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A new generation of sustainable cosmetic peptides obtained by Yeast Fermentation

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Introduction.

Cosmetic peptides can be from natural origin, as an undefined mixture of protein fragments issued from extraction, hydrolysis or fermentation of natural raw materials, or as synthetic peptides with a specific amino acid sequence. Since years, chemical synthesis of peptides is widely used whereas its most important drawback concerns the use of non-renewable carbon sources and the environmental impact of some of the chemicals and solvents used in the synthetic procedures [1,2].

Biotechnology -synthetic biology and fermentation- may offer a remarkable alternative for the sustainable production of high-quality active ingredients which are efficient and safe.

Materials and Methods.

Fermentation conditions:
Saccharomyces cerevisiae was used as host to produce and secrete a new dodecapeptide by fermentation of renewable sugars. The identity of the peptide was determined by LC-MS.

In vitro efficacy tests:
A 3D reconstructed skin equivalent (Mimeskin) was used to evaluate the performance of this biotechnological dodecapeptide. The skin equivalent was cultured for 78 days, including 3 phases: 3D dermis construction until D57, then keratinocytes proliferation until D64 and differentiation until D78.
Treatment, or not (untreated control) with the dodecapeptide at ppm doses occurred every two days. At D78, the cryosections of Mimeskin (10µm) were used to observe the effect of the peptide on Collagen I, Fibrillin-1 and EMILIN-1 (immunostaining) and elastic deformation (Atomic Force Microscopy).

In vivo efficacy tests:
Two clinical studies on human volunteers were conducted including 28 and 24 volunteers aged from 45 to 65 years, with product application by hemiface twice a day for 56 days. In the first study, the dodecapeptide ingredient at 0.7% was evaluated versus a placebo formula on skin cheek elasticity by Cutometer and on dermal density by echogenic density imaging. Measurements were done at 28 and 56 days.
In the second clinical study, the efficacy of the dodecapeptide ingredient at 0.7% on forehead wrinkle appearance, compared with a peptide benchmark at 3% in the same formulation, was evaluated by image analysis using VISIA CR and VAESTRO software. In both studies, measurements were done at 28 and 56 days.

Results and discussion

To establish a suitable Yeast Fermentation Technology, as a cell factory process for peptide production, gene constructs for the production and secretion of the dodecapeptide by Saccharomyces cerevisiae. By fermentation using renewable vegetal glucose as carbon source and downstream process, the biotechnological dodecapeptide was produced.
The performance of the dodecapeptide was validated in vitro by its stimulating effect in reconstructed skin model on Fibrillin-1 (x3.5, $p<0.001$) at the dermo-epidermal junction, on Collagen type I (x1.7, $p<0.05$) and on EMILIN-1 (x5.2, $p<0.001$) in the dermis (Figure 1).

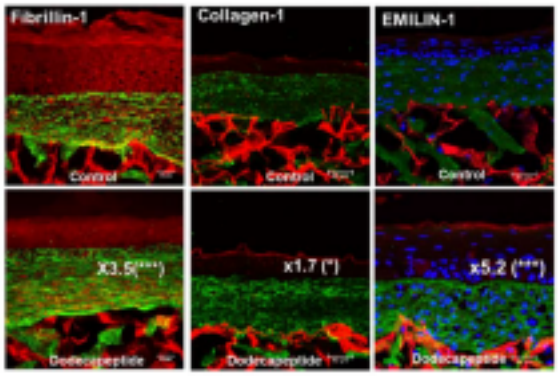
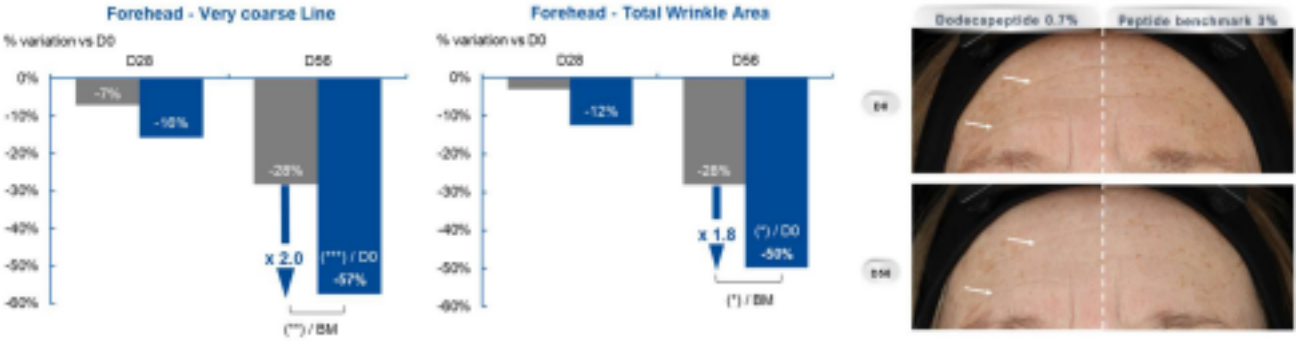


Figure 1: Effect of the dodecapeptide on Fibrillin-1 Collagen1 and EMILIN-1 (immunostaining in green) global morphology (Evan's blue in red) and cell nuclei (DAPI in blue). Statistics Immunostaining: Mean vs control, n=12; Student t test or Mann-Whitney Rank Sum test vs Control; (*) $p<0.05$, (***) $p<0.001$

On the same reconstructed skin, the elastic modulus (or Young's modulus), which measures the resistance of a material to elastic deformation [3], was reduced by 78% ($p<0.001$, data not shown) versus the untreated control. This evidences that the boosting effects on the structural components of the extracellular matrix and dermo epidermal junction resulted in a more flexible dermis.

In vivo, in 56 days, the dodecapeptide increased significantly versus its placebo formulation the skin cheeks elasticity (gross elasticity, $p<0.05$) and dermal density (SELEB and total dermis density, $p<0.05$), (data not shown). On forehead wrinkles (Figure 2), the dodecapeptide reduced significantly by 57% the very coarse lines and by 50% the total wrinkles area versus baseline ($p<0.005$ and $p<0.05$ respectively). It outperformed the peptide benchmark tested at 3% in the same formulation by 2-fold ($p<0.01$ and $p<0.05$ respectively).



A B C

Figure 2: In vivo efficacy of the dodecapeptide on forehead wrinkles by VISIA CR and VAESTRO image analysis: (A) very coarse lines, (B) total wrinkles area, and (C) illustrative picture. Histogram: Peptide benchmark (grey), dodecapeptide (blue). Statistics: % variation on 24 volunteers; Student t test or Wilcoxon test; (*) $p<0.05$, (**) $p< 0.01$, (***) $p<0.001$

Conclusion.

Using a newly developed Yeast Fermentation Technology, we can provide a new generation biotechnological dodecapeptide which ally performance and sustainability. The activity on the skin of this dodecapeptide produced through a sustainable fermentation process, has been scientifically proven through an in vitro study on 3D reconstructed skin and in two in vivo clinical study on skin elasticity, dermis density and forehead wrinkle reduction.

References

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About the speaker

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Valerie Andre has an engineer's degree in biochemistry and a PhD in biomaterials from Lyon University (France).
She joined BASF Beauty Care Solutions research team to first set up and lead the Skin Engineering platform, developing the skin model portfolio to evaluate cosmetic ingredients efficacies. Since 2014, she's one of the BASF Scouting and Communication Experts and contributes to BBCS innovation by setting up new R&D partnerships.