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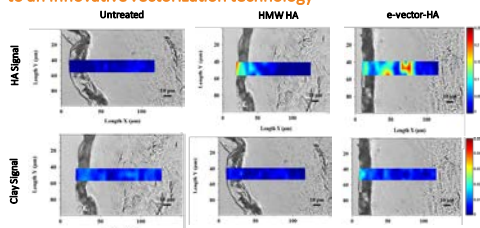
Introduction:

Skin benefits of Hyaluronic acid (HA) is well-known today and considered as an iconic cosmetic active ingredient [1][2]. According to its molecular weight, skin benefits are various and are dependent to their penetration depth [3]. Indeed, High Molecular Weight of Hyaluronic Acid (HMW HA) is known to remained at the surface and provide film-forming property, bringing protection and hydration to the skin [3].

Aiming to bring the properties of HMW HA deeper into the skin, we developed an innovative active ingredient based on vectorization process: e-vector-HA. We worked on the electrostatic properties of the HA complexed in clay in order to drive HA deeper into the skin [4][5]. On this study, we first evaluated the skin penetration enhancement of e-vector-HA in comparison with HMW HA then we confirmed our hypothesis by eliminating each question that could be asked regarding the skin penetration enhancement. Finally, we evaluated the skin benefits brought by the vectorization process on skin smoothing properties and skin brightness reduction at *ex vivo* level and clinical level.

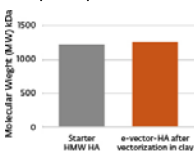
Results & Discussion:

Enhanced skin penetration of HMW hyaluronic acid thanks to an innovative vectorization technology

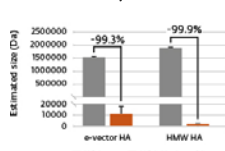


Mode of action elucidation

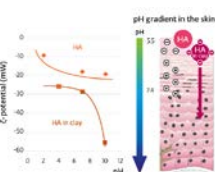
1. Impact of process



2. Resistance to hyaluronidases



3. Electrostatic attraction



The micro-imaging RAMAN spectroscopy allowed us to demonstrate that the vectorization of HMW HA improved the penetration into the skin. In 1., we demonstrate that the molecular weight was not impacted during the vectorization process. 2. The enhancement of skin penetration was not improved by the presence of hyaluronidases since both products are sensitive toward them. 3. Finally, the Zeta potential measurement demonstrated that e-vector-HA was more sensitive to a change of electrostatic charges and consequently more attracted toward the skin.

Conclusions:

Through this study, we wanted to demonstrate our innovative process of vectorization led us to create a HMW HA able to penetrate deeper into the skin and bring optimized benefits for cosmetic use. Indeed, e-vector-HA smoothed the skin by reducing fine lines of the crow's feet with immediate and prolonged effects to finally bring anti-ageing benefits.

Acknowledgements:

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References:

[1] Natalia M Salwowska, Katarzyna A Bebenek, Dominika A Zazdlo & Dominika L Wcislo-Dziadecka (2016) Physicochemical properties and application of hyaluronic acid: a systematic review. *Journal of Cosmetic Dermatology*, 15, 520-526 [2] Anca Maria Juncan, Dana Georgiana Moisa, Antonello Santini, Claudiu Morgovan, Luca-Liviu Rus, Andreea Loredana Vonica-Tincu and Felicia Loghin (2021) Advantages of Hyaluronic Acid and Its Combination with Other Bioactive Ingredients in Cosmeceuticals. *Molecules*, 26, 4429. [3] M. Essendoubi, C. Gobinet, R. Reynaud, J. F. Angiboust, M. Manfait and O. Piot (2015) Human skin penetration of hyaluronic acid of different molecular weights as probed by Raman spectroscopy. *Skin Research and Technology* 2015; 0: 1–8 [4] I. Iachina, I. E. Antonescu, J. Dreier, J. A. Sørensen, et J. R. Brewer (2019) The nanoscopic molecular pathway through human skin. *Biochimica et Biophysica Acta (BBA) - General Subjects*, vol. 1863, no 7, p. 1226-1233 [5] M. E. Lane (2013) Skin penetration enhancers. *International Journal of Pharmaceutics*, vol. 447, no 1-2, p. 12-21 [6] S. T. Stojiljković et M. S. Stojiljković (2017) Application of Bentonite Clay for Human Use. *Proceedings of the IV Advanced Ceramics and Applications Conference* [7] M. Moosavi (2017) Bentonite Clay as a Natural Remedy: A Brief Review. *Iran J Public Health*, vol. 46, p. 8.

Materials & Methods:

Skin penetration enhancement

Raman spectroscopy on skin explants after 8 hours of products application.

Mode of action elucidation

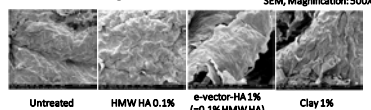
- Impact of process (measurement of molecular weight by Size Exclusion chromatography)
- Resistance to hyaluronidases (in tubo enzymatic degradation)
- Zeta potential measurement

Skin benefits

- Smoothing effect (Scanning Electron microscopy after 3 days of treatment in low hygrometry atmosphere)
- Smoothing fine lines & Mattifying effect (*in vivo* study on 39 volunteers, mean age 49.5 yo, measurement using ColorFace®)

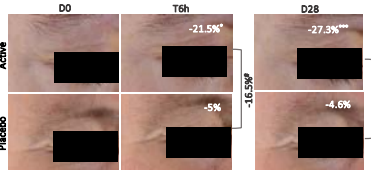
Skin benefits

1. Skin smoothing

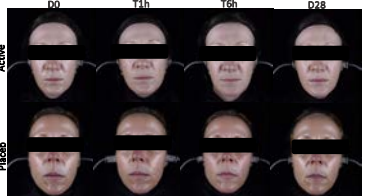
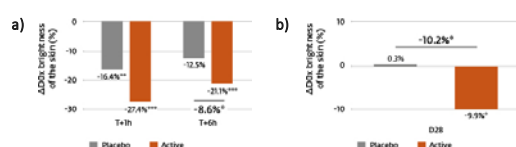


1. Analysis of images revealed that in presence of e-vector-HA completely "smooth out" the stratum corneum since we can observe that the corneocytes were no longer distinguishable in comparison to the untreated, HMW HA and clay conditions. 2. The smoothing effect was confirmed *in vivo* since fine lines were significantly reduced after only 6 hours of application up to 28 days.

2. Reduction of fine lines (short and long term efficacy)



3. Mattifying effect (short and long term efficacy)



3. The results demonstrated that e-vector-HA showed significant mattifying effect after 1 hour and 6 hours of one application (a). Then, the effect was prolonged and maintained after 28 days of application (b).