



REGAINING A YOUTHFUL LOOK

Ingredients | Replexium, a blend of two patented tetrapeptides, reduces wrinkles and firms up facial skin, turning back the clock by as much as seven years. The peptide blend improves signs of ageing by targeting the extracellular matrix, the epidermis and the dermoepidermal junction.



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Eating healthily, working out, and winding down: consumers around the world are increasingly taking a more mindful approach to the way they live their lives. But even with a healthy lifestyle, biology can't be outsmarted – time takes its toll: our skin loses its firmness, becomes more fragile, and wrinkles creep in; and the dense collagen-rich extracellular matrix network (ECM), which confers strength and mechanical support to the skin, undergoes progressive atrophy. Many people are not happy with the visible signs of ageing. Women, in particular, long for a more vibrant, youthful appearance. An online consumer survey of our company conducted among 235 North American women aged 40 to 73 revealed that 60% wished they looked 5 to 10 years younger. And most respondents trust in the potential of skin care products: 80% expected a high-quality product to make them look 5 to 10 years younger. If manufacturers can live up to these expectations, their prospects are bright. The world population is ageing, life expectancy is increasing and, according to the World Health Organization, the number of people older than 60 will nearly double from 12% to 22% of the entire population between 2015 and 2050¹.

A powerful peptide blend

Anti-ageing actives are in great demand, yet breakthroughs have remained few and far between. With **Replexium**¹, BASF has achieved a new milestone: in vivo, the blend of Acetyl Tetrapeptide-9 and Acetyl Tetrapeptide-11 (see fig. 1*) visibly reduces wrinkles within three weeks – significantly faster than a peptide benchmark. Additionally, it makes the skin look as firm as skin that is seven years younger.

The skin-bioavailable synergistic complex of the two tetrapeptides – very small molecules that can achieve a high level of efficacy in low dosages – improves the signs of ageing by targeting the epidermis and dermis as well as the membrane zone that joins them, the dermal-epidermal junction (DEJ) zone. This three-level approach promises rapid and lasting anti-ageing effects.

Replexium is a preservative-free syrupy liquid, pale yellow to yellow, which is soluble in water and insoluble in oils and fats. It contains 350–650 ppm of Acetyl Tetrapeptide-9 and 525–825 ppm of Acetyl Tetrapeptide-11 with skin-bioavailability agents. At a recommended dose of 2%, this active ingredient is incorporated

80% TRUST

that skin care products can make women look 5 to 10 years younger

The number of people older than 60 will almost double from **12% to 22%** by 2050

60% of 40-73-year-old **North American women** want to look 5 to 10 years younger

during final processing below 40 °C, or at room temperature for cold processing. On request, **Replexium** is also available as a powder without bioavailability agents under the reference **Replexium PW BC10082** with the INCI name Mannitol (and) Acetyl Tetrapeptide-11 (and) Acetyl Tetrapeptide-9; dose of use 1%).

Promising in-vitro results

For initial lab tests, our company's researchers created human skin models via 3D laser-assisted bio-printing to examine the efficacy of the peptide complex on the extracellular matrix network. This innovative methodology enables faster testing before proceeding to the in-vivo phase.

The peptide complex led to a significantly denser collagen network than the control blend, which was a typical peptide combination available on the market. This enhanced density was demonstrated using second harmonic generation, a highly precise optical process involving laser technology. In summary, photons emitted by lasers behave differently as they interact with different materials. These differences create an image, in this case, of the collagen fibres in the 3D-printed skin specimens. ▶

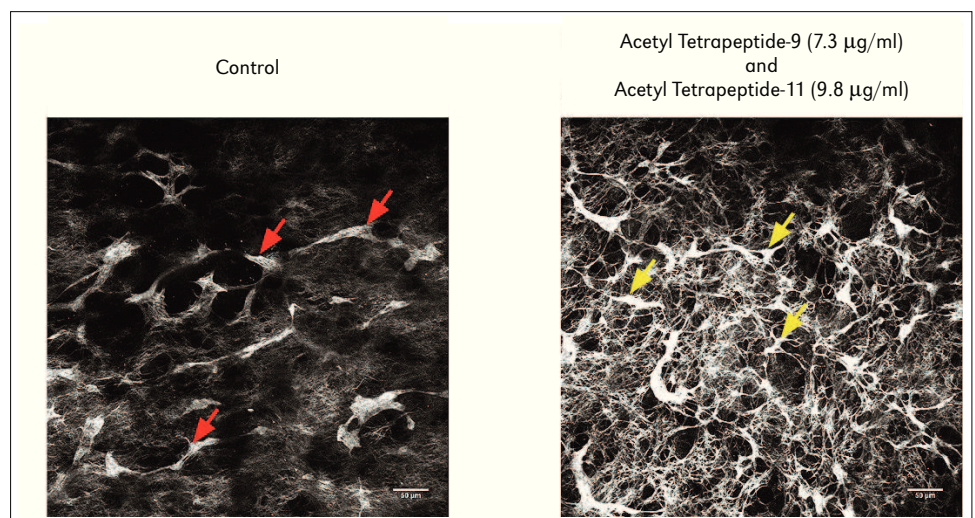


fig. 2: Visualisation by second harmonic generation (SHG) during in-vitro research. The collagen fibres in grey, are denser in the specimen using the BASF product (right) than in the control (left). Images are a 3D stack acquisition in depth of 10 planes of the upper part of the dermis.

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Fig. 2 shows a network of well-defined and very intense collagen fibres in the upper part of the dermis treated with our peptide complex, when compared to the untreated control. In the control dermis, the fibres are smaller and not well defined, forming a blurry network.

A similar improvement in the structure and organisation of the collagen network, with some collagen fibres organised in clusters, was observed deeper in the bioprinted dermis (data not shown). Overall, the **Replexium** peptide complex improved the density and organisation of the extracellular collagen fibres in the dermis of 3D bio-printed skin, for denser and firmer skin.

Powerful rejuvenation in-vivo

In-vivo studies further confirmed the efficacy of **Replexium**. In a double-blind, split-face clinical study involving Caucasian females aged 45 to 65 years, our researchers evaluated the effects of the skin-bioavailable synergistic complex for its ability to improve the appearance of signs of skin ageing, facial wrinkles and dermal density. The female volunteers all had visible forehead wrinkles, nasolabial folds and low dermal density, and considered themselves to have lost skin elasticity and firmness. They applied our peptide complex twice daily for 56 days at the recommended dose of 2% on one half of their faces, and a leading peptide-blend benchmark at its recommended dose of 3% on the other half.

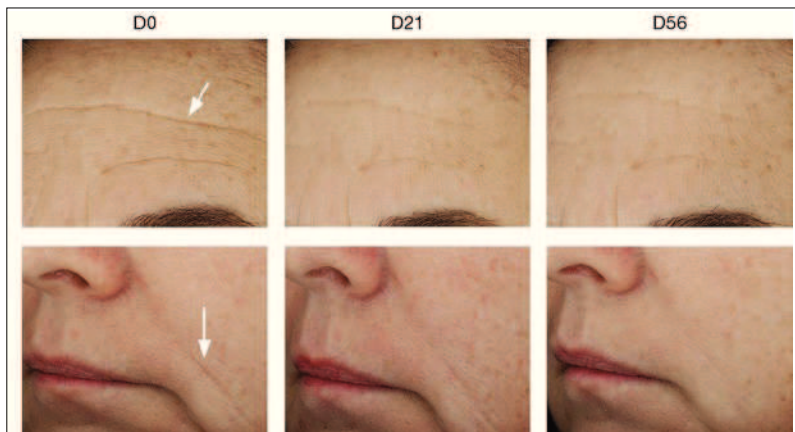


fig. 4: Effect of Replexium at 2% on the signs of ageing: D0 = before treatment, D21 and D56 = after 21 and 56 days of product application

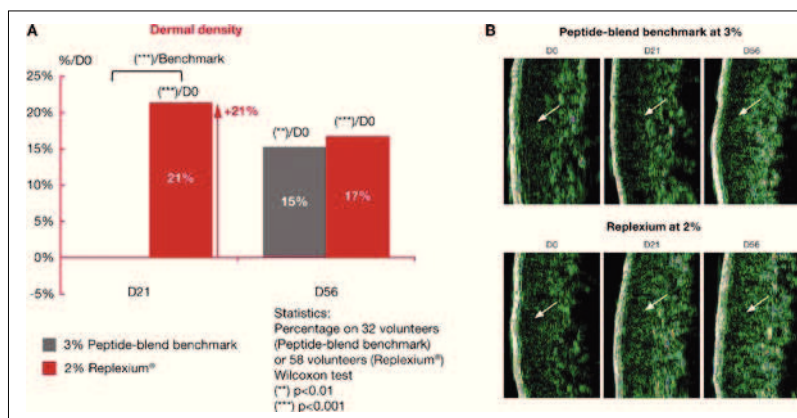


fig. 5: Dermal density evolution vs. baseline measured by ultrasounds on the face for Replexium at 2% and the peptide-blend benchmark at 3% at D21 and D56 (A), and visualisation of dermal density (in green) (B)

Fewer wrinkles and less-pronounced nasolabial folds

Replexium at 2% demonstrated a significant improvement in forehead wrinkles and nasolabial folds as graded by a clinical scientist (fig. 3a*, fig. 3b*). After 21 days of use, forehead wrinkle grades were improved by 11% and nasolabial folds by 9% vs. baseline. This an-

ti-wrinkle effect increased over time, with clinical grades for forehead wrinkles improved by 23% and nasolabial folds by 19% at D56. The results with our peptide complex at 2% are similar to the results obtained with the peptide-blend benchmark at 3%, without any significant differences between the two products (fig. 3a, fig. 3b).

The photos in fig. 4 illustrate the improvement in wrinkles and nasolabial folds achieved with our peptide complex. The effect is visible after 21 days and is even more noticeable after 56 days, as highlighted by the white arrows.

These findings indicate that our peptide complex is an important contri-

“OUR PEPTIDE BLEND REPLEXIUM ACHIEVES A SKIN FIRMNESS EQUIVALENT TO SKIN THAT IS SEVEN YEARS YOUNGER”

Philippe Moussou, R&D Project Management Manager, BASF Beauty Care Solutions

bution in the area of premium dermo-cosmetic anti-ageing products.

Firmer skin – like turning back the clock

Dermal density as measured by high-frequency ultrasound reflects the structure of the dermis and is an important indicator of skin ageing³. Improving the structure of the extracellular matrix network, as shown in fig. 2, may increase dermal density and consequently improve skin firmness.

After 21 days of application by the female volunteers twice a day, the peptide blend demonstrated a significant 21% increase in the face's dermal density value vs. baseline (D0). By contrast, there was no observable change with the peptide-blend benchmark (fig. 5). Compared to the peptide-blend benchmark, the improvement in dermal density value brought about by our peptide blend was significant ($p < 0.001$).

With the peptide-blend benchmark, significant changes in the dermal density value were only observed after 56 days of use (fig. 5). **Replexium's** effects observed at D21 were confirmed after 56 days. Overall, our peptide blend demonstrated a faster and more efficient firming effect than the peptide-blend benchmark.

The ultrasound images in fig. 5b illustrate the changes over time in dermal density (green pixels) and hypoechogenic density factor (low-echogenic pixels with black colour) brought about by the peptide-blend benchmark and **Replexium** on a female volunteer. There are more green pixels and fewer low-echogenic black pixels with our peptide blend (arrows) at D21, and no changes are visible with the peptide-blend benchmark.

For a firmness equivalent to skin that is seven years younger

With test participants exhibiting fewer visible wrinkles and firmer skin after three weeks, **Replexium** acts faster than a leading peptide-blend benchmark. Based on an internal study on dermal density, our experts have determined that this improvement achieves a skin firmness equivalent to skin that is seven years younger. As a result, our peptide blend can help manufacturers tap into a rapidly growing market segment and bring their customers one step closer to lasting youth. □

* INCI: Dimethyl Isosorbide (and) Polysorbate 20 (and) Water (and) Acetyl Tetrapeptide-11 (and) Acetyl Tetrapeptide-9

** These figures, a formulation and additional information can be found on the Internet – see Internet panel

References:

¹ World Health Organization: Ageing and Health. 2018. Available online: <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>

² Pain S, Cadau S, Berthelemy N, Poydenot P, Raul M, Guillemot F, Fayol D, Salducci M, Shao E, Jeong E-Y, Andre-Fret V.: First time use of 3D micropatterning screening and 3D skin bioprinting to further study firming actives. IFSCC 2017. Additional information can be found on the Internet – see Internet panel

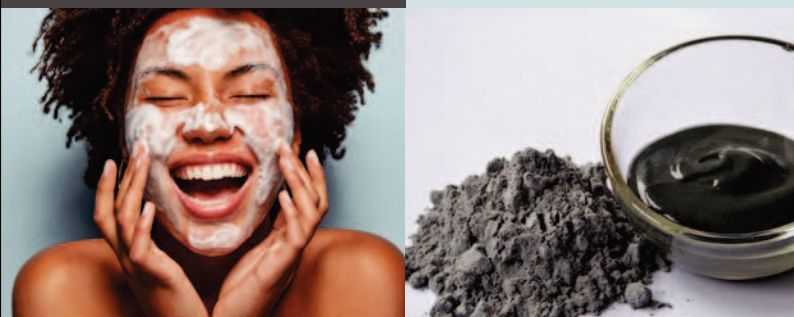
³ Crisan M, Badea R, Cattani C, Crisan D: Imagistic noninvasive assessment of skin ageing and anti-ageing therapies. Senescence, Chap 33, Ed Tetsuji Nagata, 2012.



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