Lipid submicron particles designed to deliver peptide to epidermis

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Glass skin as a skin goal

The glass skin concept is a highly popular trend from Korea of a clear, moisturised, translucent and luminous skin.

From this, the highlighter products have become a huge success in make-up

"prismatic shine"
"galactic glow"

Holographic Stick – Milk Makeup

"dewy skin"
"subtle luminescence"

High Beam - Benefit

+94 %*

of new products launched between 2015 and 2017 in this category.

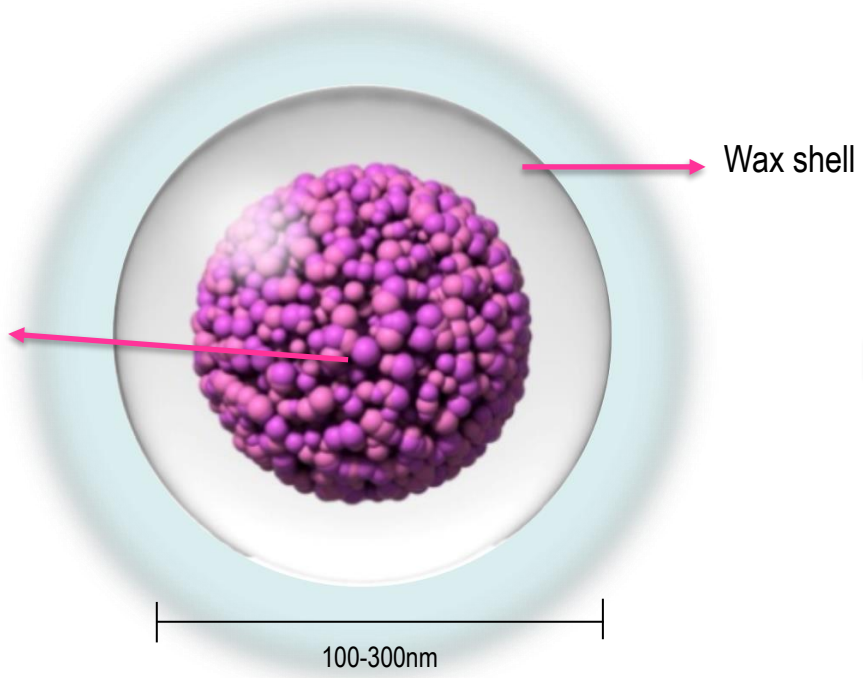
THE BIO-HIGHLIGHTER PEPTIDE

*Source: Mintel

Lipid Submicron Particles

Encapsulated active in oil core

Lipophilic actives or low aqueous solubility actives



- Controlled penetration
- Targeted penetration
- Hydration by occlusion
- Controlled release over time
- Increased active stability
- Reduction of side effects
- Increase in safety and efficacy

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New approach for peptide

PALMITOYL-LYSYL-THREONYL-PHENYLALANYL-LYSINE (Pal-KTFK)

VECTORISATION IN A LIPID SYSTEM FOR:

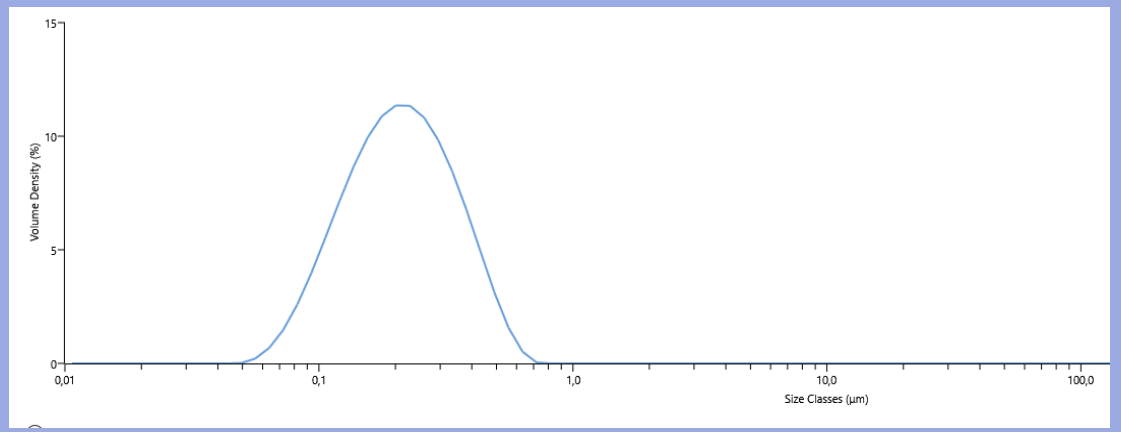
- **Optimised bioavailability** in the epidermis
- **Uniform spreading** at the skin surface
- **Efficient deliverability** with a gradual peptide release ensuring a long-term activity.

External linkage targeting epidermal delivery

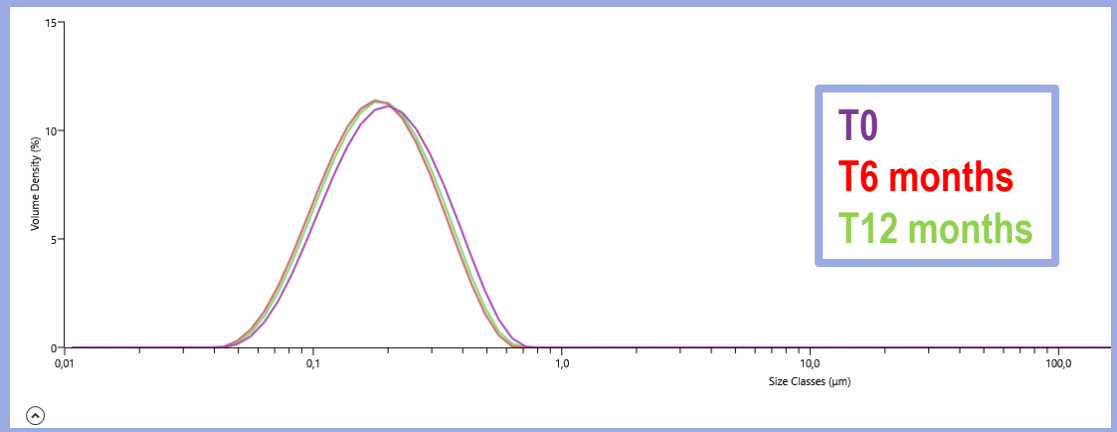
(1) MÜLLER R. H. *et al.* Nanostructured Lipid Carriers (NLC): The Second Generation of Solid Lipid Nanoparticles, 2016, p 160-185, in *Percutaneous Penetration Enhancers Chemical Methods in Penetration Enhancement: Nanocarriers*, N. Dragicevic, H.I. Maibach (eds.), © Springer-Verlag Berlin Heidelberg,

Particle Preparation

- The particles are **in suspension. No precipitation, no phase separation**
- **Solvent free** process, **biodegradable** technology
- **No need** of **thickener, no need** of **shaking** before use
- Can be incorporated **in most formulations** without the need of a suspending agent
- **Product and particles stable over time** either in formulation or standalone

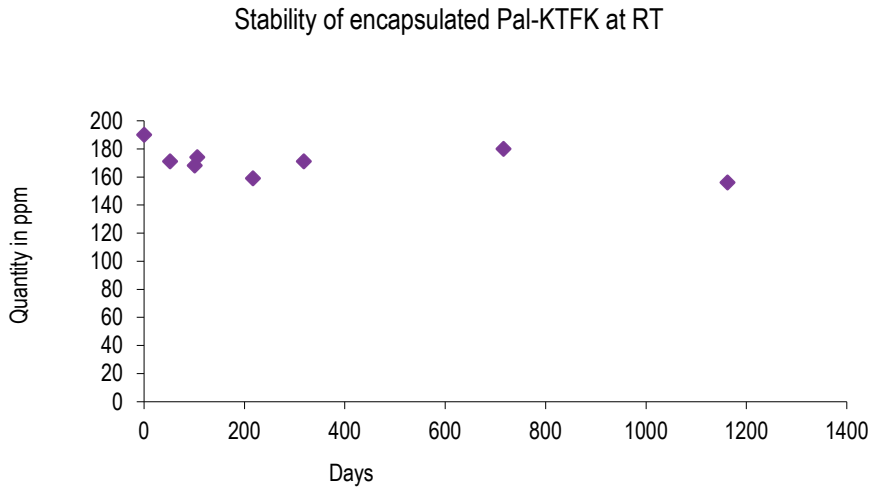


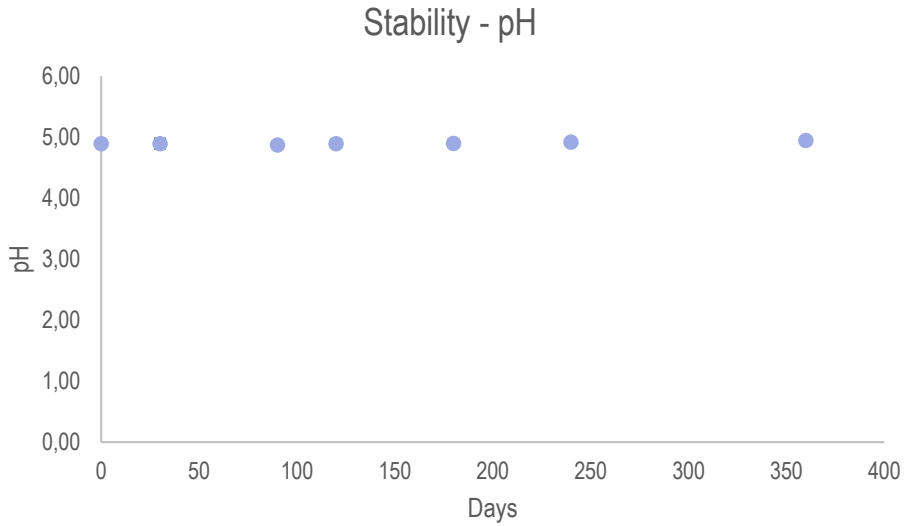
Particle average size repartition: 0.13-0.2 µm

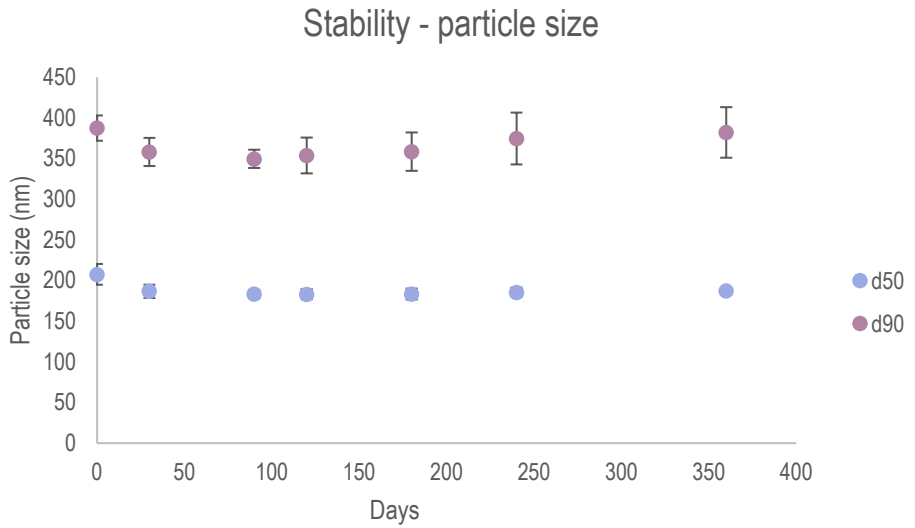


Particle stability over time

Stability

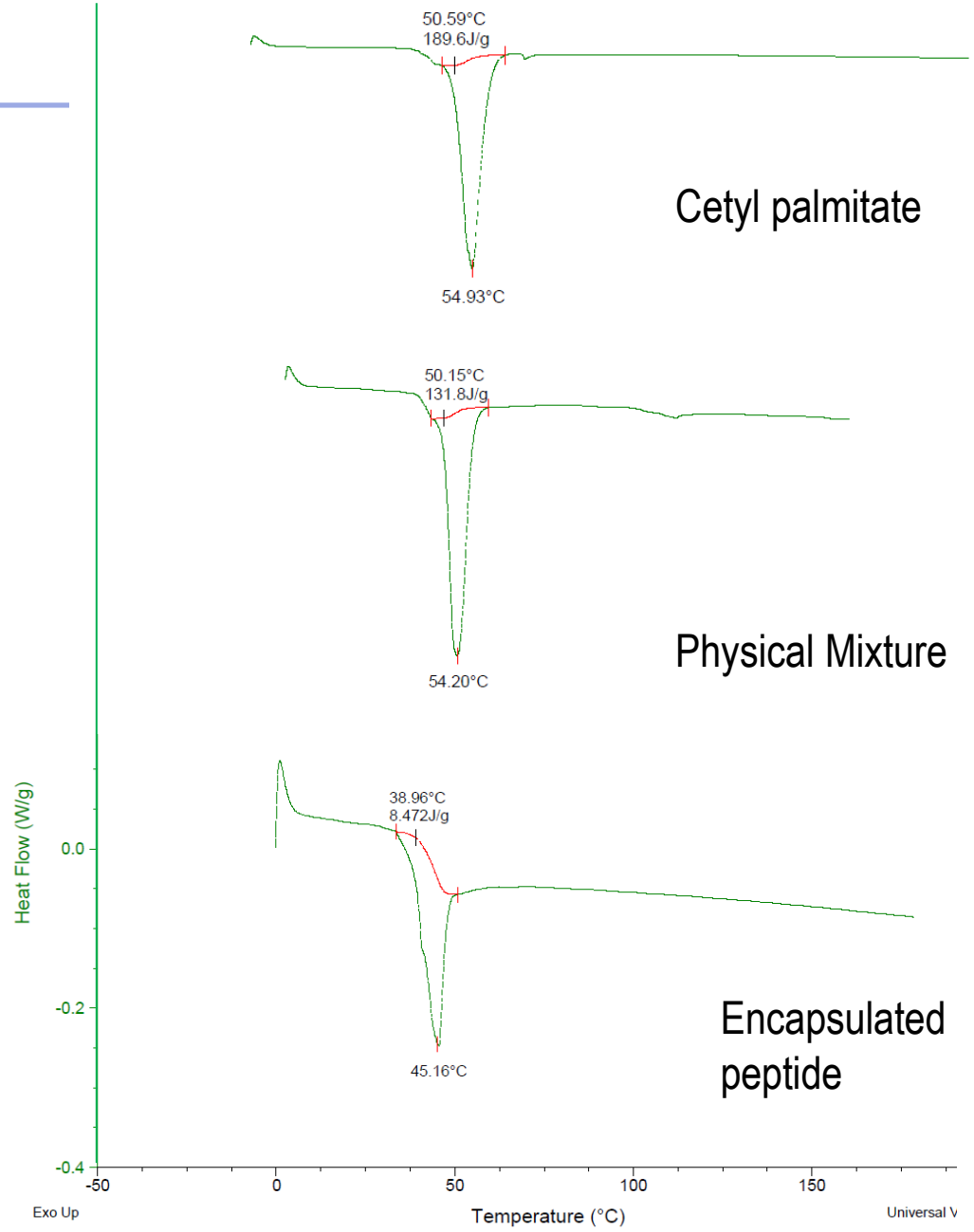






Characterization

DSC analysis – shifts in enthalpy due to encapsulation



Morphology

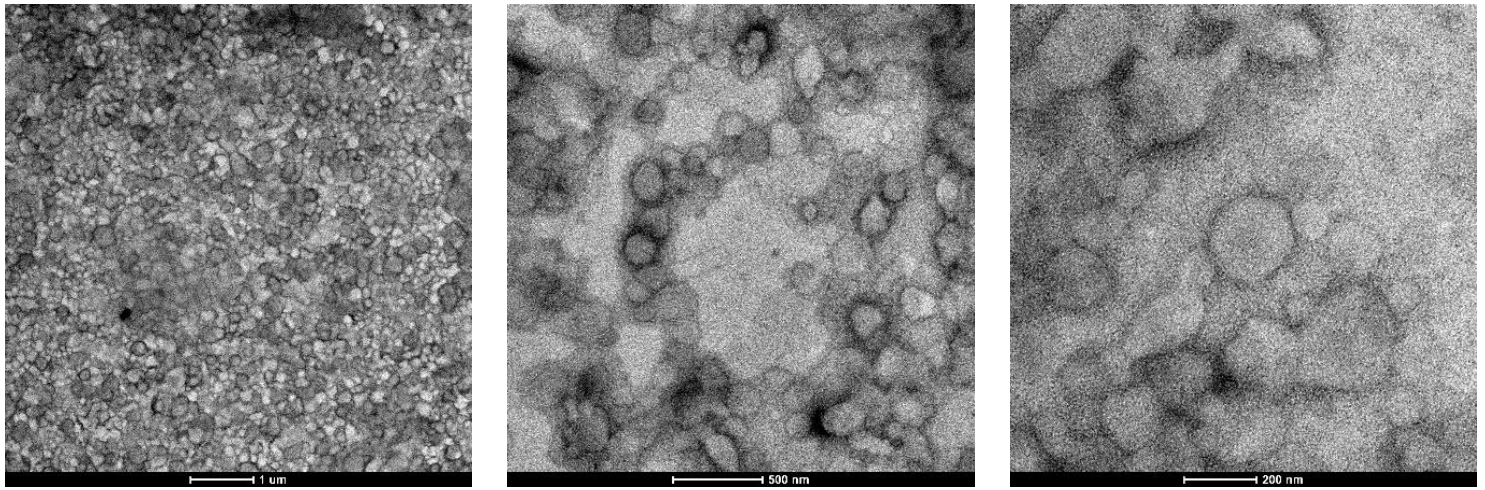
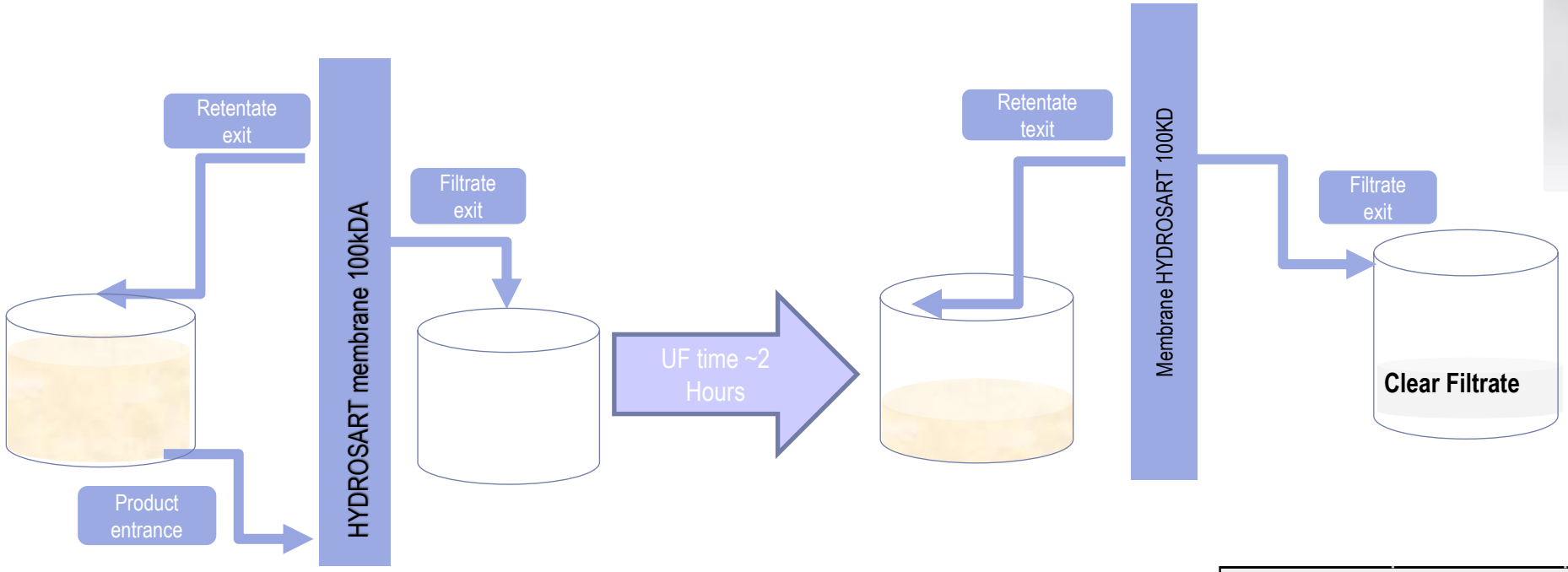


Figure 4. Microscopies in different magnifications.

Encapsulation Efficiency

➔Use of 100kDa hydrosart membrane to separate by flow filtration water/matrix
➔To determine Pal KTFK proportion driven by the« matrix »

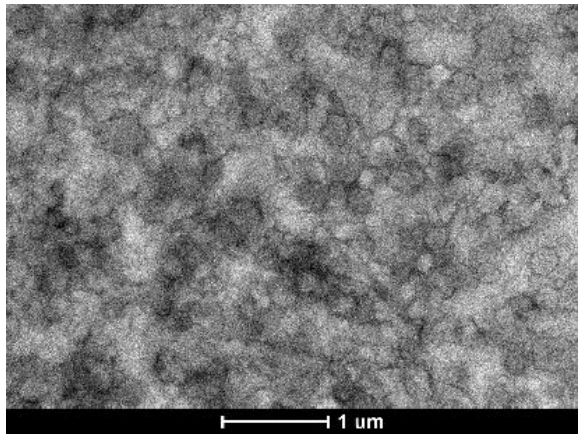


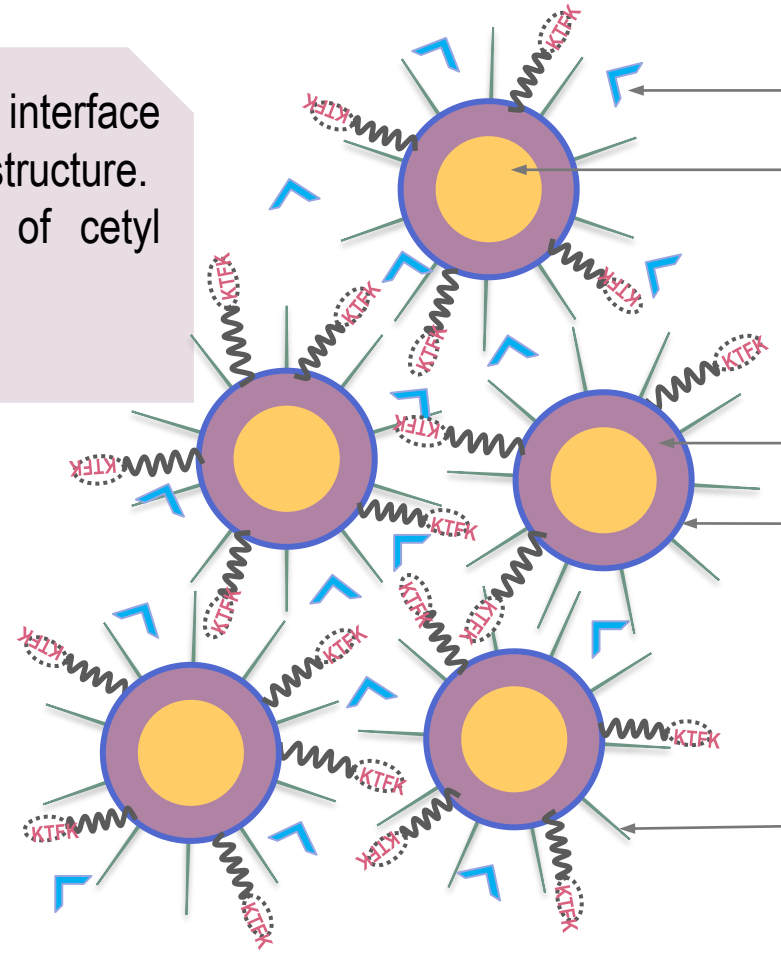
Clear filtrate collected after UF		
Filtrate quantity	Pal KTFK quantity (HPLC assay)	**% Pal KTFK "driven"**
55g	**< 0.01mg**	**< 1%**

Peptide vectorisation

By being amphiphilic, the palmitoylated peptide mainly sets at the interface of the oil soluble and water soluble phases, trapped by the waxy structure. When formulated, the progressive melting and degradation of cetyl palmitate will slowly release the peptide.

0 % free form, 100 % portage





External phase: Water

Internal oil soluble phase: Caprilic/capric triglyceride + sorbitan stearate

Inner shell: Cetyl palmitate

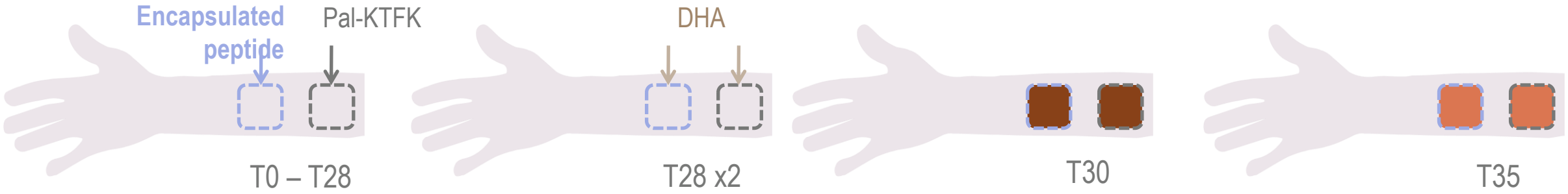
Outer shell: Hydrogenated lecithin

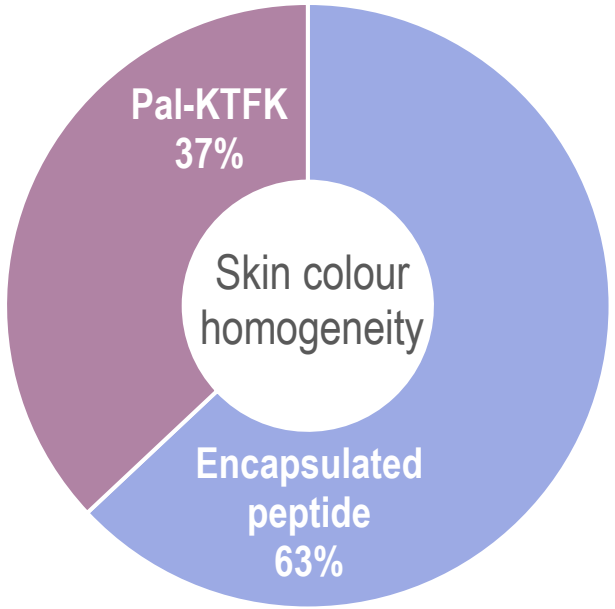
Stabilisation in the water soluble phase: Polysorbate 80

Benefits of the vectorisation

in vivo

Evaluation of the lipopeptide spreadability by assessment of the skin colour homogeneity, by C-Cube dermatoscope and 7 trained assessors. Twice-daily application on the forearm of 18 volunteers (mean age: 39.8) for 28 days of a cream with 3 % **Encapsulated peptide** against a cream with 3 % pal-KTFK. Skin colouring with DHA.





- The skin **colour** is more **homogenous** after treatment with **Encapsulated peptide**
- The skin **desquamation** process is then more **harmonious** after treatment with **Encapsulated peptide**
- Thanks to the vectorisation, the lipopeptide can **spread more homogenously** on the skin surface.

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The peptide bio-harmonical action

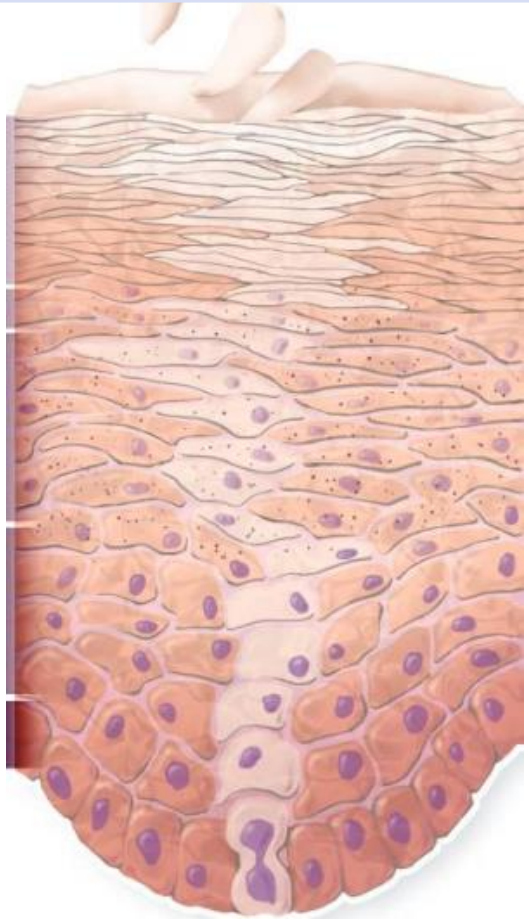
Internal or external stress

⇨ **inflammatory, epigenetic** damage, **protein denaturation**

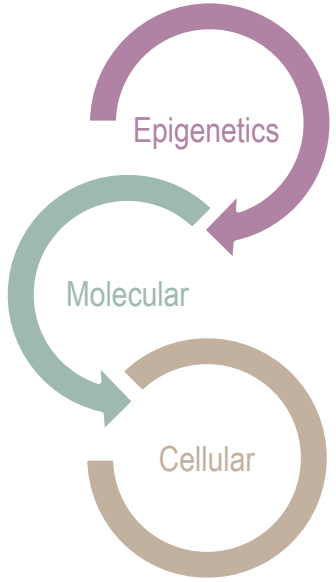
⇨ **impaired skin barrier, rough surface, loss of transparency**.

α-crystallin is the protector of skin transparency.

Chaperone protein ensuring cell proteostasis and preventing aggregation and denaturation of proteins that impairs the cell refractive index.



Encapsulated peptide bio-regulates the skin renewal at the levels of



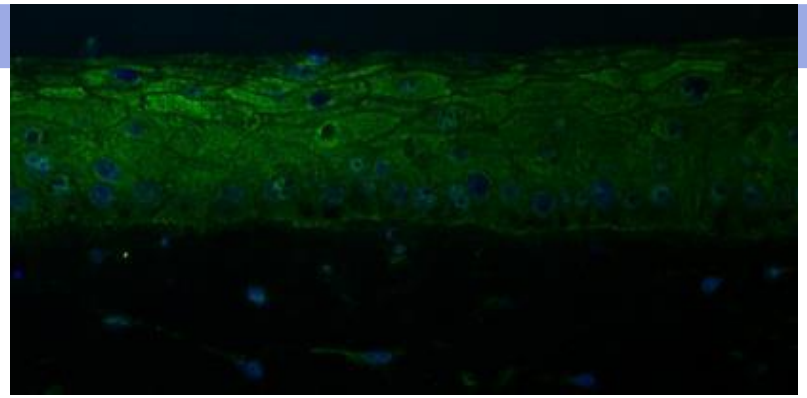
Skin clearness

in vitro

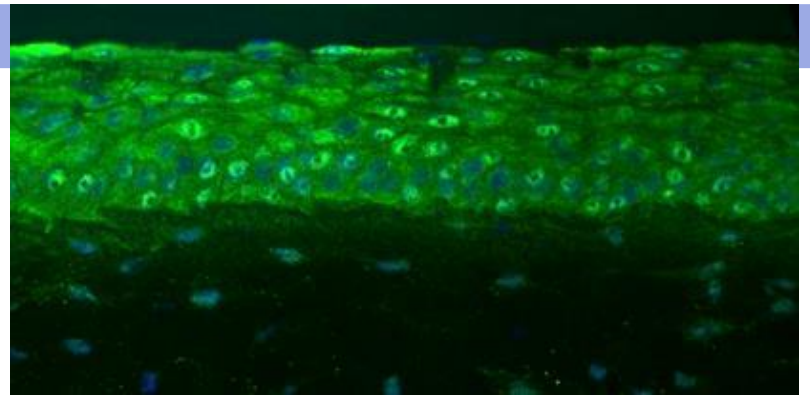
α-CRYSTALLIN

+161 %
p<0.01/control (1)

X2.19
p<0.01/control (2)



Control



Encapsulated peptide 3 %

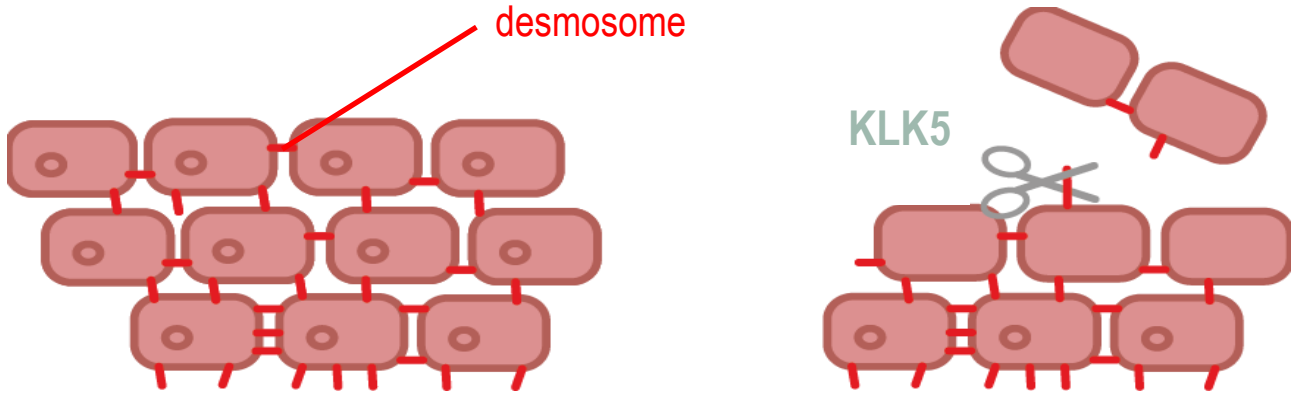
As a molecular chaperone, the **α-crystallin protein** avoids the accumulation of cellular waste.
By analogy with its role in the lens: **α-crystallin** inhibits the precipitation of denatured proteins that opacify cutaneous structures thus ensuring **the skin clearness**.

TECHNOLOGIES: (1) Skin equivalents + immunohistology, 3 %
(2) Normal human keratinocytes + LC-MS/MS, 2 %

Soft-polish effect

in vitro

Kallikrein 5 (KLK5) is a protease that digests desmosomes, thus contributing to the physiologic desquamation process for a harmonious skin renewal.



KALLIKREIN 5

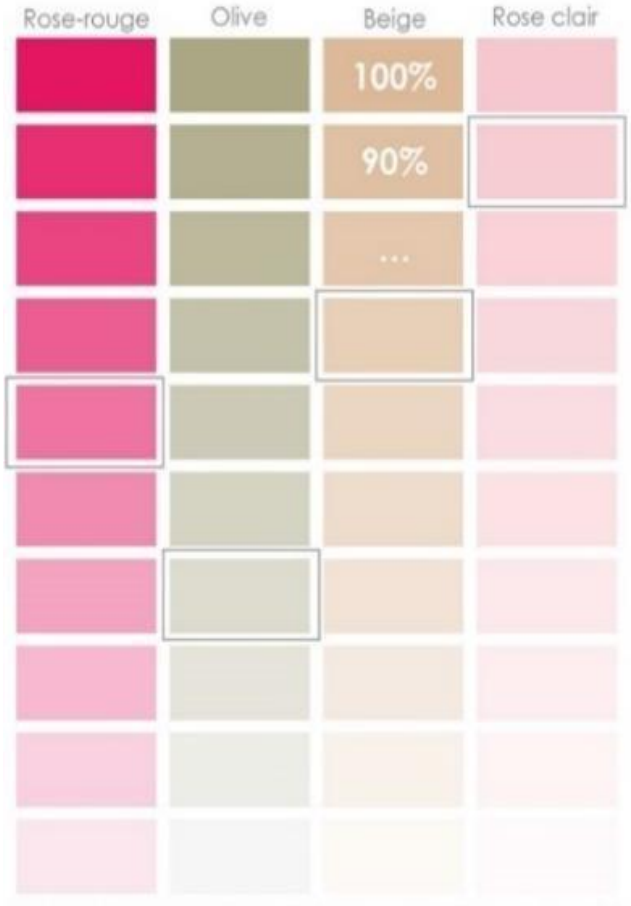
+258 %,
p<0.01/placebo

Encapsulated peptide enables the terminal cell differentiation thus ensuring skin smoothness and its healthy appearance.

Skin complexion

in vivo

Twice-daily application of a cream containing Encapsulated peptide 3 % for 6 weeks. Evaluation of the skin radiance complexion by a visual sensory analysis (CLCT method) on 26 volunteers (22-44 years old) with dull complexion and phototype I to III. Scoring by 3 expert judges.



Pink-Red	Olive	Beige	Soft pink
0 %	**-25 %*** Up to -50 % 96 % respondents	**-4 %*** Up to -10 % 100 % respondents	**+16 %*** Up to +33 % 75 % respondents

Luminosity	Clarity	Transparency
+4 %	**+4.4 %*** Up to +14 % 79 % respondents	**+7.7 %**

Very significant improvement in the skin complexion

CLCT index **+33.5 %***

81 % respondents

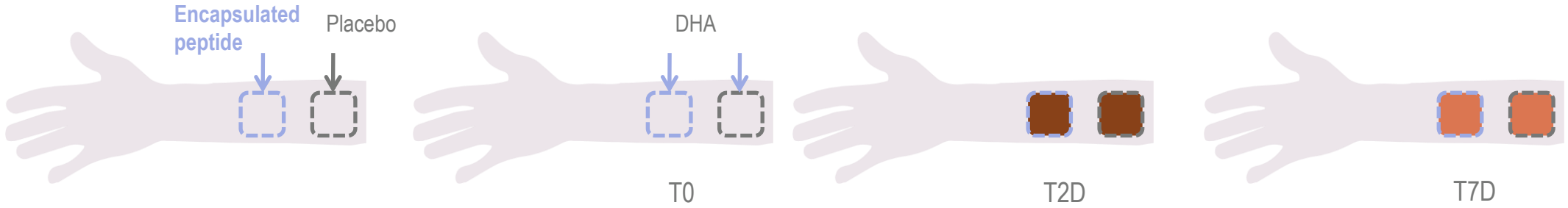
Encapsulated peptide improves the skin transparency by increasing key parameters that defined the quality of the skin complexion. Encapsulated peptide makes the skin clear and glowy.

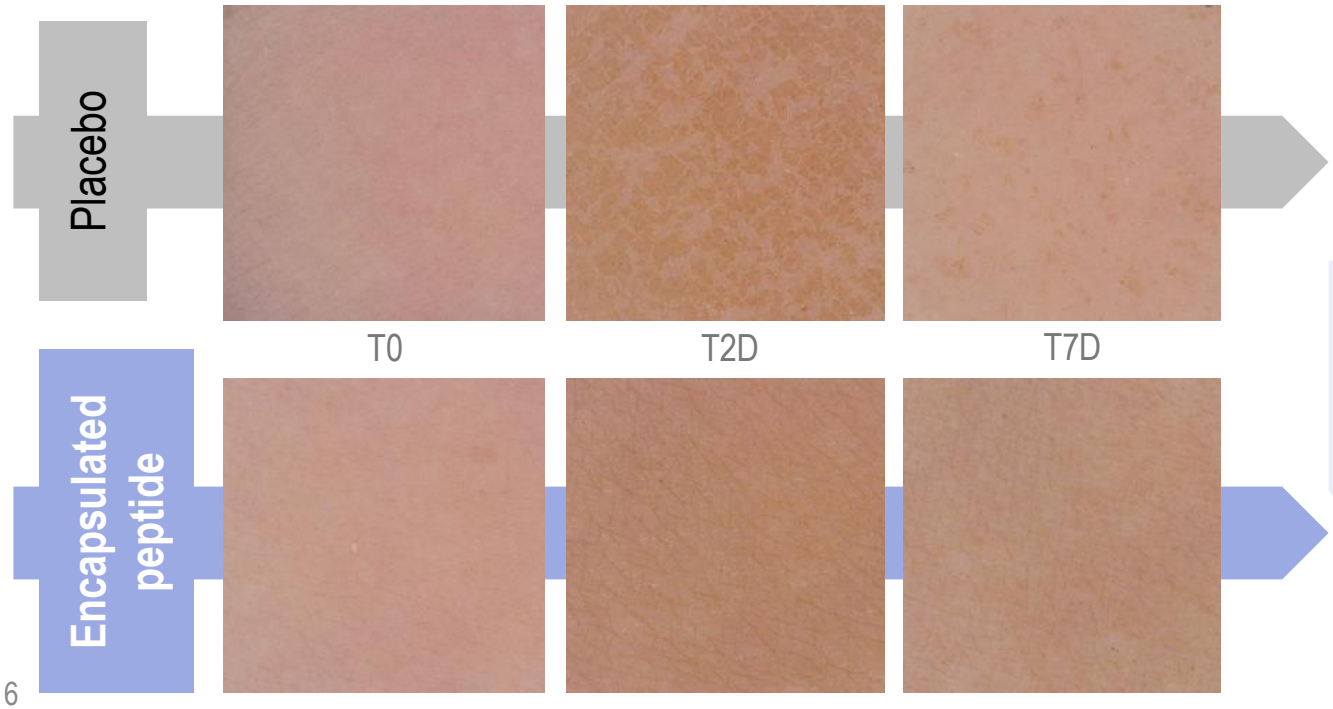
Significant: *$p<0.01/T0$

Skin uniformity

in vivo

Evaluation of the soft-polish effect by colour camera on 20 Caucasian volunteers on the forearm. 5 expert judges. Cream with 3 % **Encapsulated peptide** .





The soft-polish effect of **Encapsulated peptide** :

- enables the regular elimination of accumulated pigments in the epidermis
- restores the skin surface for a radiant appearance.

Skin smoothness

in vivo

Instrumental evaluation of the skin microrelief by LED colour camera on the forearm of 28 Caucasian volunteers.

BEFORE

AFTER 6 WEEKS

Effect also visible on the face:

MICRORELIEF DEPTH

-12.8 %* /T0

up to -29 %*

79 % respondents

MICRORELIEF COMPLEXITY

-20.9 %** /T0

up to -42 %**

79 % respondents

Encapsulated peptide smoothes the skin microrelief by significantly reducing its depth and complexity compared to the placebo.

Encapsulated peptide makes the skin as smooth as crystal for a glowing appearance.

Significant: **p*<0.01 *vs* T0 and *p*<0.04 *vs* placebo
***p*<0.01 *vs* T0 and *p*<0.05 *vs* placebo

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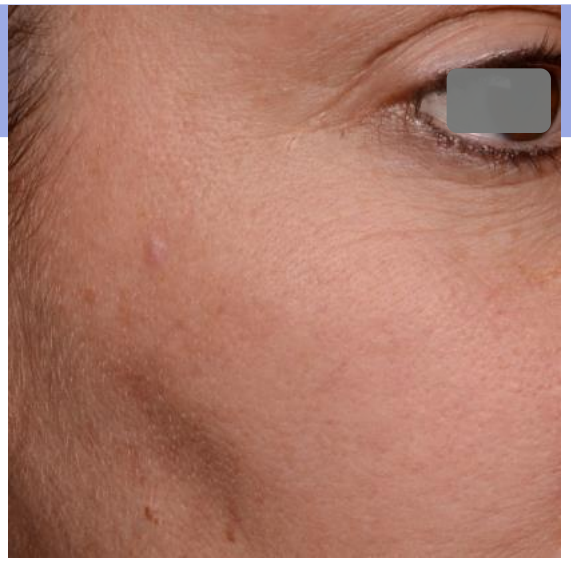
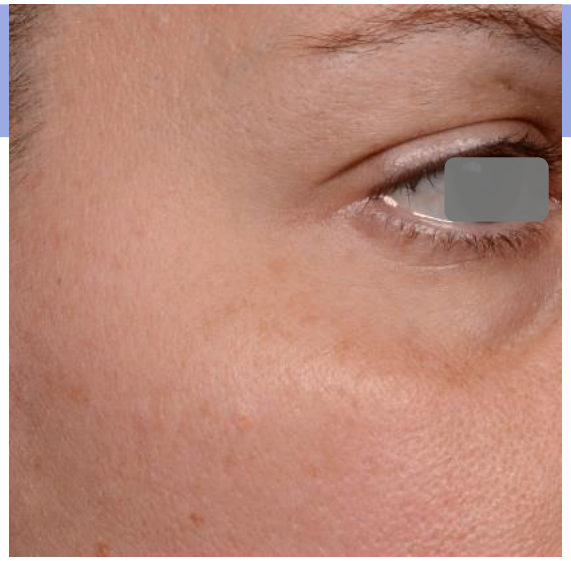
Visible crystal skin

in vivo

BEFORE

AFTER 6 WEEKS





Volunteer #18

Volunteer #17

Volunteer #11

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Conclusion

- Lipid submicron particles can deliver externally linked lipopeptide
- Stable formulations at room temperature
- Enables the harmonious epidermis desquamation
- Increased efficacy due to delivery system

Thank you

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