

H. Haeusler*

Efficacy of a Hyaluronic Acid Gel to Improve the Skin Properties

■ Summary

Since many years Hyaluronic Acid (HA) is used in various anti-aging products. In these products HA is classified by its molecular weight. It is known that HA's with masses < 200 kDa are actively involved in skin cell signaling and thus influence the extracellular matrix (ECM) (1). Finally, HA has an impact on the growth of keratinocyte cells which protect the epidermis from aging.

Higher molecular weights of HA (1000-1500 kDa) stay normally on the surface of the skin and are not able to penetrate the *stratum corneum*. By means of Raman Spectroscopy it could be demonstrated that low-molecular HA (20-300 kDa) is able to penetrate the *stratum corneum* (2).

Another work recently showed the improvement of skin moisturization of the epidermis (using HA 5 kDa) and the *stratum corneum* (using HA 100 kDa). By these measurements it was shown that HA 5 kDa permeates deeper into the epidermis. Additionally, a protein was brought into this deeper layer of the skin. The property of HA as an enhancer is coming more and more into the focus of scientific research and also into medical applications.

Based on this knowledge we have developed a mixture of hyaluronic acid of different molecular weights formulated as a gel with a classical preservative system. This gel was tested *in vivo* on 10 female persons aged between 40-60 years over a period of 4 weeks. Also a second formulated gel was applied whose component with the lowest molecular weight was en-

capsulated with lecithin, forming a liposome.

The usage of such liposomes should improve the penetration through the *stratum corneum* and should also slow down the degradation process in the skin caused by the enzyme »Hyaluronidase«. Both formulas were applied to one half of the face each.

This study was done by »Dermatest« in Muenster. In this study the following parameters were measured: skin hydration (Corneometry), water content in the *stratum corneum*, skin elasticity (Cutometry) which is based on the so called suction method where two parameters firmness and elasticity are measured, the indicators for young and fresh skin. At least the skin roughness was tested by an optical method. The surface of the skin was measured with the »Primos« 3D skin assessment device, which uses digital photos for *in vivo* analysis of wrinkles and skin roughness.

All measurements were done before and after the application of our HA Gel.

The significant result was an overall improved shape of the skin of all test persons and a very good skin compatibility of the HA Gel after 4 weeks.

■ Introduction

Diverse cosmetic formulations try to improve the properties of aged skin, for example small wrinkles round the eyes, reduction of skin elasticity and also moistening of the skin. Several cosmetic formulations could proof their long-term efficacy with quantitative measurements.

We could show through an *in vivo* study that our Hyaluronic Acid Gel is capable to improve the properties of the skin of different test persons.

Hyaluronic acid has anti oxidative properties because of the chemical double binding structure of the D-Glucuronic acid unit (4). Furthermore, HA controls the proliferation of skin cells via the receptor CD44 and HA has also some anti-inflammatory properties on the skin (6).

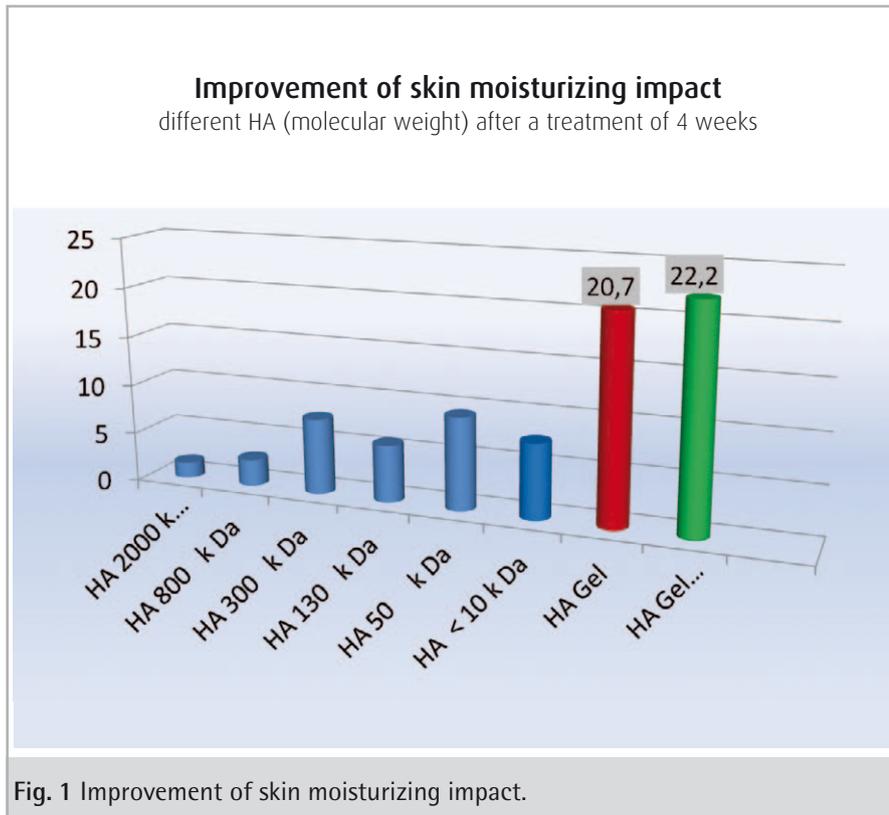
1. Improvement of Skin Hydration

Fig. 1 shows our results compared to a study which was made recently with HA of different molecular weights. The concentration level of HA used in these standard formulas is 0.1% for all molecular weights. In our opinion this concentration is too low for an effective end product. It is remarkable, however, that despite this low concentration of HA, a significant improvement could be achieved.

After 4 weeks of treatment with our HA Gel we found an average improvement of skin hydration by 20.7% for the gel and 22.2% for the gel containing the liposomes.

2. Comparison of the Increase in Skin Elasticity

Fig. 2 shows a positive effect of skin elasticity after application of HA with different molecular weights (4) as well as with our HA Gels and a cross linked hyaluronic acid. The biggest influence on this parameter was measured with HA 130 kDa as well as the low molecular 50 kDa and our HA Gels. This was



skin and environmental influences, the profile of the human skin can change dramatically.

Treatment of such skin with low molecular weight HA can lead to an improvement of this profile because of the good penetration skills compared to high molecular weight HA. In Fig.3 the values for HA 300, HA 2000 kDa and cross linked HA polymer are missing because no literature values were available for this property.

However in our HA Gels the amount of low molecular weight HA is large, which explains the fantastic impact on the skin roughness. Even only the use of HA oligomer (< 10 kDa) has a good impact.

■ **Conclusions**

By using HA with different molecular weights, a good efficacy respectively the moistening of the skin could be achieved. However we recommend a usage of at least 1% to 1.5% of HA. In order to improve the elasticity of the skin and the skin roughness a treatment with HA Gel is recommended. Depending on the skin nature of the test person before

also expected by theoretical reflections. The elasticity of the skin in the area of epidermis and the EZM is determined by HA of lower molecular weights. HA supports the formation and binding of elastin and collagen in the connective tissue and thus supports the elasticity of the skin.

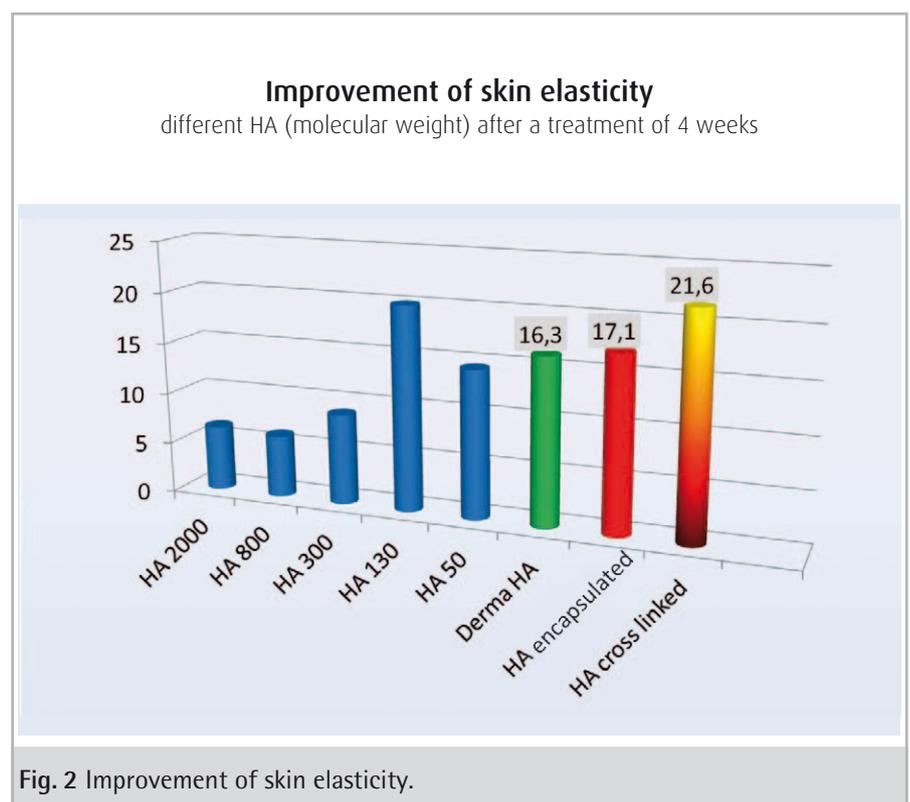
While it is difficult to explain the measurement result for HA 130 kDa, in general the positive effects of lower molecular HA on skin elasticity could be confirmed. As well the gels, the chemically modified (cross linked) HA and also HA 50 kDa are showing a significant improvement on elasticity.

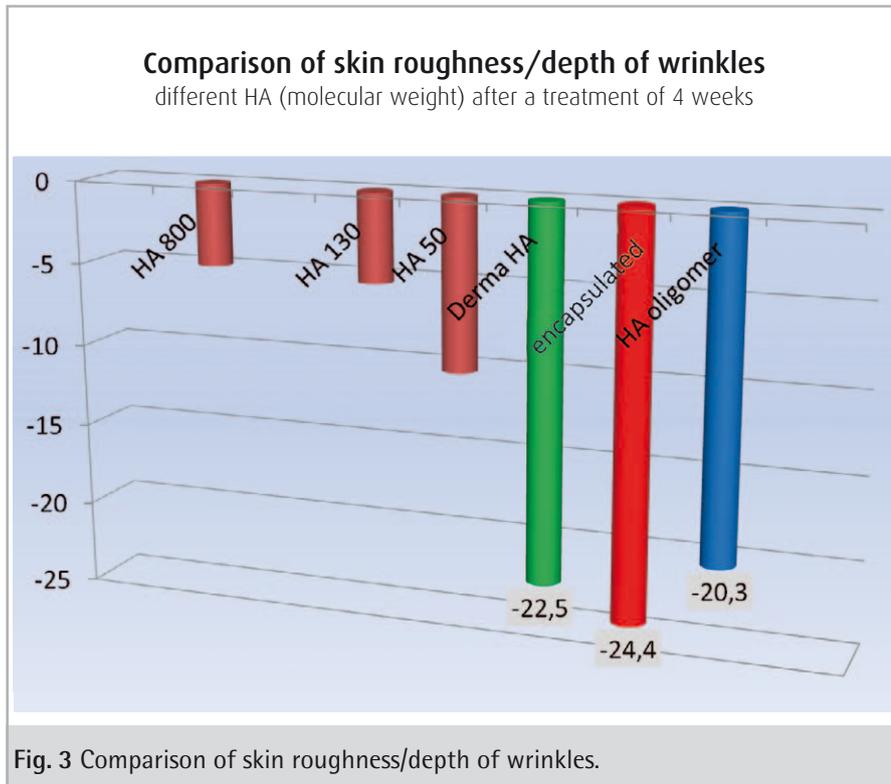
The positive impact of the cross linked HA can be explained by the longer availability on the skin surface compared to normal HA and it is known that the enzymatic degradation of a cross linked HA is slower than for a »normal« HA.

3. Comparison of Wrinkle Depth/Skin Roughness

Like for the elasticity property, the skin roughness is determined by the loss of

water in the dermis and in the connective tissue. Depending on the age of the





treatment, improvements between 5 and 28% could be observed. All our Gels had a concentration of about 2.5% HA, standard preservation as well as customized solutions are possible. The HA Gels can also be used in natural cosmetic formulations. ExperChem Ltd is producing these HA Gels and can also offer all the hyaluronic acids of different molecular weights.

Literatur

- (1) *Wohlrab W, Neubert R, Wohlrab J.* Hyaluronsäure und Haut, Trends Clin Exp Dermatol, Aachen, Shaker, 2004, vol3
- (2) *Essendoubi M, Gobinet C, Reynaud R, Angiboust JF, Manfait M, Piot O.* Human skin penetration of hyaluronic acid of different molecular weights as probed by Raman.

Spectroscopy Skin Res Techn 2015, Apr 16. doi:10.1111/srt12228

- (3) *Witting M, Boreham A, Brodwolf R, Vavrova K, Alexiev U, Friess W, Hedtrich S.* Interactions of hyaluronic Acid with skin Mol Pharm. 2015, May 4, 12(5), 1391-1401. doi:10.1021/mp500676e
- (4) *Pavlic T, Gauglitz GG, Lersch P, Abdellaoui K, Malle B, Korting HC, Farwick M.* Efficacy of cream base novel formulations of Hyaluronic Acid of different molecular weights in Anti-wrinkle treatment. J Drugs Dermatol, 2011; 10(9): 990-1000
- (5) Produktdatenblatt; Bloomage Freda Biopharm Co., Ltd.. Hyacross™ Hyaluronic Acid Elastomer. Vortrag INCOSMETICS, Barcelona 2015
- (6) *Cutting KF.* Wound healing through synergy of hyaluronan and an iodine complex. Journal of Wound Care, Vol 20, No. 9 September 2011, 424-430

*Author's address:
Dr. Henry Haeusler
ExperChem Ltd.
Lortzing Str. 7
69469 Weinheim
Germany
Email: henry.haeusler@experchem.com

