

A. Bürger<sup>1</sup>, U. Scherдин<sup>1</sup>, U. Koop<sup>1</sup>, S. Gallinat<sup>1</sup>, M. Moers-Carpi<sup>2</sup>, M. Carpi<sup>2</sup>, J. Mergell<sup>1</sup>, F. Rippke<sup>1</sup>

<sup>1</sup> Beiersdorf AG, Hamburg, Germany | <sup>2</sup> hautok, Munich, Germany

### Abstract

Facial wrinkles are often considered as stigmatizing and thus may have profound effects on people's self-image, self-esteem, and sense of physical well-being. As a consequence, products counteracting these signs of ageing are in great demand. We investigated efficacy, skin compatibility and cosmetic performance of two anti-aging face creams (a day and a night care product) containing soy saponin and hyaluronic acid as active ingredients. Anti-wrinkle efficacy of the test products was assessed in a two month study with 30 female volunteers by phase-shifting rapid *in-vivo* measurement of skin (PRIMOS) as well as by photo evaluation. In a second study, 24-hours skin moisturizing efficacy was analyzed by corneometric measurements in 28 female subjects. Furthermore, tolerability and cosmetic performance of the products were evaluated in an open multicenter study in 35 patients. After two months of product use PRIMOS measurements demonstrated a significant decrease in mean peaks height of the surface which is mainly based on wrinkle depth. These results were substantiated by optical grading of digital photographs taken from the foreheads of participating subjects at baseline, after one month and after two months of product application. Skin moisturization measurements after a single product application showed a significant increase in skin hydration after 2, 5, and even after 24 hrs. A dermatological in-use study revealed highly statistically significant effects on skin dryness, tension, wrinkles and redness. Results of the clinical study demonstrated "very good" or "good" skin compatibility of both products in the vast majority of patients even in subjects after hyaluronic acid injections for wrinkle filling. Patients' feedback was completely in line with the physicians' evaluation. Consequently most patients were in favor of using the products and the physicians recommended the product in most cases. Our data demonstrates that the tested anti-wrinkle face creams are skin compatible and highly effective products which even can be recommended for use after skin augmenting injections.

### Introduction

Skin aging goes along with numerous functional and structural changes including depletion of dermal extracellular matrix components like collagen and hyaluronic acid (HA). HA is an extremely hygroscopic polysaccharide abundant in youthful skin and, amongst various other functions, responsible for the maintenance of its turgor. Reduced dermal HA levels lead to an impaired water-binding capacity of the connective tissue and, consequently, wrinkle formation. In the past years, cosmetic-dermatological treatments of facial wrinkles with dermal injections of skin fillers have attracted much attention and, only recently, HA was approved for this indication in the US and some European countries. Its unique safety profile as biodegradable, nonimmunogenic and nontoxic compound, even at very high concentrations, provides numerous advances over other filler substances. As dermal bioavailability of topically applied HA is limited, we researched into phytochemicals for their ability to induce dermal HA formation. As a result, we identified a specific soy germ extract rich in saponins as most effective, enhancing HA synthesis of human dermal fibroblasts by more than 250%. Soy saponins are bioactive glycosides with numerous inherent properties including antioxidant and immunoprotective effects. In the studies presented here we investigated the clinical anti-wrinkle efficacy and skin compatibility of two novel face care creams (Eucerin® Hyaluron Filler Day and Eucerin® Hyaluron Filler Night, Beiersdorf AG, Hamburg, Germany) containing HA and a specific soy extract with a high portion of saponins (14%) on facial wrinkles and rhytides.

### Materials and Methods

#### Preparations

Eucerin® Hyaluron Filler Day and Eucerin® Hyaluron Filler Night are based on O/W emulsions and contain soy saponin and hyaluronic acid as active ingredients. Hyaluron Filler Day additionally contains UVA and UVB filters (SPF 15 plus high UVA protection) and Hyaluron Filler Night regenerating dexpantenol and pure vitamin E, respectively. No other skin care products were allowed to be used in the course of the studies.

#### Evaluation of anti-wrinkle activity

30 females between of 31 and 55 years of age with mild to moderate facial wrinkles and crow's feet were enrolled in this blind, split-face, in-use study with left-right randomization. The products, Hyaluron Filler Day and Hyaluron Filler Night, were each applied to one half of the face by the subjects in self-application. The participants had to refrain from using anti-wrinkle or anti-age face care products during the last 2 weeks and from face care products in general during the last 3 days prior to the baseline visit. Forehead wrinkles were assessed before use (baseline evaluation), as well as after one and two months of regular product use by means of *in-vivo* topometry (Phase-Shifting Rapid *In-vivo* Measurement Of Skin, PRIMOS analysis) and by photo evaluation. Photo images were judged independently by 10 non-expert evaluators. After blinding the notation of the pre-treatment / post-treatment images, photographs taken from the same patient were compared and differences in wrinkle appearance between the images were graded on a 9-point scale from -4 (worsening) to +4 (improvement). The 10 grades for each comparison were averaged.

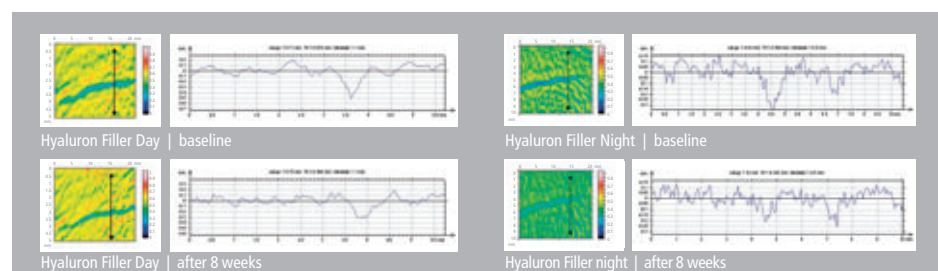


Figure 1: Profiles of forehead skin surface with wrinkle before and after 8 weeks of applying Hyaluron Filler Day or Hyaluron Filler Night

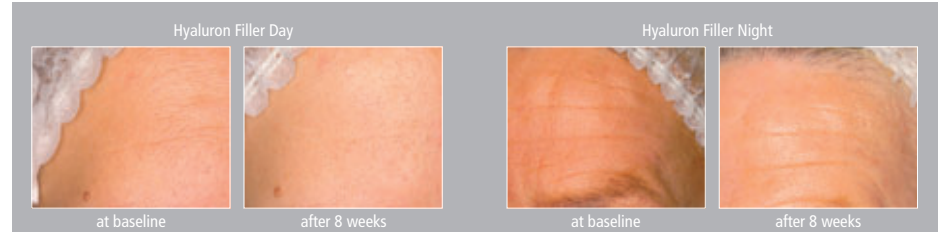


Figure 2: Representative photographs taken from the forehead of a female volunteer at baseline and 8 weeks after using Hyaluron Filler Day or Hyaluron Filler Night.

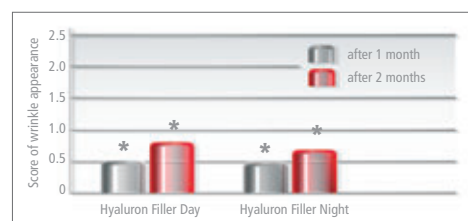


Figure 3: Grader assessment of blinded images for forehead wrinkles after treatment with Hyaluron Filler Day and Hyaluron Filler Night. Given are means of differences in comparison to baseline. Positive values indicate an improvement in wrinkle appearance, the wrinkles are visually reduced. \* p < 0.05

#### Evaluation of skin moisturization

56 females between 25 and 65 years of age with dry skin (Corneometer values less than 35) were enrolled in this randomized, blinded in-use study. After 3 days of preconditioning prior to the baseline visit (no use of skin care products and special cleansing products as shower oils) either Hyaluron Filler Day or Hyaluron Filler Night was applied onto the inner forearm of the participants. Skin moisture was examined by Corneometer measurements at baseline as well as after two, five and 24 hours after treatment.

#### Dermatological in-use study

24 female patients with normal or dry facial skin (average age 48.6 yrs.) were included into the open, dermatologically controlled study. The patients applied Hyaluron Filler Day twice daily for four weeks. Dermatological assessments at start and end of the study included dryness, wrinkles, tension, and reddening. Furthermore, photo images were taken from the crow feet regions at baseline and 15 min. after product application at the first and the last study day. Finally, skin compatibility and product performance were evaluated.

#### Clinical in-use study

A total of 70 patients patients between 30 and 50 years of age with normal or dry facial skin were enrolled in

the clinical in-use study. Approximately half of all patients had skin augmenting injections with hyaluronic acid in the week prior to the baseline visit. 35 participants received Hyaluron Filler Day while the remaining ones were asked to use the Hyaluron Filler Night. Skin compatibility and product performance was evaluated by physicians (visual assessment) and by the patients at the end of the 2-week study period.

### Results

#### Evaluation of anti-wrinkle activity

After 2 months of product use PRIMOS measurements revealed a significant decrease (p < 0.05) in forehead wrinkle value Sc (mean peaks height of the surface) when compared to baseline. Improvement in skin wrinkles was demonstrated after use of Hyaluron Filler Day as well as after application of Hyaluron Filler Night (fig. 1). Results of the photo evaluation were in line with the *in-vivo* topometry data and demonstrated a visible improvement in wrinkle structure (fig. 2). A significant decrease in forehead wrinkle

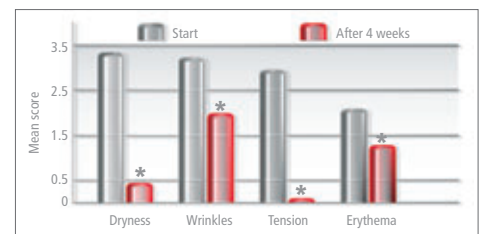


Figure 5: Highly significant improvement (\*p < 0.001) of facial skin parameters in dermatological in-use study.

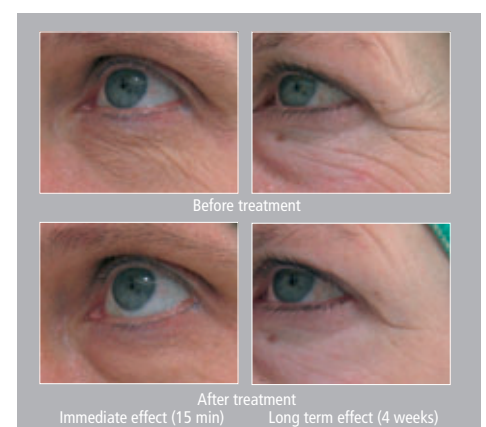


Figure 6: Visible improvement of wrinkles in the crow feet area.

#### Clinical in-use study

Visual assessment of solicited symptoms at baseline and after the 2-week study showed significant improvements especially for the most frequently reported skin parameters dryness, scaling, tension and erythema (fig. 7). An overall improvement of the skin condition was seen in 94% of patients using the Hyaluron Filler Day and 77% of patients who applied the night care product. Skin compatibility of both products was rated in the vast majority of patients to be "very good" or "good" even in subjects after hyaluronic acid injections. Patients' satisfaction with the performance of the products was very high. Best mean scores with ratings above 6 on a 7-point scale were recorded for skin feeling, reduction of tension, moisturizing efficacy and skin compatibility. Consequently, most patients were in favor of using the products and the physicians recommended the product in most cases.

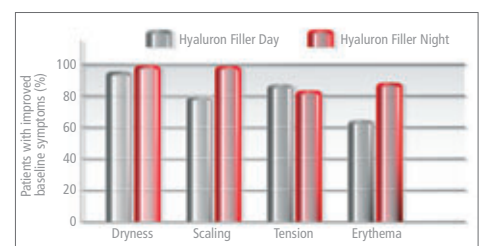


Figure 7: Significant improvement (p < 0.05) in skin parameters in clinical in-use study after 2 weeks.

score was demonstrated in subjects using the Hyaluron Filler Day as well as in those who applied the night care product. Data of the mean pre-treatment / post-treatment differences revealed a significant improvement compared to baseline even after just one month of using the products (fig. 3).

#### Evaluation of skin moisturization

When compared with the untreated control area and baseline, application of both face care products resulted in a significant increase in Corneometer values after 2, 5, and 24 hours (fig. 4). Even 24 hrs after a single application, skin moisture was still elevated by approx. 19% (relative to untreated control and baseline), demonstrating excellent skin moisturizing efficacy of both face care products.

#### Dermatological in-use study

The clinical evaluation revealed highly statistically significant improvements of skin symptoms at the end of the 4 week treatment course (fig. 5). In single cases remarkable effects were observed, as illustrated in fig. 6. Skin compatibility was rated "very good" in all cases by the investigator and in 95.8% by the patients themselves. All cosmetic product properties were assessed as very good by the patients (above 6 on a 7-point scale).

### Discussion and Conclusion

This data, obtained from four studies including altogether 180 volunteers, clearly demonstrates an intensive skin moisturizing and wrinkle diminishing efficacy of the tested formulations. Furthermore, skin compatibility was high even when used in conjunction with injections of dermal filling substances. The anti-wrinkle effects are attributable to the active ingredients hyaluronic acid and soy saponin. HA has long been known for its hygroscopic properties, immediately increasing skin moisture content. In the area of cosmetic dermatology it has recently seen a revival, as regulatory approval has been granted for its use as dermal filler. The application of soy saponins enables an additional enhancement of skin's own HA synthesis, as shown by *in-vitro* studies. The production of HA in human dermal fibroblasts was also significantly induced by this specific soy extract with an increase by more than 250%. Taken together the tested products can be considered effective and safe in the dermatological treatment of facial wrinkles and rhytides, also in conjunction with the intradermal application of dermal filling substances, namely HA.