Tech Session 2: Delivery Technologies in Consumer and Diversified Industrial Products (C&DP 1)

CRS 2022 Annual Meeting & Expo

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Advanced Delivery Science

Inspired by Nature: Biomimetic stabilizers for smart cosmetic active ingredient encapsulation

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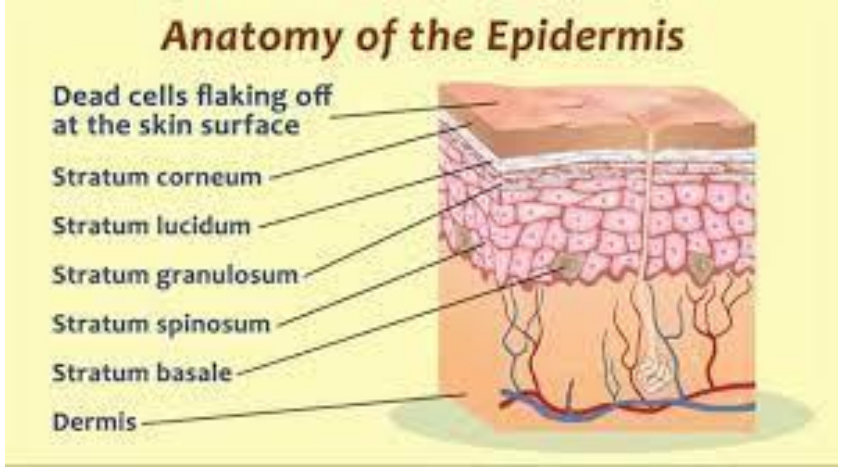
Skin conditions



The skin is the largest organ of the human body that protect from the sun, bacteria, keep the body temperature and is composed of 2 main layers: epidermis and dermis.

Epidermis (0.05-1.5 mm) is structured of different sublayers that are continuously regenerated.

Skin photo-damage

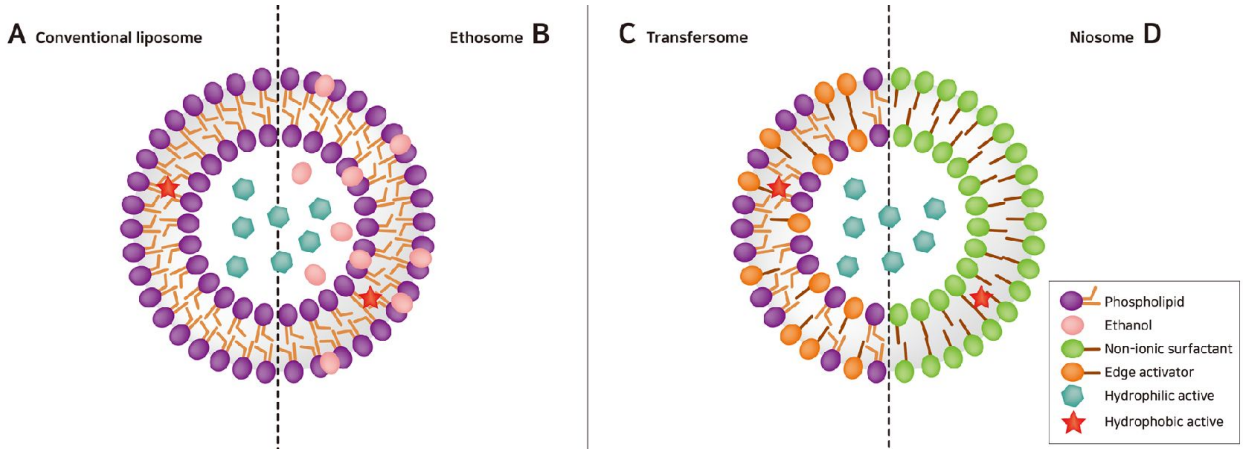
Redness, itching, Inflammation which is translated to increase in IL, overexpression of MMP, hyaluronidase, increase of skin pH…

Cosmetic active ingredients can be used...

… but how can we improve their performances?

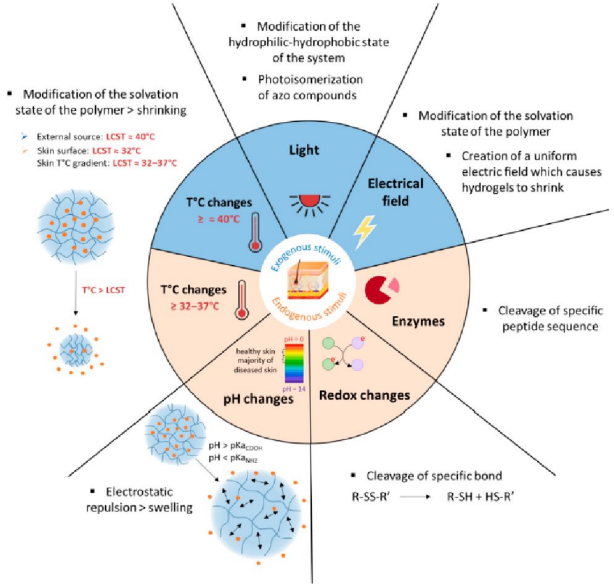
Delivery Systems for Skin Application

Lipid based delivery systems[1]



Liposomes are the most used systems and already on the market. However, most are lacking responsiveness for triggered release.

Responsive delivery systems[2]

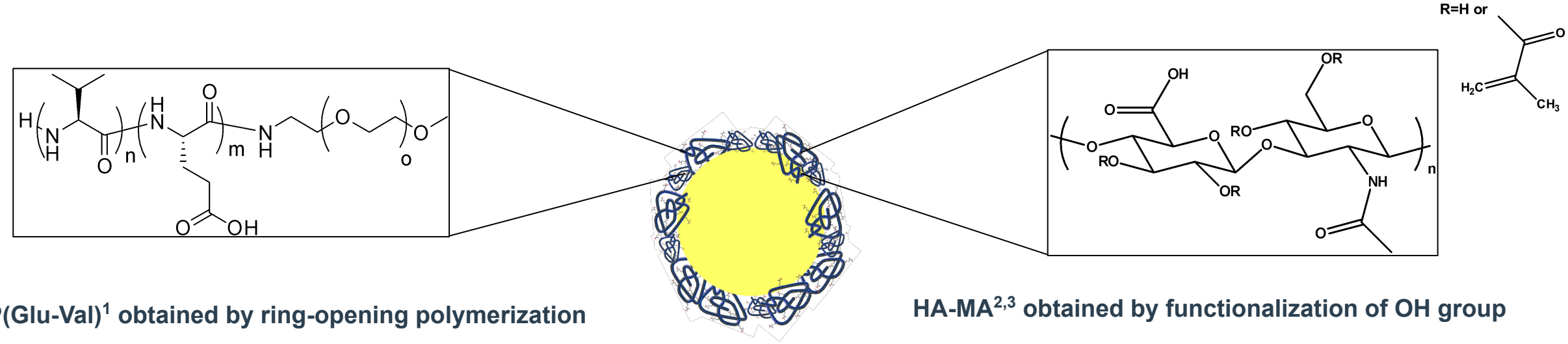


Nanogels are quite versatile and offers a lot of option for responsiveness. However, they are mainly based on non-sustainable polymers.

Can new carrier be designed with responsiveness and from more biofriendly polymers?

1. Kim et al. Biomedical Dermatology 2020, 4, 10.
2. Van Gheluwe Polymers 2021, 13, 1285

Biomimetic stabilizer for emulsion-based delivery systems



PEG-P(Glu-Val)[1] obtained by ring-opening polymerization

HA-MA[2,3] obtained by functionalization of OH group

COOH group of the Glu moieties are used to confer pH-responsiveness

Enzymatic response conferred by:

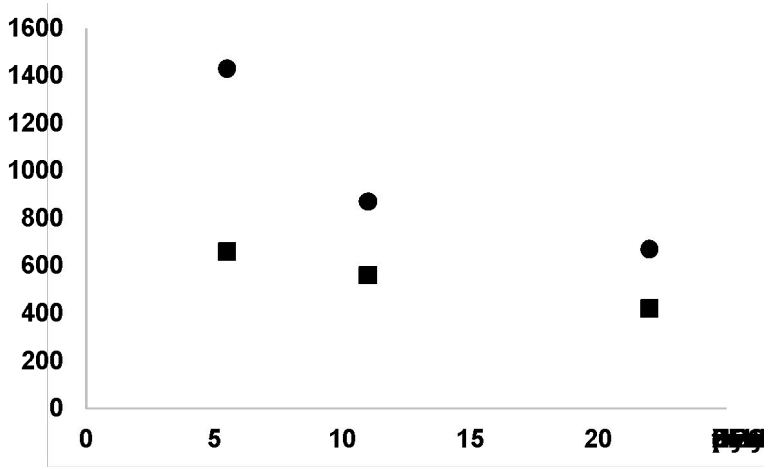
- HA itself through hyaluronidase
- The presence of ester group make the polymer reactive towards lipase

First, can they stabilize Oil-in-Water emulsions?

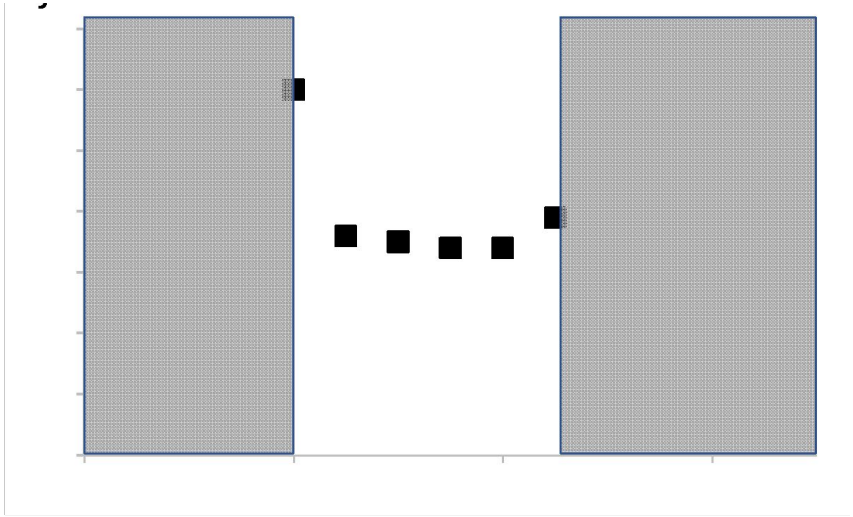
1. WO2019068936A1, NEW POLYMERIC EMULSIFIER AND USES THEREOF FOR THE ENCAPSULATION OF HYDROPHOBIC OR HYDROPHILIC ACTIVE COMPOUNDS.
2. WO2021122942A1 NATURAL ORIGIN STABILIZER FOR OIL IN WATER EMULSIONS.
3. Navascuez et al. Chem. Comm., 2021, 57, 4540-4543

Stabilizers properties

PEG-P(Glu-Val)

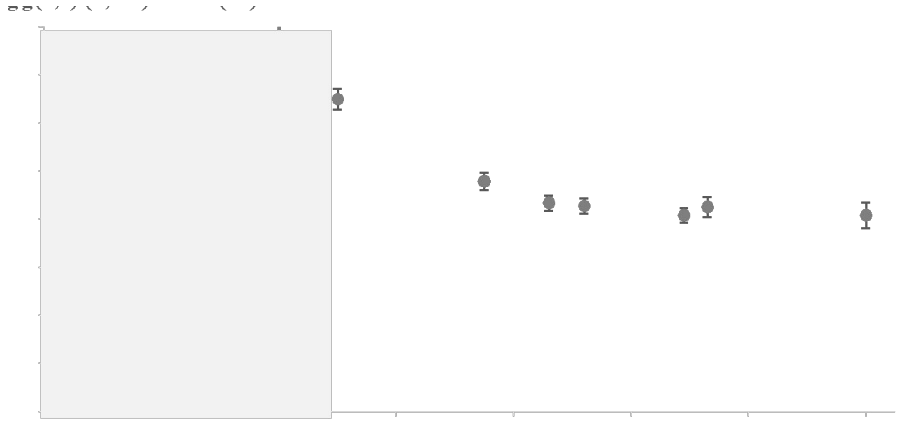


Increasing Dp of PEG block results in smaller droplets. The same was observed for P(Glu-Val) block.

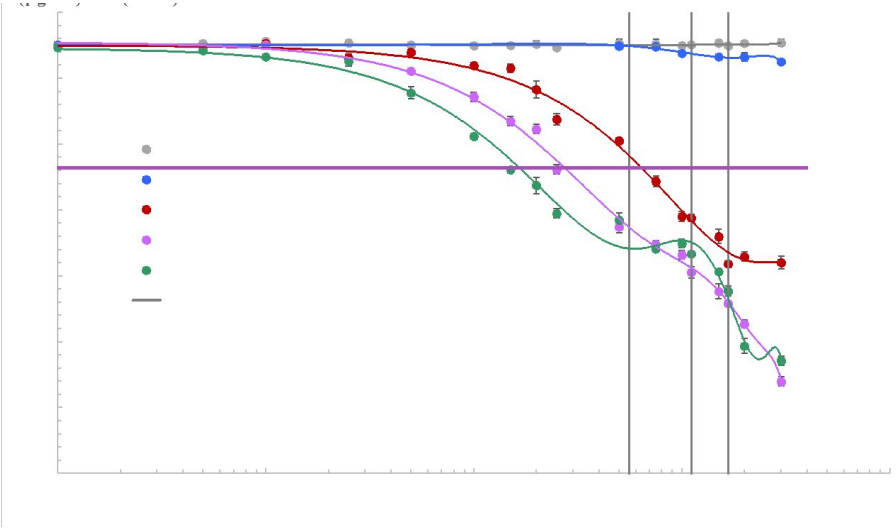


Stable emulsion can only be obtained in a very narrow pH range.

HA-MA



DS of MA > 50% to produce stable emulsion.



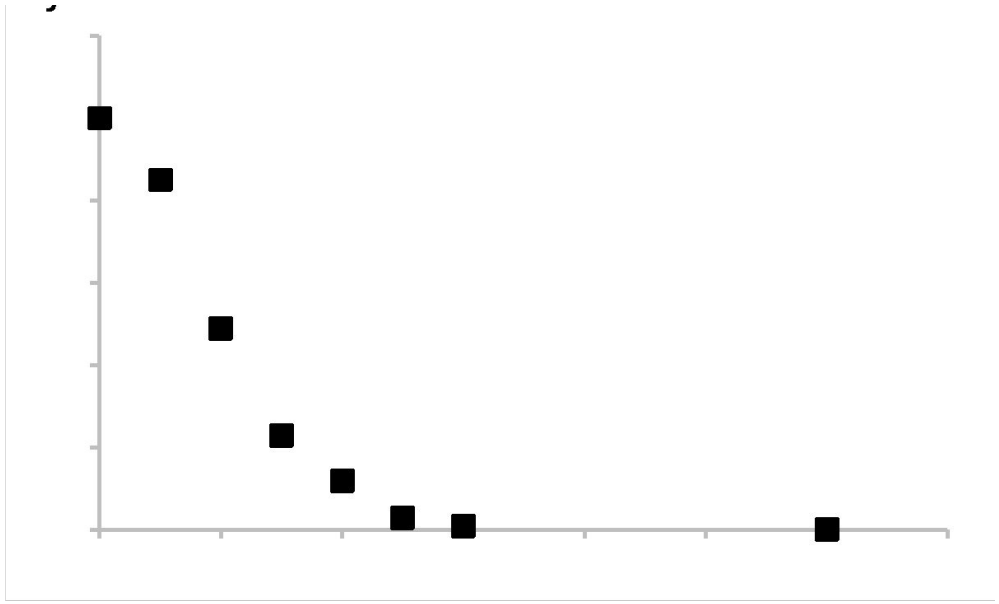
ST studies confirmed that at 10wt% HA-MA: < 63 mN/m was required.

PEG-P(Glu-Val)

Responsiveness of the stabilizers

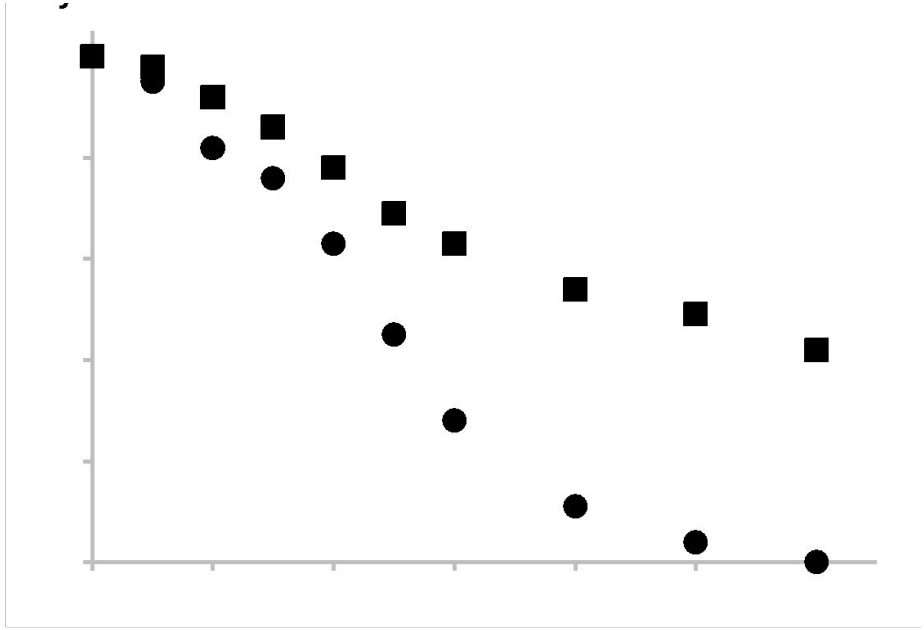
HA-MA

Demulsification kinetics of PEG-P(Glu-Val) emulsions in PBS monitored by laser diffraction



Demulsification occurred very fast within 30 min in PBS

Demulsification kinetics of HA-MA stabilized emulsions in the presence of hyaluronidase (●) and lipase (CAL-B, ■)

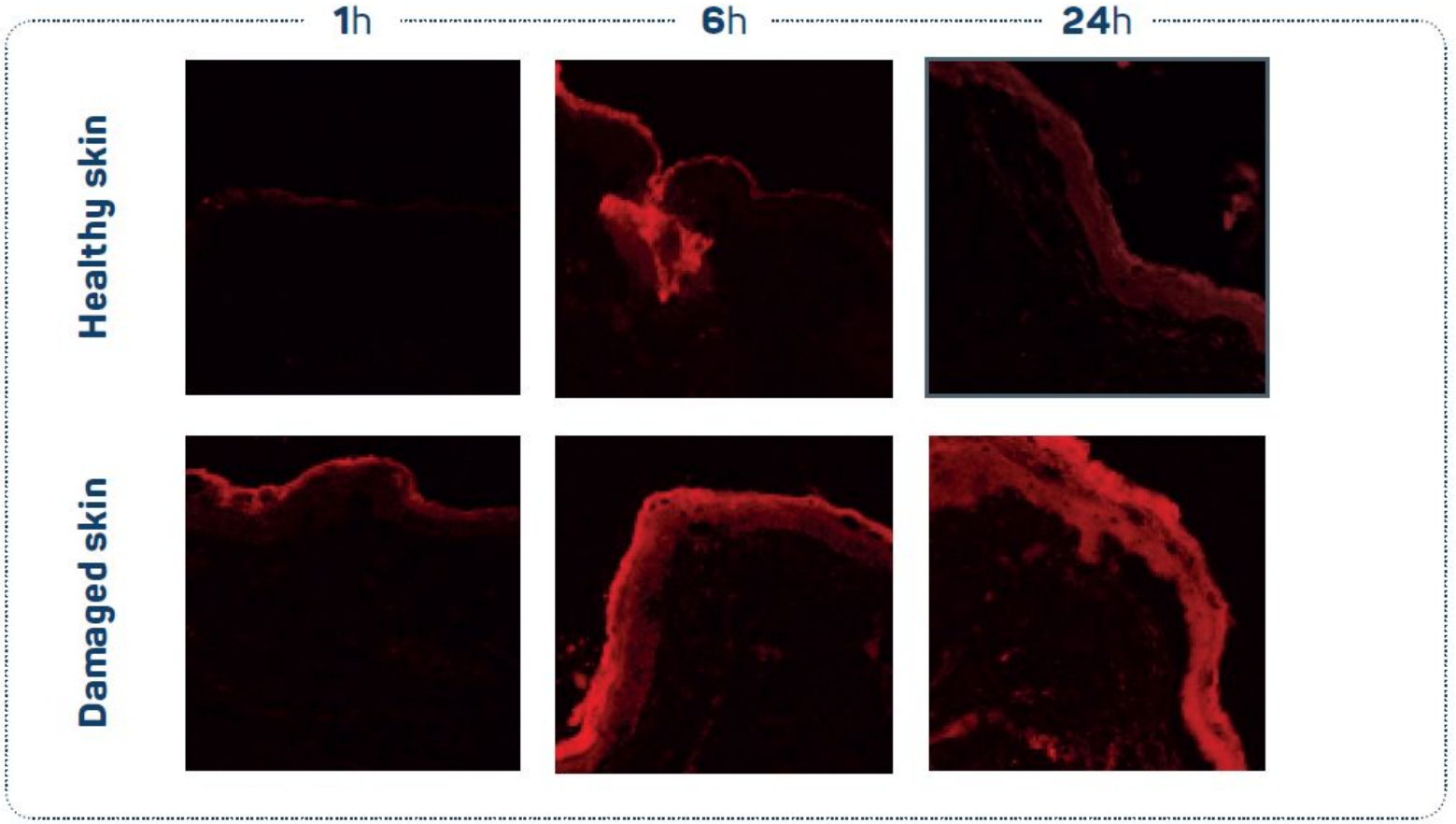


Demulsification kinetics depend on the enzyme, as the ester are mor difficult to reach.

Focus on PEG-P(Glu-Val) system

Skin biodistribution on damaged skin

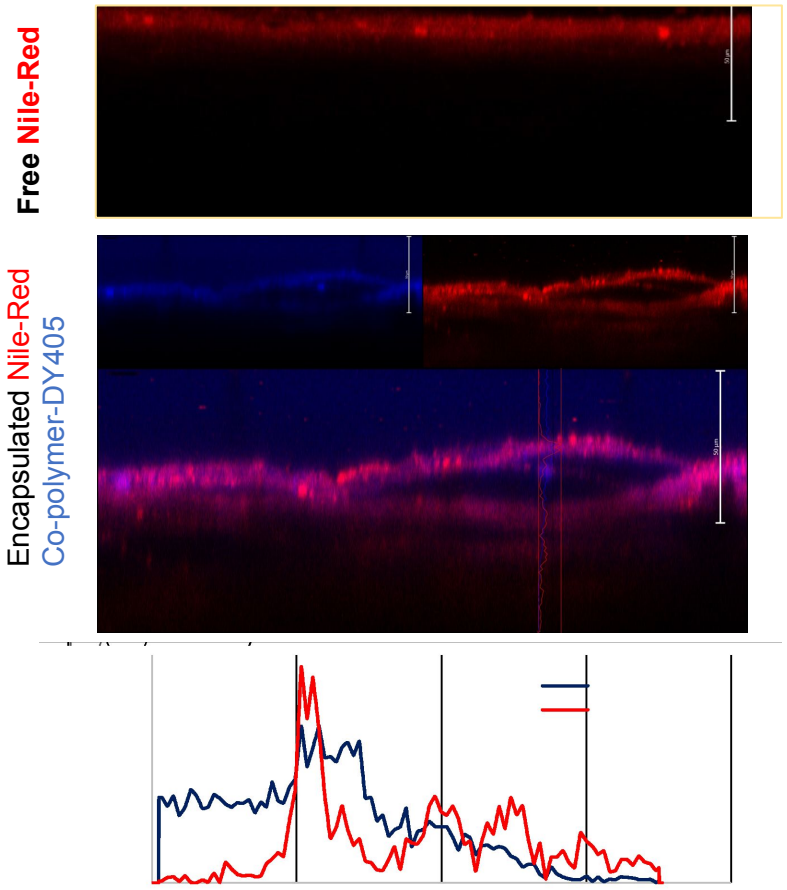
PEG-P(Glu-Val)-stabilized emulsion containing Nile Red in the oil phase which was used to visualize its distribution when applied on Human Skin explant without any treatment (healthy) and treated with 10% SDS to induce irritant contact dermatitis.

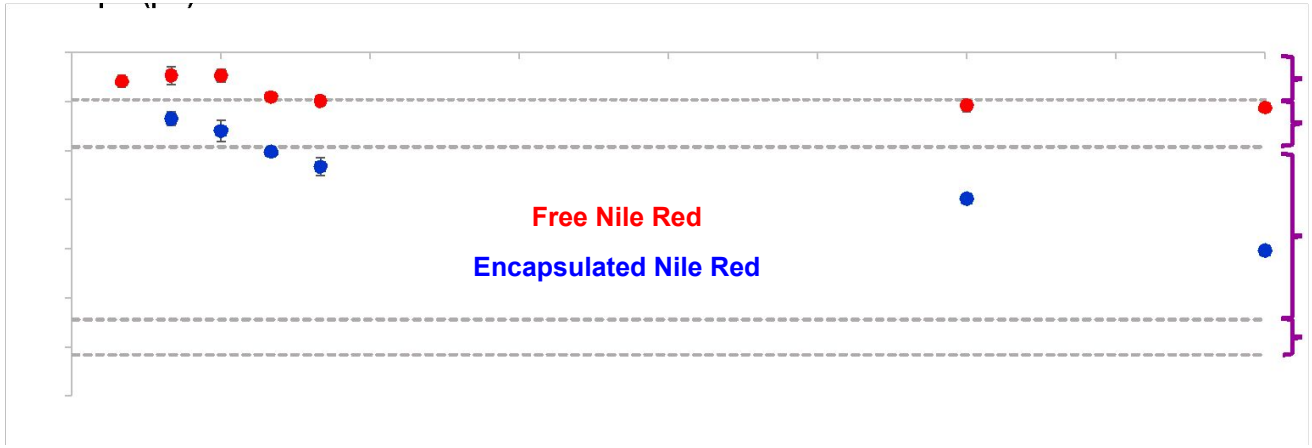


As expected, most of the Nile Red was located in the whole epidermis faster (< 6hours) on damaged skin, due to its higher permeability

Skin biodistribution on healthy skin 24 h

At 24 hrs

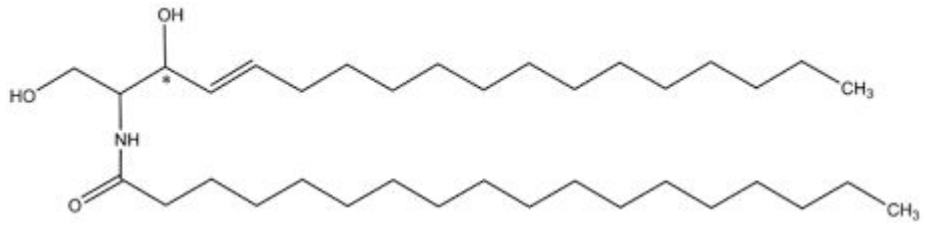




- **PEG-P(Glu-Val) allowed a faster and deeper penetration of Nile Red in the epidermis.**
- **To some extent, it appears that some of the stabilizer and the Nile Red are going together.**
- **Unexpectedly, only PEG-P(Glu-Val) could be observed in the upper layer the epidermis, acting as penetration enhancer.**

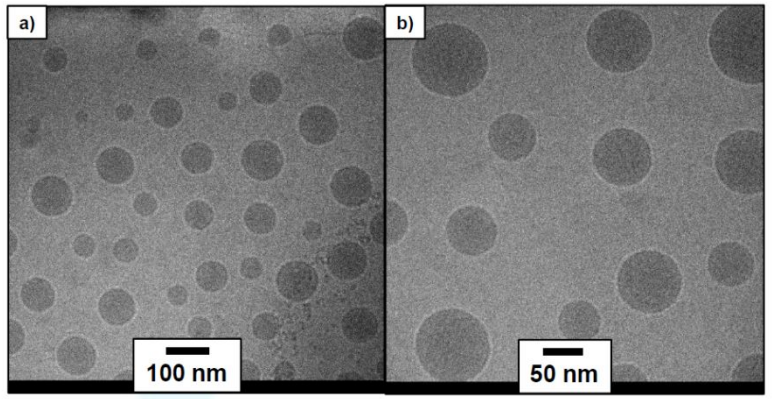
Case of ceramide

Ceramide TIC-001



A sphingolipid identical to a lipid found in the skin. Help retain moisture constant in SC

Homogenized



Hydrodynamic diameter = 153 nm

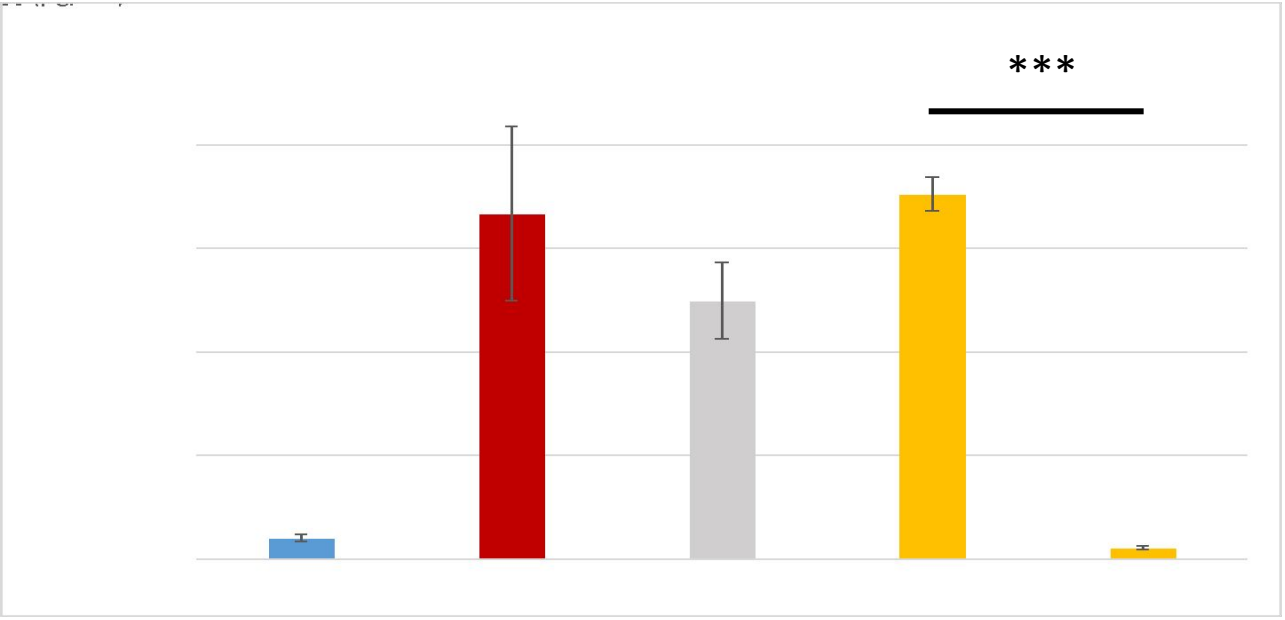
- **Production of 10 Kg of emulsion at 10wt% solid content using High Pressure Homogenizer.**
- **Ceramide concentration in the final product 1wt%.**

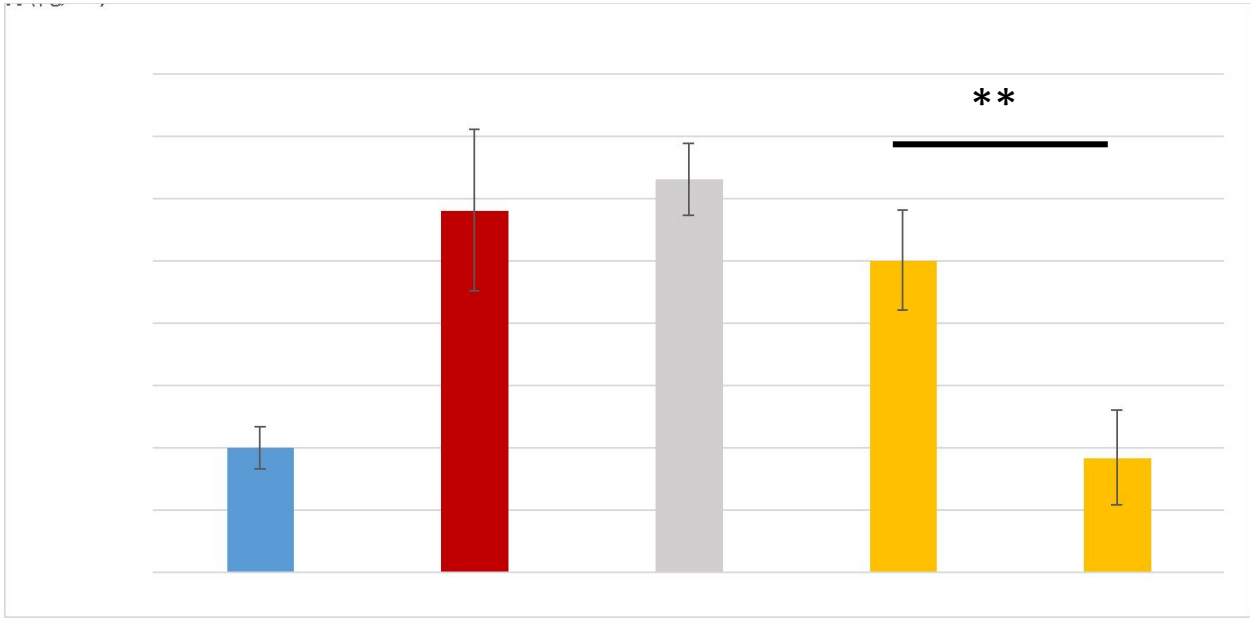
Stability of the product has been demonstrated (freeze-thaw) and accelerated test over 9 month (and ongoing).

Can PEG-P(Glu-Val) increase the properties of ceramide?

Inflammation studies on damaged skin

Inflammation model: 7 days treatment of a human skin explant with corticoids and testing product. After 7 days exposure, the skin was treated with lipopolysaccharides extracted from E. Coli. Interleukin levels are measured after two hours of exposure.



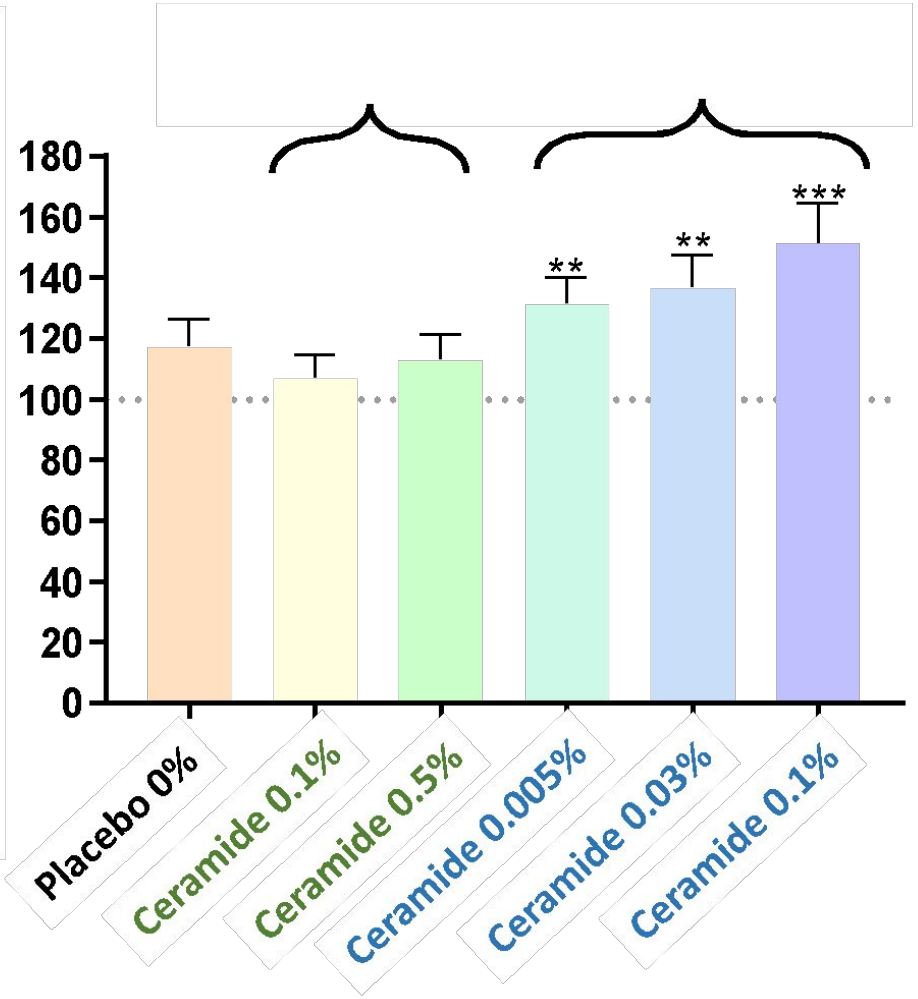


PEG-P(Glu-Val) emulsion containing 1 wt% ceramide, allowed the values of IL-6 and IL-8 for healthy skin to be recovered, whereas free ceramide did not show any significant anti-inflammatory property.

Test on consumers: Skin moisturising

Clinical assessment – topical treatment – 28 days, 2 groups of 20 volunteers.

Corneometry after 28 days

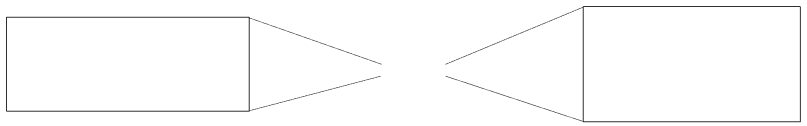


Topical treatment with 0.005%, 0.03%, and 0.1% significantly increased skin hydration levels by 31.5 ± 8.7 %, 36.8 ± 10.9 %, and 51.5 ± 13.2 %, respectively, after 28 days of treatment, compared to basal values at Day 0 (paired Student's t-test).

Significant differences were also observed between the encapsulated at 0.1% compared to free ceramide at 0.1 and 0.5%.

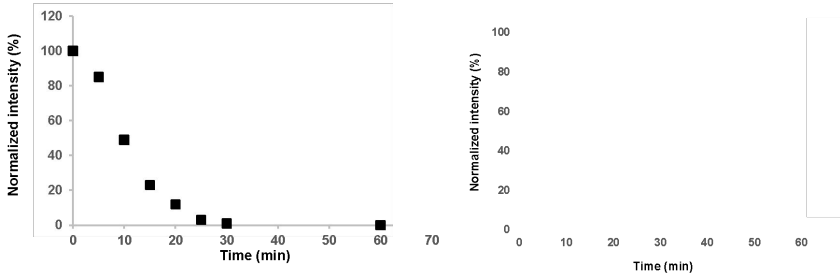
PEG-P(Glu-Val) can increase the skin hydration properties of ceramide.

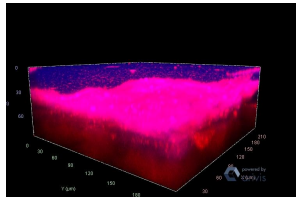
Conclusions



2 biomimetic stabilizers were designed to stabilize oil-in-wáter emulsions.

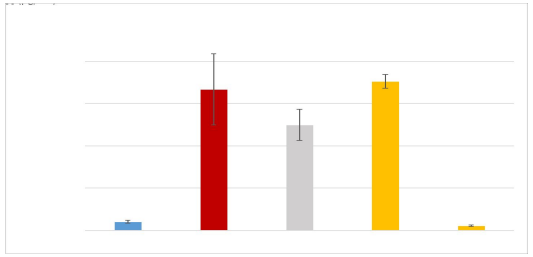
Both systems showed responsiveness to pH or enzyme for PEG-P(Glu-Val) and HA-MA, respectively.





PEG-P(Glu-Val)-stabilized emulsions penetration was faster on damaged skin and allowed the active to reach deeper layers of the epidermis on healthy skin.

The anti-inflammatory and skin hydration properties of ceramide were enhanced when encapsulated in the emulsions stabilised by PEG-P(Glu-Val).



Acknowledgments

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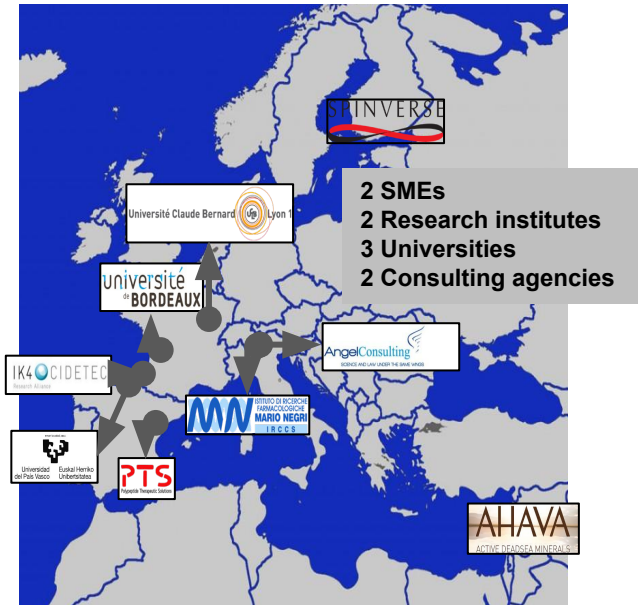

Thank you for your attention