

HyaCare®

New Hyaluronic Acid with unique anti-wrinkle benefits
– A breakthrough in safety and purity –

- Replenishes the skin's natural short and long-term moisturization
- Promotes the appearance of younger looking skin
- Provides a perceivably more elastic skin feel and reduces the appearance of wrinkles
- Provides a soft, smooth and silky texture to the skin
- High purity
- New production process

Personal Care

INCI name (CTFA name)

Sodium Hyaluronate

Chemical and physical properties (not part of specifications)

Form	Powder
pH (0.5 % aqueous solution)	5 – 8.5
Solubility in water	1 g/100 g

Sodium hyaluronate is the sodium salt of hyaluronic acid, a glycosaminoglycan consisting of D-glucuronic acid and N-acetyl-D-glucosamine disaccharide units. Since the discovery of hyaluronic acid in 1934, many different production methods have been used. The ethically dubious method of extracting hyaluronic acid from rooster combs was replaced in the 1990s by more modern *Streptococcus* fermentation technology.

It is, however, time to think again! HyaCare®, a biosynthetic non-animal derived hyaluronic acid, is now available. HyaCare® is based on a unique production method by fermentation of a novel strain, *Bacillus subtilis*, a safe and non pathogenic host. The method is based on a patented, advanced and safe fermentation and purification process. No organic solvents are to isolate it, and due to its high and constant level of purity, HyaCare® will reduce the risk of allergy. HyaCare®, has an average molecular weight (MW) of 550 – 1000 kDa .

Hyaluronic Acid is a natural substance found in great abundance in young skin, synovial fluid and other tissues in humans and animals. It plays an important role in tissue hydration, lubrication and cellular function, and is able to hold 70% more water than any other natural substance. (Removed because redundant in this paragraph)

Over time, oxygen radicals, produced largely through exposure of skin to pollutants and sunlight, degrade and destroy hyaluronic acid. Fifty year olds are estimated to have less than half the hyaluronic acid they had in youth. It is well documented that fetal tissues contain large amounts of hyaluronic acid and that decreasing hyaluronic acid content correlates with aging and wrinkling.

Properties

The skin needs an optimal proportion of water to retain its softness and suppleness. Water-binding ingredients incorporated into cosmetic emulsions can provide the skin with a moisturized feel. Hyaluronic acid is a special mucopolysaccharide occurring naturally throughout the human body. It is the most effective humectant available, and has been shown in scientific literature to bind water within the intercellular structure of the skin. Its unmatched hydrating properties may result in skin which appears smoother, feels softer, and wrinkles appear less pronounced.

The consistency and tissue-friendliness of hyaluronic acid allows it to be used in skin-care products as an excellent moisturizer. It is one of the most hydrophilic molecules in nature and can be described as "Nature's moisturizer".

In-vitro efficacy study

The determination of the water-binding capacity, by Differential Scanning Calorimetry, of different types of hyaluronic acid (various molecular weights and sources) (Fig. 1) shows that HyaCare® (800 kDa) has a higher water-binding capacity when compared to hyaluronic acid isolated from *Streptococcus* fermentation (750 kDa or 1450 kDa).

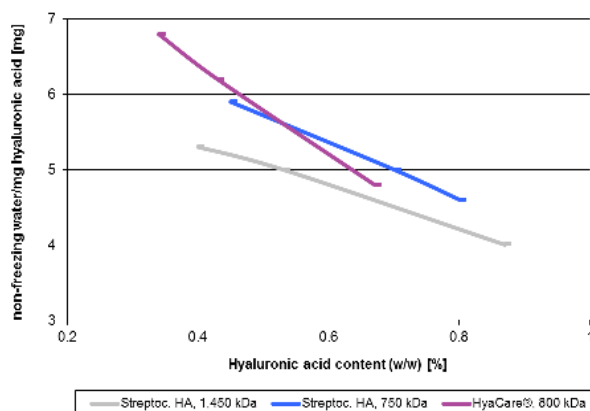


Fig. 1: Water-binding capacity of various hyaluronic acids

In-vivo efficacy studies: Short-term evaluation of transepidermal water loss (TEWL) and skin hydration

- Study Design:

Studies were performed at the ISPE srl., Milan (I) to measure transepidermal water loss (TEWL) and skin hydration after a single application of an O/W cream containing 0.1 % HyaCare® in comparison to a vehicle and to an untreated area.

The studies were carried out in a climate-controlled room (24 °C; 50 %rh) ensuring that temperature and humidity during the measurements remained constant.

Each of the 12 volunteers was asked not to cleanse or moisturize the forearms for 3 hours before baseline measurements were performed. The assessment was taken on the volar area of each forearm, in three areas each measuring 9 cm² (one area treated with the HyaCare® containing cream, another area treated with the vehicle and the third area left untreated). The selected areas were randomized among the subjects. A fixed amount of the two creams were applied on the previously delimited areas. Measurements were performed before and at 30, 60, 120 and 180 minutes after the application.

- TEWL

Measurements show TEWL reduction related to the untreated skin areas on the volar forearms at

different time points (Fig 2).

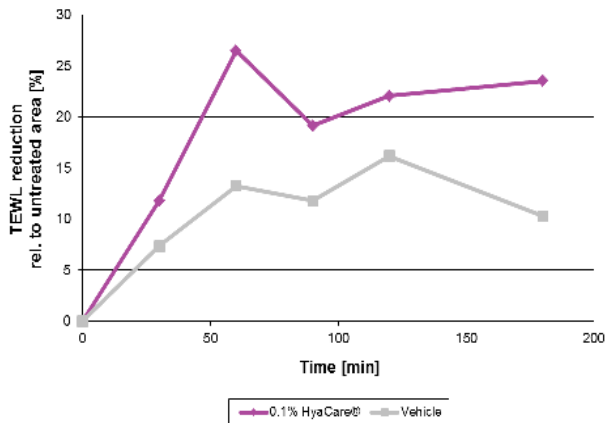


Fig. 2: Transepidermal water loss (TEWL) after singular application of test formulation

The graph demonstrates that a singular application of the cream containing HyaCare® noticeably reduces the TEWL when compared to vehicle alone.

- Skin hydration

There is also an increase in moisturization relative to the untreated skin areas using Corneometer (Fig. 3). This indicates that a one-time application of the HyaCare® containing formulation results in a clearly visible increase of skin hydration compared to vehicle alone (p-value?) even at 180 minutes following application.

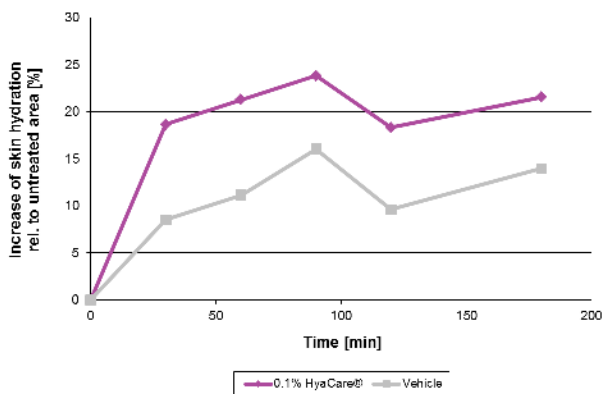


Fig. 3: Skin hydration after singular application of test formulation

In-vivo efficacy studies: Long-term evaluation of skin hydration, elasticity and roughness

- Study Design

The studies were performed at the ISPE srl., Milan (I). Hydration, elasticity and roughness evaluations of skin following application of an O/W cream containing 0.1 % HyaCare® in comparison to a vehicle were obtained.

The studies were carried out in a climate-controlled room (24 °C; 50 %rh) ensuring that the temperature and the humidity during the measurements remained constant. Each of the 12 volunteers was

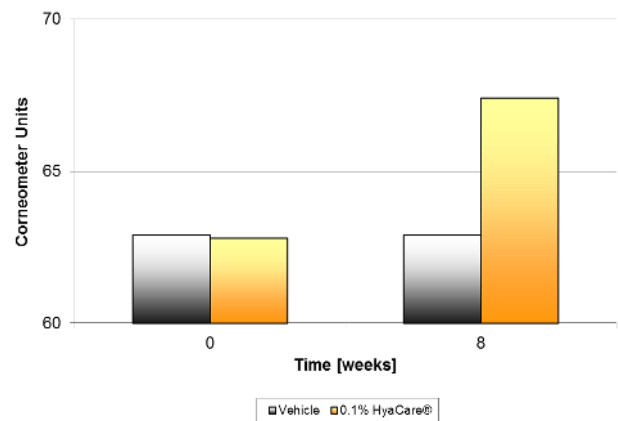
asked not to wash their face for at least 3 hours before performing the measurements.

The assessment was performed on the face, where half of the face was treated with the cream containing HyaCare® and the other half with the vehicle cream, respectively. The side of application on the face (left or right) of the two products was randomized. At the beginning of the study, instrumental evaluations of skin elasticity, hydration and roughness were carried out onto the left and right peri-ocular areas, marked out in a reproducible way. The volunteers applied twice daily the test formulations over a period of 8 weeks. At the end of the treatment, the volunteers returned to the laboratory for the final instrumental measurement.

- Long-term Skin Hydration

Increased moisturization was observed in the areas exposed to the HyaCare® formulation in comparison to the vehicle (Fig. 4). A dramatic increase in skin hydration was detected after 8 weeks, confirming the long-term moisturization properties of HyaCare®.

Fig. 4: Skin hydration after 8 weeks application of test



formulation

Based on long term skin hydration, there was an overall improvement of skin resiliency following application of HyaCare® formulation in comparison to the vehicle.

A significant increase of more than 27% was detected in the area treated with HyaCare® formulation (Fig. 5).

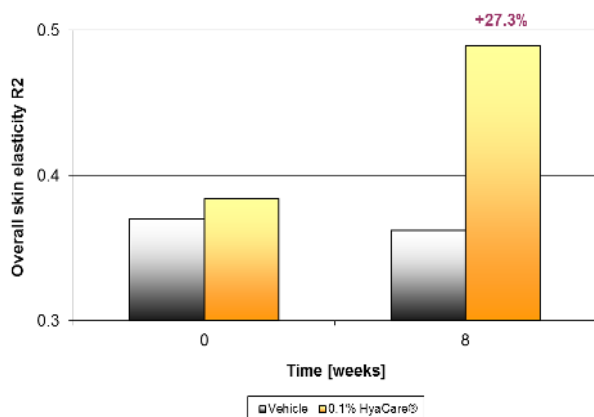


Fig. 5: Overall skin hydration and improvement of skin resiliency after 8 weeks application of test formulation

Finally, skin image analysis showed a significant decrease in maximum skin roughness of more than 10 % of the area treated with HyaCare® formulation (data not shown). These data further show that this decrease in skin roughness leads to a reduction in deep wrinkle perception.

Preparation

HyaCare® is completely soluble in water and shows good compatibility with other ingredients.

Recommended usage concentration

0.01 – 0.2% of HyaCare®

Applications

HyaCare® is suitable as an additive for hydro-regulative cosmetics of all kinds:

- Moisturizing products (facial and body care)
- Anti-aging creams and lotions
- After sun products

Storage

For short term (few weeks), the product can be stored at room temperature. For long term (over several months), the product should be stored in a cool place (4°C). Avoid freezing. The product is expected to be stable up to 36 months.

Handling

Sterile gloves should be used to handle the product in order to prevent any microbial contamination. The container should be hermetically sealed after sampling.

Packaging

0.5 kg package

Hazardous goods classification

Information concerning

- classification and labelling according to regulations for transport and for dangerous substances
- protective measures for storage and handling
- measures in accidents and fires
- toxicity and ecological effects

is given in our material safety data sheets.

Guide Line Formulations

Skin Repair Cream with HyaCare® and SK-Influx® Mac 481/3/3		
Phase A		
TEGO® Alkanol S 2 P (Steareth-2)		2.4 %
TEGO® Alkanol S 20 P (Steareth-20)		0.6 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)		3.0 %
Stearic acid		1.0 %
Isohexadecane		6.0 %
TEGOSOFT® APS (PPG-11 Stearyl Ether)		3.0 %
Cyclomethicone		1.0 %
Phase B		
Glycerol		3.0 %
HyaCare®		0.2 %
SK-influx® (Ceramide 3; Ceramide 6II; Ceramide 1; Phytosphingosine; Cholesterol; Sodium Lauroyl Lactylate; Carbomer; Xanthan Gum)		5.0 %
Water		73.4 %
Preservative		<i>q.s.</i>
Phase C		
TEGO® Carbomer 134 (Carbomer)		0.2 %
Mineral Oil		0.8 %
Phase D		
NaOH (10 %)		0.4 %
Preparation:		
1. Solubilize HyaCare® in water and add the other ingredients of phase B.		
2. Heat phase A and B to 80°C.		
3. Add phase B to A without stirring and homogenize.		
4. Cool with gentle stirring to 60°C and add phase C. Homogenize again for a short time.		
5. Cool with gentle stirring below 40°C and add phase D.		
6. Cool down with gentle stirring to 30°C.		

Cream Gel with Moisturizing Properties F 31/02-23	
Phase A	
TEGOSOFT® DC (Decyl Cocoate)	8.0 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	5.0 %
TEGOSOFT® CR (Cetyl Ricinoleate)	2.0 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	1.0 %
Tocopheryl Acetate	0.5 %
Phase B	
TEGOSOFT® PSE 141 G (Sucrose Stearate)	2.0 %
TEGO® Care CG 90 (Cetearyl Glucoside)	0.5 %
Propylene Glycol	4.0 %
Glycerol	4.0 %
Panthenol	0.5 %
HyaCare®	0.1 %
Water	40.93 %
Phase C	
TEGO® Carbomer 341 (Acrylates/C10-30 Alkyl Acrylates Crosspolymer)	0.45 %
Water	29.55 %
Phase D	
NaOH (10 %)	0.675 %
Phenoxyethanol; Methylparaben; Butylparaben; Ethylparaben; Propylparaben (Uniphen P-23, Induchem)	0.5 %
Perfume	0.3 %
Preparation:	
<ol style="list-style-type: none"> 1. Solubilize HyaCare® in water and add the other ingredients of phase B. 2. Heat phase A and B separately to 75-80°C. 3. Add phase A to phase B with stirring ¹⁾. 4. Homogenize. 5. Cool with gentle stirring. 6. Add phase C at approx. 45°C with stirring. 7. Homogenize for a short time. 8. Add phase D at 40°C while stirring. 	
¹⁾ Important: If phase A has to be charged into the vessel first, phase B must be added without stirring .	

W/O Cream with HyaCare® and TEGO® Cosmo C100 Mac 481/1/4	
Phase A	
ABIL® EM 90 Cetyl PEG/PPG-10/1 Dimethicone)	2,0 %
ISOLAN® GI 34 (Polyglyceryl-4 Isostearate)	1,0 %
Microcrystalline Wax	1,2 %
Hydrogenated Castor Oil	0,8 %
TEGOSOFT® OS (Ethylhexyl Stearate)	5,0 %
Mineral Oil (30 mPa s)	12,0 %
Phase B	
Sodium Chloride	0,5 %
TEGO® Cosmo C100 (Creatine)	0,5 %
HyaCare®	0,2 %
Water	Ad 100%
Preservative	<i>q.s.</i>
Preparation:	
<ol style="list-style-type: none"> 1. Heat phase A to approx. 80°C. 2. Solubilize HyaCare® in water and add the other ingredients of phase B. 3. Add phase B to A slowly with stirring. 4. Homogenize for a short time. 5. Cool with gentle stirring below 30°C and homogenise again. 	

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