

TAKING ADVANTAGE OF ELECTROSTATIC INTERACTIONS

for unprecedented skin moisturizing!



NEW YORK
Society of Cosmetic
CHEMISTS

*HYDRATION +
HERO INGREDIENTS*

=

Solving the equation of
young beauty consumers' obsessions!

Young beauty consumers are craving for long-lasting hydration!

When it comes to the main benefits young consumers are looking for in their skincare routine¹, **moisturising is by far their number one priority**, right before **mattifying** & **correcting ageing first signs**.



73%

of young consumers rank
« long-lasting hydration »
in their top 5 skincare claims

(that's at least 14% more than any other claim)

Obviously shared with other demographics, this hydration desire is a key marker of a young generation conscious that **it all starts with a super moist skin**.

1. Givaudan Active Beauty CMI study // (Beauty Snapshot) performed online in France, 695 respondents (women from 16 to 51 years old), April 2021



Another strong driver...

... Hero ingredients, such as HA!

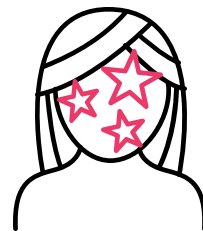
Another significant characteristic of Beauty consumers is their interest in **hero molecules**.

One of the gold standard being hyaluronic acid (HA), first and foremost recognised as being the champion ingredient when it comes to hydration¹.



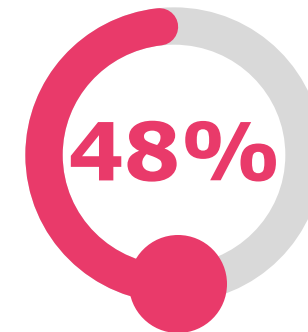
72%

of consumers check
the ingredient list
'always or most of the time'



72%

of consumers
like or love HA



spontaneously
associate
hydration to HA

1. Givaudan Active Beauty CMI study // (HA focus) performed online in 3 countries (France, China, USA), 1145 respondents (80% women, 20% men, from 18 to 65 years old), March 2020

Now to the challenging part...

How to get HMW HA into the skin?

High molecular weight HA (HMW HA) has the best hydration properties versus smaller molecular weights, which offer other benefits, such as anti-ageing, skin repair or anti-microbial defences.

However, HMW HA **does not spontaneously penetrate into the skin**, preventing any long-lasting benefits.

Givaudan Active Beauty white biotechnology experts have therefore been working on this challenge, looking for **the most efficient way to vectorise HMW HA into the skin**.



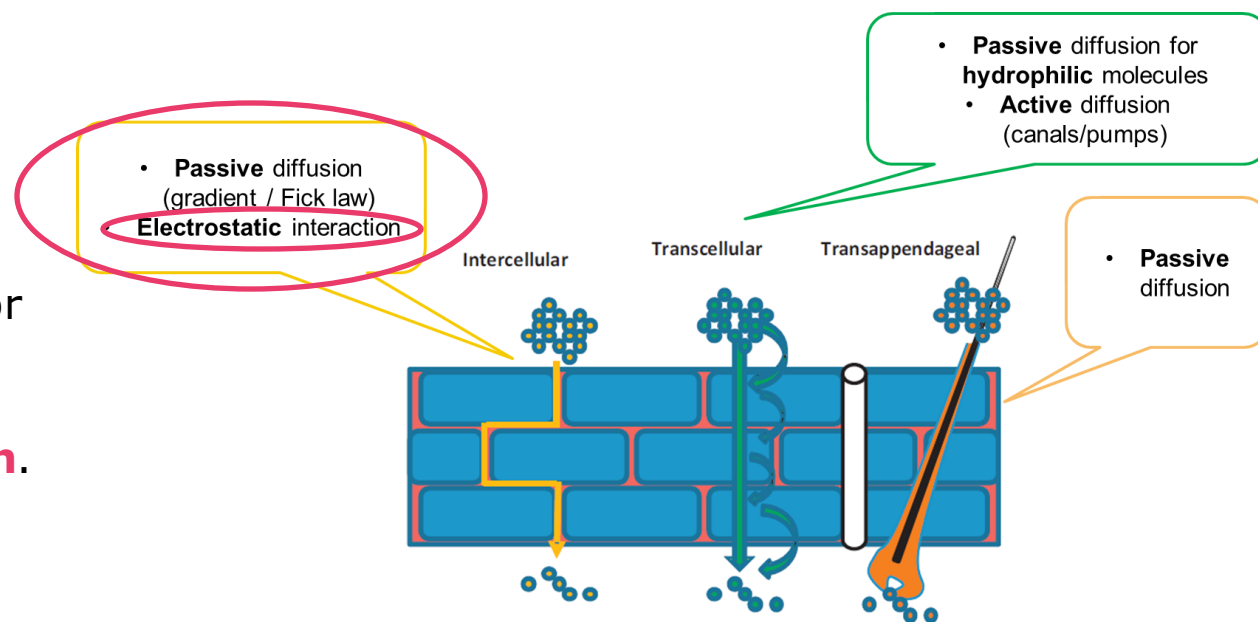
How can molecules penetrate into the skin?

Various possible mechanisms, but...

For molecules to penetrate into the skin, only a limited number of mechanisms are described in the literature: **transappendageal** (through appendages, such as the pilosebaceous unit), **transcellular** or **intercellular**.

Only this last one can be identified as realistic for a “large” molecule such as HA. But even though, **HMW HA does not penetrate if only applied on top of the skin, through passive diffusion**.

To help it penetrate, it is necessary to exploit **electrostatic interactions**, by modulating the charges on the molecule.



Electrostatic interactions and their benefits...

... are actually already known in the Beauty industry!

“Ionophoresis (or Iontophoresis) is an electrical treatment used to help move substances across the skin [...]”



Back in the 1900's...



... and still today!

Source: <https://www.cosmeticsandskin.com/>

How to play on electrostatic charges... ... without any hardware?!

Bentonite is a specific type of clay (from the Smectite family, made of a majority of Montmorillonite) obtained from volcanic ash sediments.

Well-known in skincare applications, for its sensorial benefits, or for its mattifying and exfoliating properties, **clay is another comforting ingredient** in consumers' minds.

Our experts identified bentonite (sourced in Mediterranean European countries) as an interesting **vectorisation** candidate, as it presents a specific organisation, in a so-called **lamellar structure**, an aggregate of lamellar platelets, packed together by **electrochemical forces**, and containing interposition water.



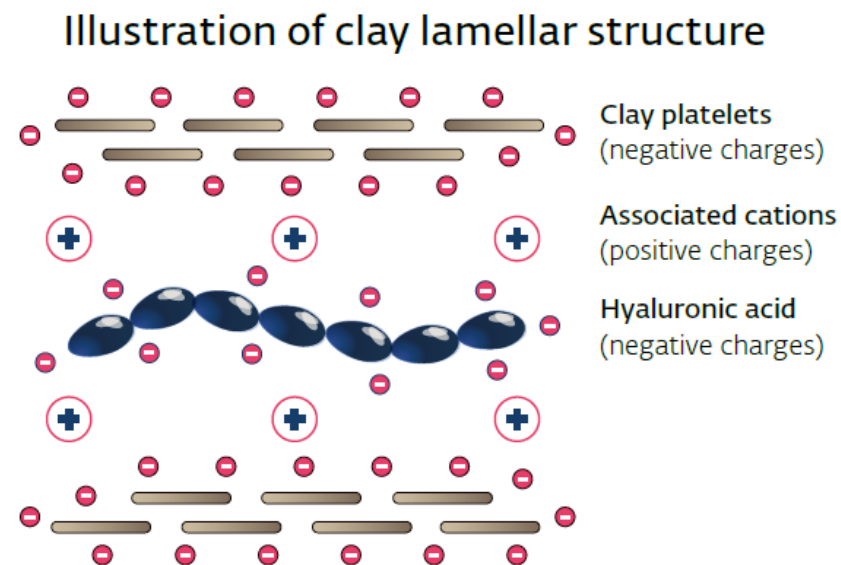
Deep skin penetration of HMW HA

Made possible thanks to clay!

To equilibrate the natural negative charges of the bentonite itself, its lamellar structure usually entraps **exchangeable cations** in the interstitial water, such as calcium, sodium, or magnesium.

Thanks to a patented and proprietary process, bentonite can be activated to entrap molecules of HMW HA.

This results in **a complex between HA and clay**, where HA molecules are strongly negatively charged (in contact with cations), and thus benefit from an **electrical attraction from the skin's deep layers**.



Deep skin penetration of HMW HA

Modification of HA electrical potential for skin attraction

To demonstrate the modification of electrostatic behaviour of our complex, Zeta potential of HA/Clay complex was compared to the one of HMW HA alone.

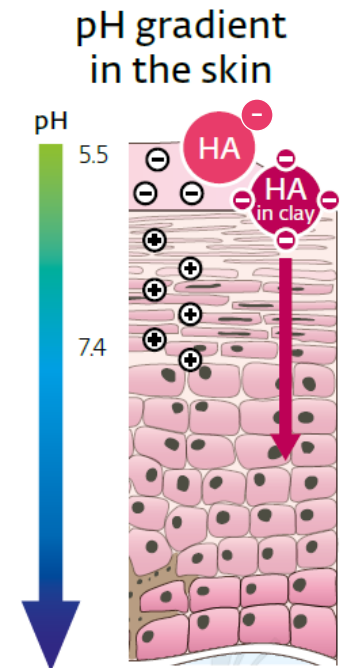
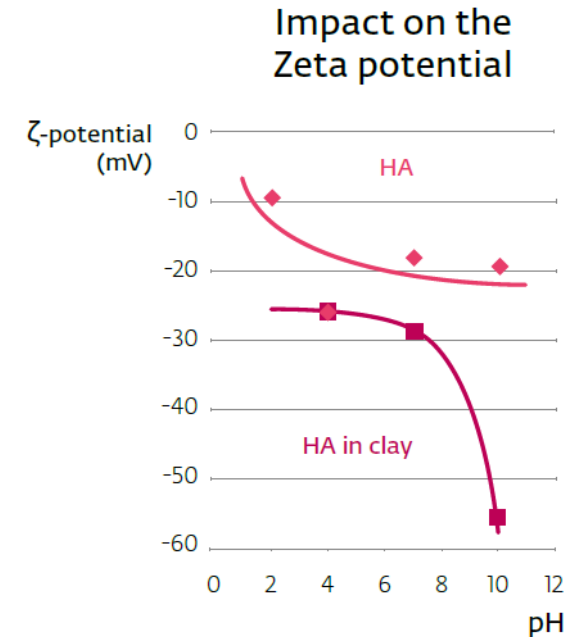
Results:

HA/Clay complex presents **a Zeta potential profile which is significantly different from HMW HA alone**, specifically at "high" pH (>7), demonstrating that our **HA/Clay complex bears more negative charges than the HMW HA alone**.

This behaviour improves the affinity of HA molecules for the skin depth, and can thus explain a better penetration.

Indeed, there is a natural pH gradient in the skin¹, with an increase of pH when going deeper into the epidermis.

This leads to an **electrostatic attraction** (Coulomb law) of the negative HA molecules present in the clay complex, ultimately resulting into an **enhanced skin penetration**.



Deep skin penetration of HMW HA

RAMAN spectroscopy (*ex vivo*)

Skin explants (47 y.o. donor) were topically treated for 8 hours with HMW HA at 1%, HA/Clay complex at 10% (eq to 1% HA), or left untreated.

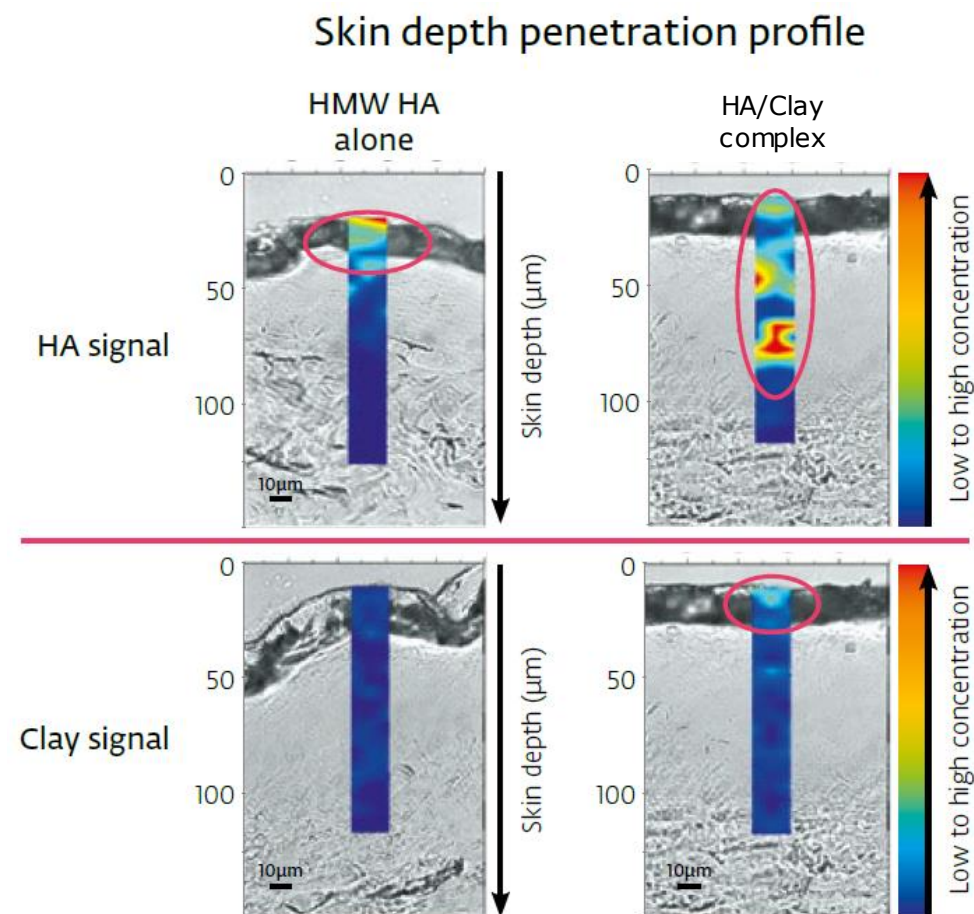
Raman spectroscopy was then performed to assess products penetration profiles.

Results:

Standard HMW HA shows no skin penetration, and remains at the surface of the skin.

HA/Clay complex enables HMW HA to penetrate into the skin, up to 60-75µm.

In the meantime, it can be observed that the clay does not penetrate the skin.



Biological evaluation

Hydration, smoothing,
detoxification

Long-lasting hydration

Atomic Force Microscopy (*ex vivo*)

Skin explants (22 y.o. donor) were topically treated and incubated for 8 and 24h, with:

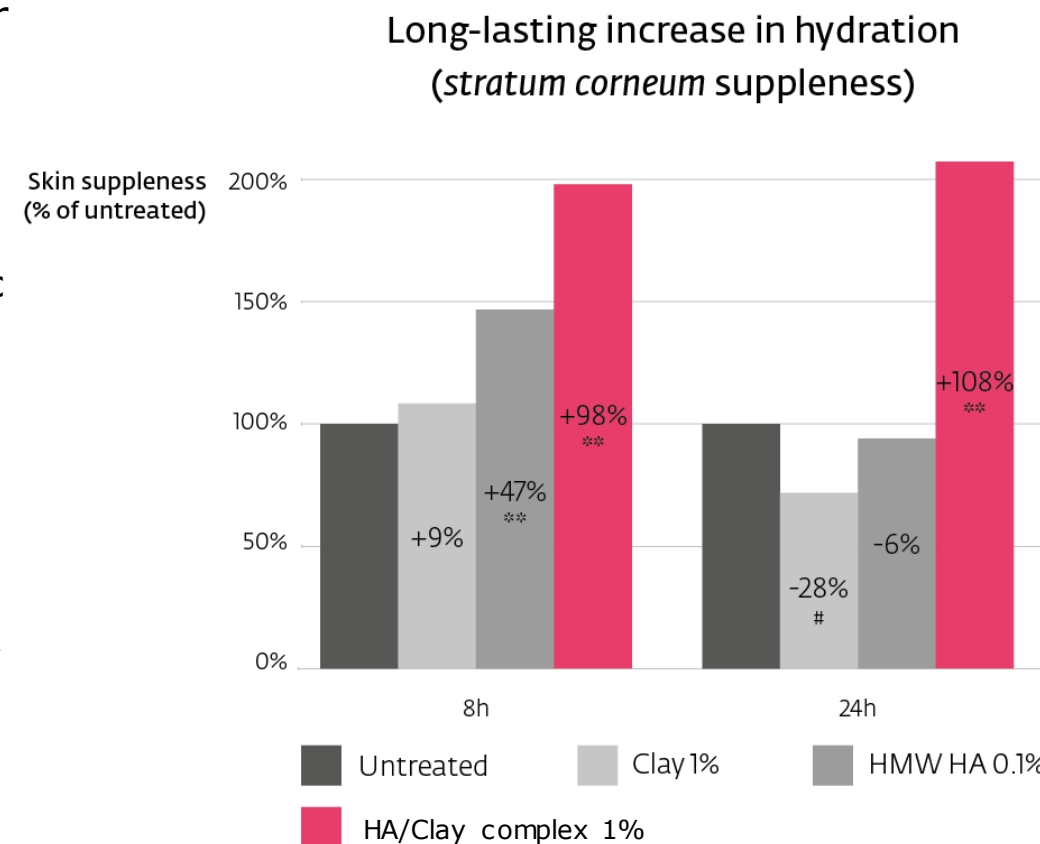
- HMW HA at 0.1%,
- HA/Clay complex at 1% (eq to 0.1% HA),
- Clay at 1%,
- or left untreated.

Force measurements were then performed using AFM, and the elastic modulus (E_a , related to the suppleness of the *stratum corneum*) was then quantified thanks to BioMeca Analysis®.

Results:

After 8h, both HMW HA and HA/Clay complex result in a significant increase of the *stratum corneum* suppleness, respectively by +47% and +98%. Clay alone has no significant hydration benefit. After 24h, both clay and HMW HA are back to a basal level (or lower), with no impact on the hydration level.

Only HA/Clay complex is able to provide a prolonged long-lasting hydration, by +108% vs untreated conditions.



Mann Whitney test: # $p < 0.1$, * $p < 0.05$, ** $p < 0.01$

Smoothing of the skin's surface

Scanning Electron Microscopy (*ex vivo*)

Skin explants (55 y.o. donor) were topically treated and incubated for 72h under reduced hygrometry (mimicking dry skin condition) with:

- HMW HA at 0.1%,
- HA/Clay complex at 1% (eq to 0.1% HA),
- Clay at 1%,
- or left untreated.

Scanning Electron Microscopy (SEM) measurements were then performed to assess the condition at the skin's surface.

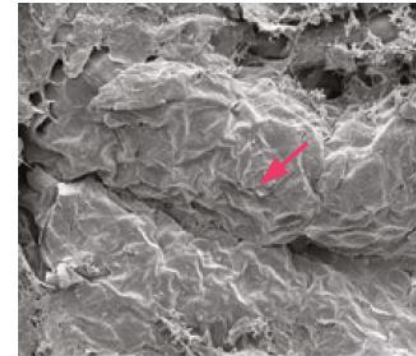
Results:

Compared to untreated conditions, no significant change can be observed on the explants treated with clay only. The skin is not smoothed, and corneocytes can still be visualised very easily. The use of HMW HA enables a slight smoothing of the skin, but corneocytes can still be observed clearly.

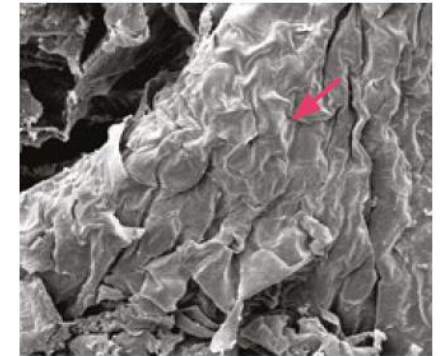
The use of HA/Clay complex results in a significant smoothing of the skin, as the corneocytes can not be distinguished easily anymore.

Scanning Electron Microscopy
pictures of skin's surface

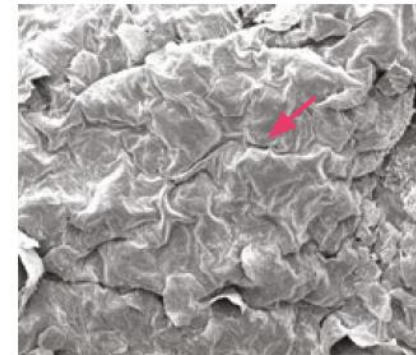
Untreated



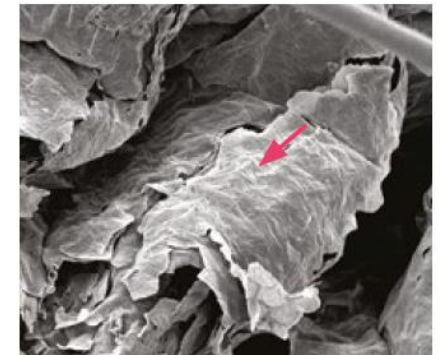
Clay 1%



HMW HA 0.1%



HA/Clay complex 1%



Anti-adhesion and detoxification benefits D-squame (*ex vivo*)

Skin explants (57 y.o. donor) were topically treated either with HA/Clay complex at 1% or left untreated.

They were then photographed, and 3mg of carbon particles were applied to mimic an exposure to pollution. Skin explants were again photographed, then particles were rinsed and a D-squame® sample was taken on each zone in order to quantify the remaining particles at the surface of the skin explants.

Results:

The quantity of particles found after carbon application was significantly lower in presence of HA/Clay complex, down to -50%, demonstrating **an anti-adhesion benefit of the active**.

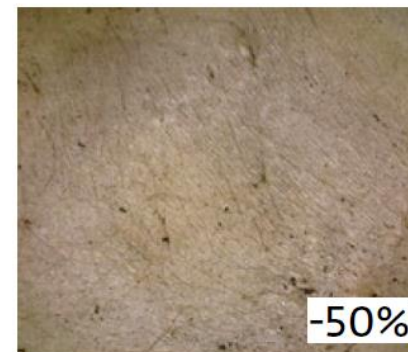
After rinsing, the quantity of carbon particles was significantly reduced in comparison to untreated condition, down to -29%, showing that **the skin was detoxified in presence of HA/Clay complex**.

After carbon particles
application

Untreated

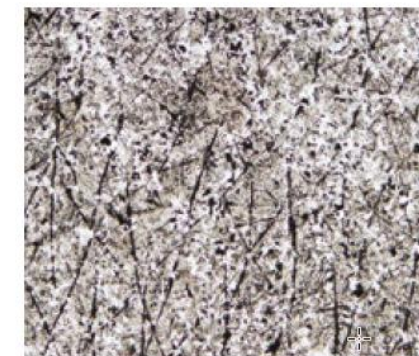


HA/Clay complex 1%

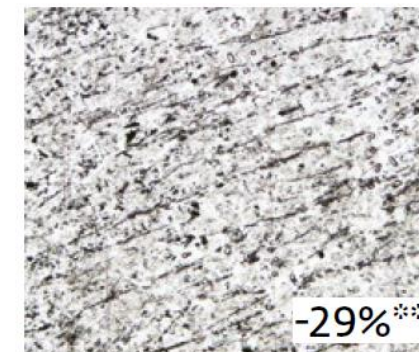


After rinsing
(D-squame® image)

Untreated



HA/Clay complex 1%



After carbon particles application: Student's *t*-test: #*p*<0.1
After rinsing, Mann Whitney test: ***p*<0.01

Fine lines smoothing & mattifying
From flash-efficacy
to long-term benefits!

Clinical study

Fine lines smoothing & mattifying

Protocol:

- Double blind *versus* placebo
- 39 female volunteers
(average age 49 years old, from 35 to 55)
- Dry skin & fine lines on the crow's feet area
- Application twice a day for 28 days
- Full face (2 groups), with a formula containing 1% HA/Clay complex, or a placebo (same formula without the active)

Evaluation by ColorFace® technology:

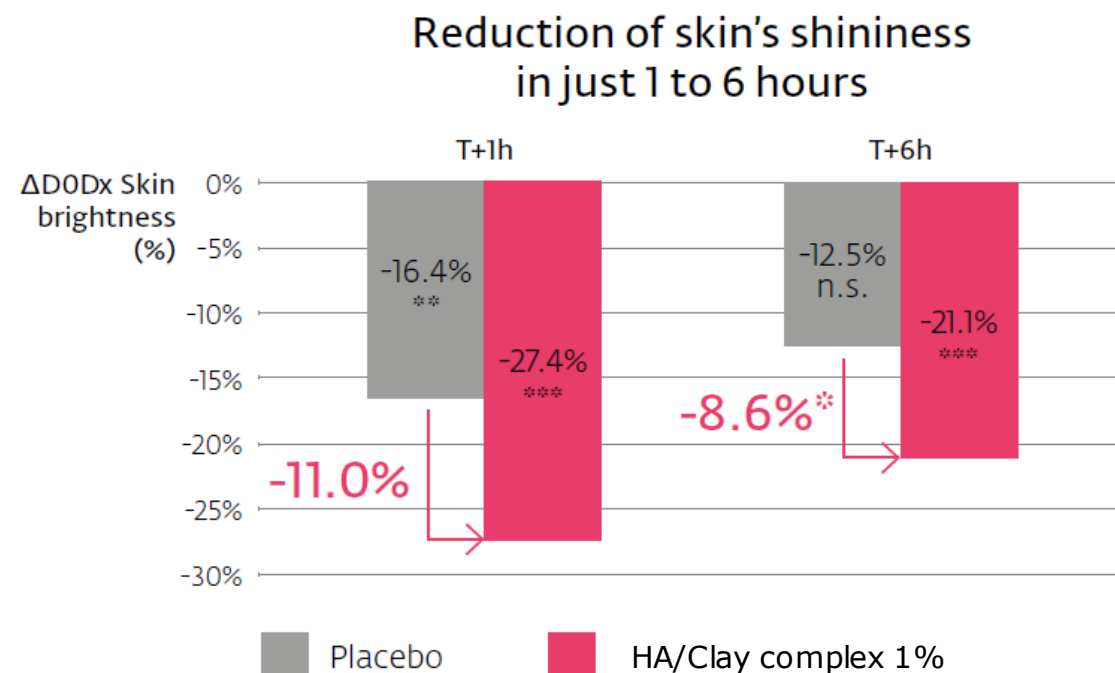
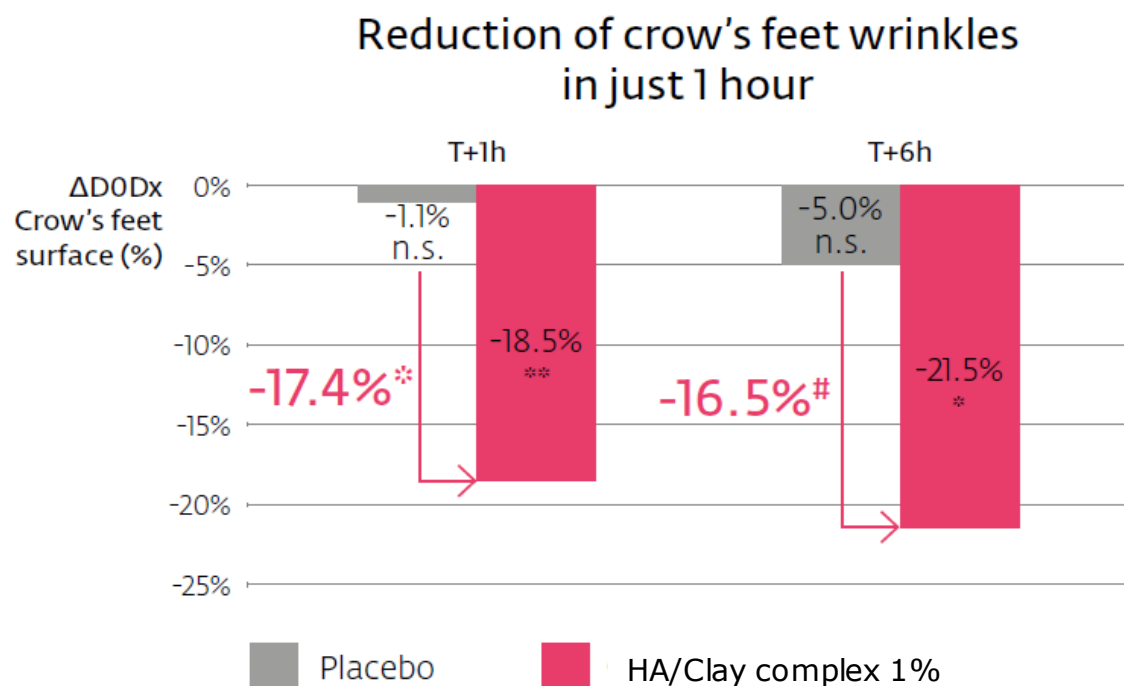
- on the first day after just one application of the product, T+1h and T+6h,
- after 28 days.

Note: last application on D27 evening, so that there's no product left on their skin, no "surface" effect from the clay).



Instant gratification in just 1 to 6 hours

Reduction of crow's feet wrinkles & shininess

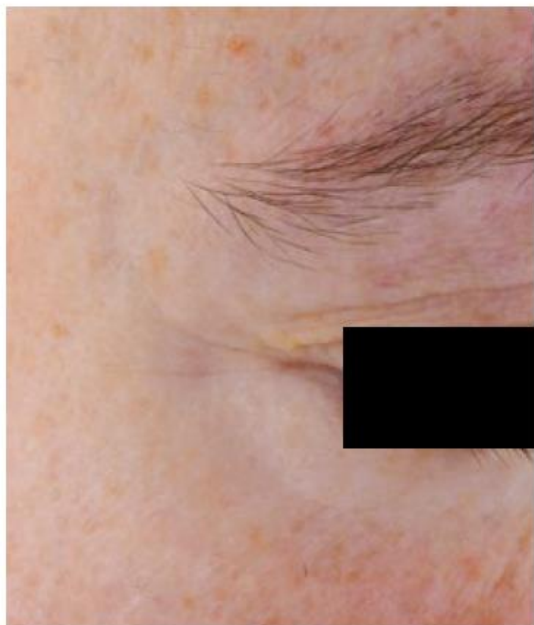


Wilcoxon test vs D0, Mann Whitney test vs placebo:
#p<0.1, *p<0.05, **p<0.01

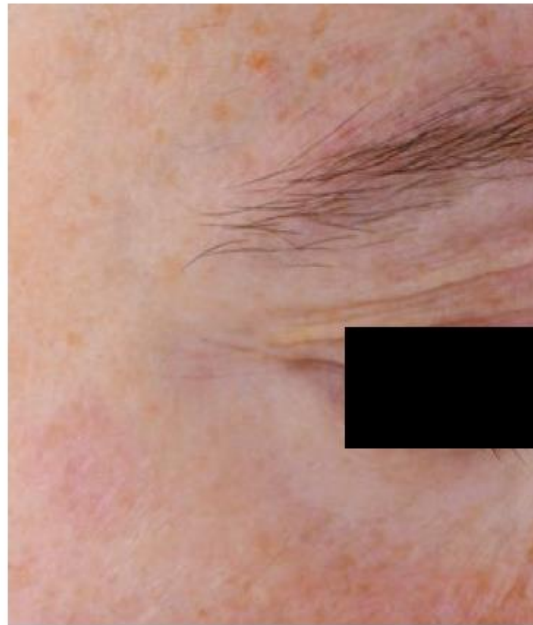
Instant gratification in just 1 to 6 hours

Reduction of crow's feet wrinkles & skin's shininess

Illustrative pictures of a volunteer using HA/Clay complex at 1%
(Vol #16 - crow's feet wrinkles, left // Vol #22 - skin shininess, right)



T0



T+6h



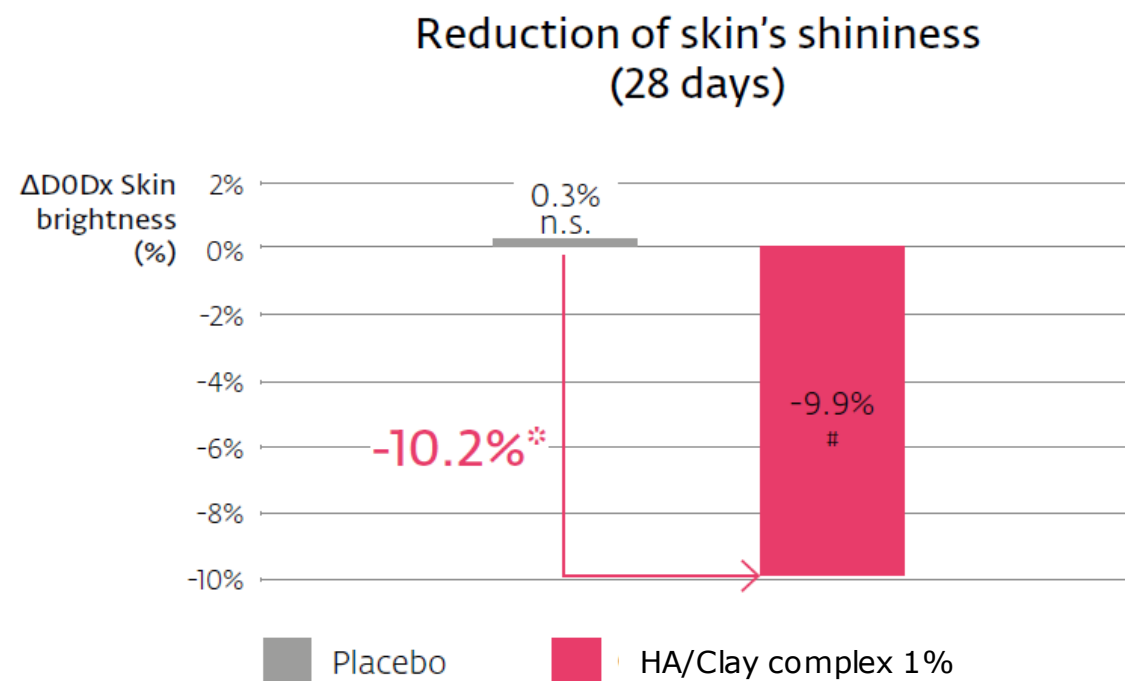
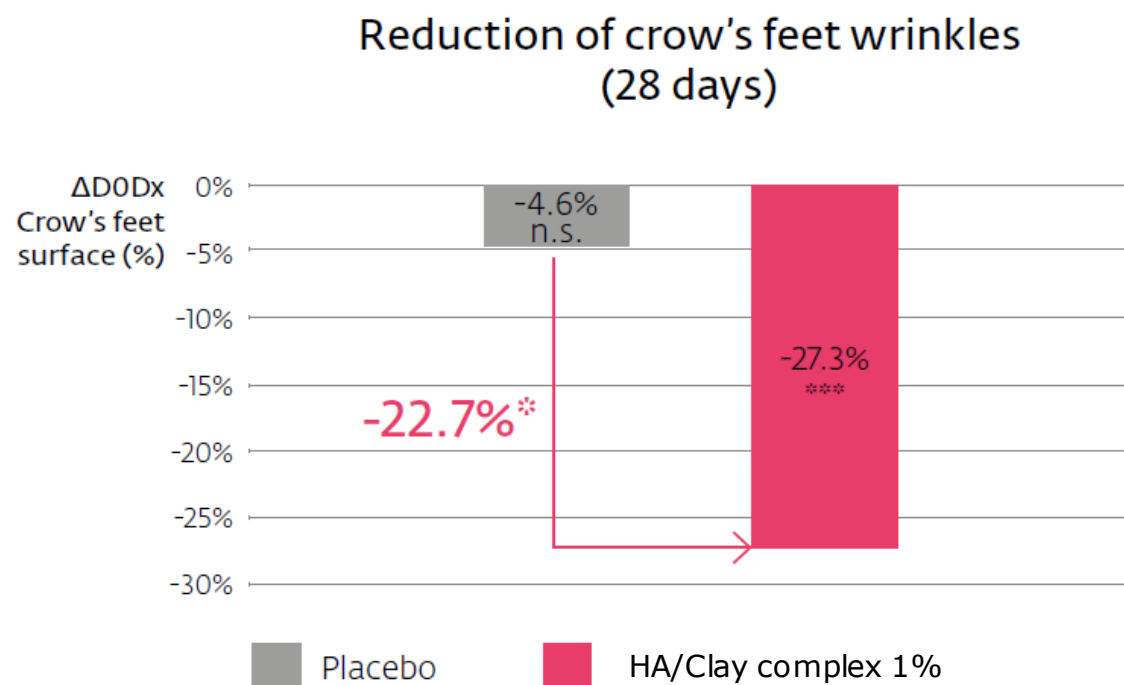
T0



T+6h

Long-term benefits after one month

Reduction of crow's feet wrinkles



Wilcoxon test vs D0, Mann Whitney test vs placebo:
* $p < 0.05$, *** $p < 0.001$

Long-term benefits after one month

Reduction of crow's feet wrinkles & skin's shininess

Illustrative pictures of a volunteer using HA/Clay complex at 1%
(Vol #16 - crow's feet wrinkles, left // Vol #36 - skin shininess, right)



D0



D28



D0



D28

HYDRATION +
HERO INGREDIENTS

=

Solving the equation of
young beauty consumers' obsessions!

THANK YOU

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