial layers of stratum corneum while deeper epidermal layers keep unchanged integrity. Cohesivity of stratum corneum was tested by stripping after 21 days of HyActive application. Total protein content was measured in the third to eighth strip.

After treatment period, when old and abnormally thickened corneocyte scales peel off, more cohesive layers of new corneocytes with more regular run of desquamation appear. Decreased protein content in deeper strips confirms this hypothesis, as well as represents the evidence of unaffected desquamation in these layers.

The effect of HyActive lies in normalizing of superficial stratum corneum desquamation, which is down-regulated predominantly in elderly skin.

OXIDATIVE STRESS REDUCER

Changes of UV-induced catalase activities in the presence of 1% HyActive in vivo

Catalase is an enzyme eliminating hydrogen peroxide generated in tissue upon oxidative stress. After skin irradiation with UV light, its activity is initially suppressed. Only after several hours enzyme activity reaches the original level and then increases.

The skin of volunteers was treated for 21 days with 37 kDa HyActive and then irradiated by UVA/UVB (1.5 MED). 24 hours later, an increase in the catalase activity over control was found in the HyActive treated skin by tape stripping method, which means a better ability of skin to resist free radicals.