Biotechnological Active Ingredient

Epidermist 4.0 is a Marine Exopolysaccharide secreted by a planktonic microorganism in the Aber Benoît (Brittany - France).

The Aber-Benoît is a coastal river in the Pays de Léon region of Northwest Finistère, Brittany (Northwest France).

An Aber (Celtic word meaning estuary) is a river valley flooded by the sea. Abers are rich and varied ecosystems in which organisms and microorganisms thrive in both salt water from the sea and fresh water.

Epidermist 4.0 is produced by culture in a bioreactor to obtain a pure and natural molecule that has no land-based equivalent.

It is composed of galactose, and N-acetyl-glucosamine, which one is involved in the synthesis of GlycosAminoGlycans (GAGs): the main water reservoir of dermis.

Galactose + N-acetyl-glucosamine

\[
\text{Galactose} + \text{N-acetyl-glucosamine}
\]
PERFECT SKIN, A COMPREHENSIVE STRATEGY

Perfect skin - new skin - skin as fresh and radiant as a baby’s is achieved through a multi-faceted approach. Skin colour, shine, surface condition and texture are all factors which play a role. To respond effectively, a comprehensive strategy is needed: the three major skin functions must be rebooted:

- physical barrier function
- chemical barrier function
- hydra memory function

This reboot involves readjustment of the 4 parameters of “good” skin health:

- skin renewal
- innate immunity
- chronic inflammation
- rehydration

With its multi-faceted approach, Epidermist 4.0 provides skin with an overall perfecting action

- Cell renewal is optimised
- Skin's natural defences are reactivated
- Pro-acne bacteria growth is inhibited
- Skin reactivity is reduced
- Skin’s intrinsic ability to rehydrate itself is strengthened
- Skin texture is smoothed
- Pores are less visible
- Skin is in better health

People who have tested Epidermist 4.0 have found their skin to be softer, smoother and in better health... as if restored.
REBOOTING THE PHYSICAL BARRIER FUNCTION

Disorganisation of the skin’s physical barrier leads to skin dehydration and increased skin roughness; it also causes a loss of skin radiance (dull complexion). An impaired skin barrier also facilitates contact with allergens and the development of unwanted bacterial flora.

Keratinocyte differentiation and epidermis renewal are the two main mechanisms affecting physical barrier quality.

EPIDERMAL DIFFERENTIATION

The primary function of the epidermis is to produce the stratum corneum which forms a semi-permeable protective layer. It is formed through the differentiation of keratinocytes from the basal layer to the skin’s surface layer. Many proteins and enzymes are involved at each stage of keratinocyte differentiation.

### Differentiation proteins

<table>
<thead>
<tr>
<th>Protein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>INVOLUCRINE (INV)</td>
<td>involved in forming the cornified envelope</td>
</tr>
<tr>
<td>TRANSGLUTAMINASE 1 (TGM1)</td>
<td>ensures assembly of proteins that make up the cornified envelope</td>
</tr>
<tr>
<td>SMALL PROLINE RICH PROTEIN (SPRP)</td>
<td>precursor proteins in the formation of the cornified envelope</td>
</tr>
<tr>
<td>LATE CORNIFIED ENVELOP (LCE)</td>
<td>precursor proteins in the formation of the cornified envelope</td>
</tr>
<tr>
<td>CORNEODESMOSINE (CDSN)</td>
<td>pivotal role in cohesion of the stratum corneum</td>
</tr>
<tr>
<td>NICE 1</td>
<td>involved in terminal differentiation of keratinocytes</td>
</tr>
</tbody>
</table>

### Chronology of differentiation protein expression

The chronology of differentiation protein expression is as follows:

1. **Basal layer**: INV (Junctional INV)
2. **Spinous layer**: TGM1
3. **Granular layer**: SPRP, LCE, CDSN, NICE1
4. **Cornified layer**: INVOLUCRINE (INV)
**IN-VITRO TEST**

Used at 1%, Epidermist 4.0 increases differentiation protein synthesis

**Protocol:**

Assessment of genes expression on human reconstituted epidermis treated with 1% Epidermist 4.0 applied topically.

**RESULT:**

The increase in differentiation proteins contributes to the formation of a higher quality physical barrier, and activation of stratum corneum renewal.

![Graph showing gene expression increase](image)

**CLINICAL TEST:**

Used at 1%, Epidermist 4.0 improves skin renewal

**Protocol:**

- 17 volunteers aged between 18 and 59
- Application of a coloured cream containing 5% DHA, 1 day before start of treatment.
- From Day 0, lotion containing 1% Epidermist 4.0 applied twice a day for 2 weeks.

Skin pigmentation by the DHA enables monitoring of cell renewal; pigmentation will be eliminated faster if cell renewal activated.

**RESULT:**

Cell renewal rate is doubled in just 1 week.

By improving the skin’s natural renewal process, Epidermist 4.0 helps to eliminate dead cells on the skin’s surface and avoid the formation of a too thick and rough stratum corneum.

![Graph showing cell renewal rate](image)

**Benefits associated with rebooting the physical barrier function**

Improved keratinocyte differentiation and cell renewal activation promotes better epidermal cohesion and better elimination of dead skin cells and skin roughness. Rebooting the skin’s physical barrier provides a smoothing and softening effect on skin texture, appreciated by the volunteers.
REBOOTING THE CHEMICAL BARRIER FUNCTION

The chemical barrier function brings 2 defence modules into play: innate immunity made up of proteins and antimicrobial peptides, and inflammatory reaction.

Innate immunity, unlike acquired immunity, is already present within a child when it is born. It is the first line of defence against the infectious agents and pathogens which surround us. Innate immunity is activated immediately and works for 4 days.

Inflammatory reaction is triggered by the release of pro-inflammatory molecules by keratinocytes under attack; it causes the appearance of redness, stinging, inflammation, etc.

IN-VITRO TEST

Used at 1%, Epidermist 4.0 reinforces innate immunity and reduces inflammation

Protocol:

Assessment of genes expression by human reconstituted epidermis treated with 1% Epidermist 4.0 applied topically.

INNATE IMMUNITY RESULTS

Epidermist 4.0 stimulates 4 of the main antimicrobial peptides of innate immunity:

- **Defensin beta (DEFB103)**
  Deconstructs exogenous bacteria membrane; known for its effectiveness against Staphylococcus aureus

- **Secretory Leucocyte Peptidase Inhibitor (SLPI)**
  Inhibits proteases and especially elastase, activated by bacteria to penetrate deeper into the tissues

- **Ribonuclease Rnase 7 (RB RNASE 7)**
  Breaks down bacterial and viral RNA

- **S100 Calcium Binding Protein A10 (S100A10)**
  Inhibits bacterial growth by interacting on their cell cycle

INFLAMMATION RESULTS

Epidermist 4.0 reduces 5 inflammatory mediators:

- **S100 Calcium Binding Protein A7 (S100A7)**
  Also called Psoriasin, promotes the action of collagenase and elastase during inflammation.

- **Toll-like Receptor 2 (TLR2)**
  Recognizes bacterial lipopolysaccharides and activates TNFa

- **TNFa**: activates CXCL5 and CXCL10 chemokines

- **CXC Ligand 5 & 10 (CXCL5 & CXCL10)**
  Chemokines involved in the migration and activation of neutrophils on site
**CLINICAL TEST:**

Used at 1%, Epidermist 4.0 reduces bacterial growth and skin reactivity

**BACTERIAL GROWTH CLINICAL TEST**

Protocol:
- 20 volunteers (aged 35 to 45) - lotion with 1% Epidermist 4.0 applied twice a day for 4 weeks.
- The effect on bacterial growth is assessed by porphyrin quantification: bacterial shedding (characteristic among other P.acnes). Easy to quantify porphyrin because it turns fluorescent under UV.

RESULT:

Average reduction: -10%
Maximum reduction: -54%

The reduction of porphyrin on the skin’s surface is evidence of inhibited growth of unwanted bacteria.

**SKIN REACTIVITY CLINICAL TEST**

Protocol:
- 30 volunteers (aged 30 +/- 2 years) - Application of a gel containing 1% Epidermist 4.0, twice a day for 1 week.
- Evaluation of skin reactivity score. Use of stinging test.

RESULT:

by application of lactic acid on the skin. 76% of volunteers observed a reduction in their skin’s reactivity after 1 week of treatment

**p<0.01 Student test

Benefits associated with rebooting the chemical barrier function

Epidermist 4.0 reinforces skin’s innate immunity and reduces inflammation. Bacterial growth is curbed, thereby reducing acne characteristics. Skin is less reactive and less sensitive. Epidermist 4.0 improves skin health by rebooting the skin’s chemical barrier in this way.
REBOOTING SKIN’S HYDRA MEMORY

Environmental attacks, chemical products, friction... all play a daily role in drying out skin. Applying moisturising products helps to rehydrate damaged skin, but not all skin types recover their optimal hydration levels in the same way.

This ability to recover optimal hydration levels can be called:

HYDRA MEMORY

This Hydra Memory involved a mechanism of pumping water into the dermis to rehydrate the upper layers: epidermis and stratum corneum. The skin’s Hydra Memory will be all the more effective if the physical and chemical barrier functions perform well. This memory can also be improved by reinforcing the skin’s ability to retain moisture, as does hyaluronic acid.

WATER RESERVOIR OF THE DERMIS

Within skin, in the dermis, the proteins of the extracellular matrix synthesised by fibroblasts create “a sort of water reservoir”.

Hyaluronic acid, the main component, acts like a water magnet to trap hydration molecules and gradually disseminate them to the skin’s outer layers.

It is thanks to this water reservoir that the skin is able to rehydrate autonomously after dehydrating stress.

IN-VITRO TEST

Used at 0.02%, Epidermist 4.0 stimulates the synthesis of hyaluronic acid

Protocol:

human dermis fibroblasts cultivated with or without Epidermist 4.0. Dosage of the amount of hyaluronic acid synthesized, in culture medium.

RESULT:

The increase in hyaluronic acid synthesis by fibroblasts promotes an increase in dermis hydration level, which represents the main water reservoir of the skin and is essential to its good hydration.

***p<0.001 Student test
EX-VIVO TEST

Used at 1%, Epidermist 4.0 improves autonomous skin rehydration

Protocol:

We tested the ability of a skin explant pre-treated with Epidermist 4.0 to autonomously regain (without added moisturiser) its optimal level of hydration after severely dehydrating stress (use of salt crystals). Hydration levels are measured using corneometry.

RESULT:

The explants were subjected to severe dehydration: approx. -40% hydration. Only the explant treated with Epidermist 4.0 was able to regain its initial hydration levels: 96%, 1 hour after the dehydration process and 99% after 24 hours.

Benefits associated with rebooting the water memory function

Rebooting the water memory function contributes to improving the comfort levels of mature and reactive skin types, and also resolving the issue of skin dryness in oily, acne-prone skin types.
NEW SKIN BUILDER

Skin renewal is about regaining soft, brighter skin with smoothed skin texture and less visible pores – skin that looks renewed and in good health.

CLINICAL TEST: 🌸

Overall perfecting action of Epidermist 4.0 used at 1%

Protocol:

20 volunteers aged between 35 and 45
Lotion containing 1% Epidermist 4.0 applied twice a day for 28 days
Use of the VISIA tool to visualise skin texture smoothing effect and visibility of pores

ANALYSIS OF SKIN ROUGHNESS

Average reduction: -19%***
Maximum reduction: -56%
***p<0.001 Student test

Rebooting the physical barrier function, improvement of skin renewal and reactivation of water memory help to obtain smoother skin texture, less rough and softer skin.

ANALYSIS OF NUMBER OF VISIBLE PORES

Average reduction: -7%
Maximum reduction: -41%

ANALYSIS OF TOTAL SURFACE OF VISIBLE PORES

Average reduction: -11%
Maximum reduction: -58%

Rebooting the chemical barrier function, reduction of bacterial growth and improved skin renewal help to obtain a reduction in the number of pores and total surface area of pores visible.
CLINICAL TEST:

Overall view of Epidermist 4.0 new skin effect on a volunteer

With its multi-faceted approach, Epidermist 4.0 provides skin with an overall perfecting action:

After a single application:
- Improved ability of skin to autonomously rehydrate: +17%

After 1 week’s use:
- Improved cell renewal: +31%
- Reduced skin reactivity: -37%

After 4 week’s use:
- Reduced bacterial growth: -10% porphyrin
- Smoother skin texture: -19% roughness
- Less visible pores: -7% of pores and -11% of total surface area of pores visible

CLINICAL TEST:

Volunteers self assessment

My skin is softer approved by 82% of volunteers
My skin is healthier approved by 73% of volunteers
My skin is smoother approved by 68% of volunteers
My skin is brighter approved by 64% of volunteers

With its multi-faceted approach, Epidermist 4.0 provides skin with an overall perfecting action:
EPIDERMIST 4.0: New Skin Builder

Cosmetic Actions

- Improves skin renewal
- Smooths skin texture
- Reinforces innate immunity
- Reduces bacterial growth
- Reduces skin reactivity
- Reduces the number of pores and total surface area of pores visible
- Improves skin health

INCI name

- EPIDERMIST 4.0 PA: Water (and) Plankton extract (and) Phenethyl alcohol
- EPIDERMIST 4.0 P: Water (and) Plankton extract (and) Phenoxyethanol

% of recommended use

- EPIDERMIST 4.0 PA: 1 %
- EPIDERMIST 4.0 P: 1 %

CODIF
R & N

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Iris, water mint, flowering rush, willows etc... now form part of the image of the brand which is recognized for its commitment to the preservation of natural resources.