SKIN RESURFACING STRATEGIES & CORNEOTHERAPY

CODIF R&N
Flawless skin: TOP 5 consumers concerns

Multitasking products suitable for all skin types.
High Definition skin grain
Immediate effect + long lasting benefits.
New segment in anti-aging strategies.

Key Words
Immediate smoothing action
Resurfacing
Blur
Flawless skin
Perfect skin
Pixel-perfect skin
PERFECTIONISTS & BLURS

On the Market

L’OREAL
Skin Perfection
Discover our 1st skincare to help transform the appearance of skin quality, for perfect looking skin even without foundation.

Magic Touch Instant Blur
Pixel-perfect your skin. Enriched with Optical Blur Polymers the formula optically blurs the appearance of shine, pores and irregularities for a soft-focus finish. In your 20's and 30's your skin is still young but not always perfect. Stress, fatigue and an unbalanced lifestyle can affect skin quality causing irregularities to appear: imperfections, enlarged pores and an uneven skin texture.

CLARINS
Instant Smooth Perfecting Touch
Just like magic! The Clarins Instant Smooth Perfecting Touch is an invisible 'second skin' base that smoothes surface skin and minimizes the appearance of wrinkles, fine lines and dilated pores. It is a perfect marriage of make-up and skin care that creates a spectacular beauty effect.

KIEHL’S
Micro-Blur Skin Perfector
Lightweight skin smoother visibly transforms skin in seconds and over time. Instantly diminishes the appearance of pores and refines skin texture. Provides long-lasting pore and texture correction. Appropriate for all skin types and skin tones.
PERFECTIONISTS & BLURS

Which Innovative Strategies?

THE CONCEPT

SKIN PERFECTIONISTS
Blurs, Idealist, Perfectionist, Instant Smoother... they all meet the growing demand for instant zero-defect skin but which then lasts.

THE CUTANEOUS TARGET

STRATUM CORNEUM
This upper layer of the skin incorporates several adaptive mechanisms to maintain and re-establish its structural integrity. When these mechanisms are altered the skin becomes irritated, dry, loses its softness and brightness.

THE BIOLOGICAL ANSWER

CORNEOTHERAPY
a treatment centered on the renovation of the corneal layer to correct the entire skin
CORNEOTHERAPY
Benefits & Innovation Potential
First used by the American dermatologist Pr. Albert KLIGMAN in the mid 1960’s.

- Described the effect of vitamin A in acne and wrinkles
- Created “cosmeceuticals” and “photo-aging” terms.

Showed that substantial clinical effects could be achieved by treating the disturbed balance of the skin through the repeated topical application of substances that had humectant and emollients properties - now known as «Moisturizers».
International Association for Applied Corneotherapy (I.A.C.)

Innovative thinkers that changed the way to consider skin today

• Pr A. Kligman, M.D. PhD., Univ. Pennsylvania, Philadelphia, USA
• Pr Peter M. Elias, M.D., Univ. California, San Francisco, USA
• Pr Ronald Marks, Cardiff, Wales
• Dr Paul J. Matts, UK
• Dr Hachiro Tagami, MD, PhD, Sendai, Japan
• Dr Anthony Rawlings, Great Britain
• Dr Lars Norlén, MD, Karolinska University, Sweden

World map of IAC members
“The skin care concept of the future”

• Combines cosmetics and dermatology
• Treatment centred on renovation of the corneal layer to correct the entire skin: “OUTSIDE-IN THERAPY”.

“Long term effects of therapeutic treatment of the corneal layer could assist repair of the underlying structures of the skin such as the epidermis and dermis”.

STARTING IDEA OF CORNEOTHERAPY

Science Of Corneotherapy

The most modern trends in the science of healthy skin

Corneotherapy has been practiced unwittingly by dermatologists from the earliest times

Many studies have been conducted by Professor Albert M. Kligman at the intersection of science, resulting in cosmetology and medicine appear such terms as "keratinizing" and "corneotherapeutic" and "corneotherapy".

Albert Montagu Kligman (March 17, 1926 - February 8, 2005), Professor of Dermatology, University of Pennsylvania School of Medicine, co-founder of the science of cosmeceutics, which were the scientific basis of dermatology.

Dr. Kligman was first to describe the human hair growth cycle, investigated the pathogenesis and treatment of acne, photosensitization, and keratinization of the skin, and discovered the "keratinizing" skin disease, psoriasis. He described the effects of sunlight on the skin.

"Corneotherapy refers to preventive interventions that are primarily directed to the correction and restitution of the stratum corneum barrier that has been rendered defective and impaired by disease, genetics and a variety of mechanical, physical, chemical and psychological exogenous insults and stresses."

The skin gate for moisture from "inside", by the diffusion of fluid from the blood vessels, the stratum corneum prevents the permeability of water from the "outside".

The stratum corneum is the skin barrier function, it prevents the penetration of pathogens, toxins, and environmental factors. The permeability of the stratum corneum is 0.05-0.5 microns, a barrier that is even more important to maintain the skin barrier and hydration. The permeability of the stratum corneum is 0.05-0.5 microns, a barrier that is even more important to maintain the skin barrier and hydration.

At the base of corneotherapy, the need to protect and to restore the stratum corneum, the destruction of which leads to the appearance of skin diseases, allergies, infections, dehydration and dryness. Stratum corneum is the outermost layer of the epidermis and is largely responsible for the initial barrier function of the skin.

For the first time, it is demonstrated that the stratum corneum is not a "nonliving" barrier that is capable of self-regulation and interaction with other layers of the epidermis and dermis.

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"Corneotherapy refers to preventive interventions that are primarily directed to the correction and restitution of the stratum corneum barrier that has been rendered defective and impaired by disease, genetics and a variety of mechanical, physical, chemical and psychological exogenous insults and stresses."
The **stratum corneum**

- Outer layer of the skin
- First protective barrier against outside attacks.

Uses several adaptive mechanisms to maintain and re-establish its structural and functional integrity:

- Readjustment of Trans-Epidermal Water Loss
- Reinforcement of its lipid barrier during reconstruction processes.
- Maintenance of cutaneous pH.

When these adaptive mechanisms are altered, deeper structural disruption occurs and the skin becomes irritated, dry and wrinkled.
Formulations characterized by a selection of active compounds that:

- allow the skin to breath or regenerate
- could be degraded in the skin
- are compatible with the skin barrier or corresponds to the physiology of the skin (« bio-mimetism »)

Corneotherapy involves “CORNEO BIOLOGY” AND “CORNEO BIOCHEMISTRY”
**Preventive treatments**
Prevents the alteration of stratum corneum barrier

**Curative treatments**
Correction and restoration of the stratum corneum barrier that has been rendered defective and impaired by many intrinsic and extrinsic factors of life (solar radiation, pollutants, cold dry environment, bacteria...).

**MEANS?**
Restoring the skin disrupted barrier defence with substances that mimic skin structure and function
HOW DOES CODIF EXPLORE CORNEOTHERAPY?
HOW DOES CODIF EXPLORE CORNEOTHERAPY?

- Skin Related Actives
  - Skin Related Structures

- Outside in Therapy
  - Extended Outside in Therapy

- Corneotherapy

- Repairing Corneotherapy
  - Correcting Corneotherapy

- Codif R&N
  - Innovative Strategy

2 High Precision Tools
2 HIGH PRECISION TOOLS

CORNEOSTICKER DS

SKIN RELATED STRUCTURE
Corneo-mimetic

SKINPERF LWG

EXTENDED OUTSIDE IN THERAPY
AHA Perfusion
SKINPERF LWG
NEW TOOL FOR OUTSIDE-IN-THERAPY

SKINPERF LWG (Lamellar Water Gel) was designed to diffuse AHAs in a progressive and controlled way into the skin.

This is a completely new way of releasing AHAs which equals the performance of conventional AHA treatment while avoiding the problems of burns and inflammation.

It consists of:
- A biomaterial developed using green chemistry, forming a lamellar gel which behaves like an intra-cutaneous reservoir of AHA.
- A synergy of alpha-hydroxy acids: 15% glycolic, 7% lactic and 6% citric acids adsorbed onto the lamellar biomaterial.

This new system means that low concentrations of AHA can be used while maintaining its exfoliating performance.
To demonstrate the benefits of Lamellar Water Gel (LWG) technology, we compared its diffusion properties with a conventional Carboxy Methyl Cellulose (CMC) gel. CMC does not have any special diffusion properties, this control is thus similar to a formulation containing free AHAs.

The two LMG and CMC structures both contain 28% AHA. They were deposited on the surface of an agarose gel in which AHA diffusion is measured thanks to infrared spectroscopy. This procedure enables the measure of AHA diffusion kinetics.
LAMELLAR WATER GEL TECHNOLOGY
BENEFITS FOR PROGRESSIVE AND CONTROLLED DIFFUSION OF AHA

The kinetics of AHAs diffusion show a stationary step (diffusion equilibrium) reached after:

- 5h 25 min for the CMC technology.
- 9h 12 min for the LWG technology.

This means that the AHAs are released much more slowly with LWG technology but also in a more progressive and continuous manner.

We can therefore expect 2 types of benefits:
- Extended contact time giving high performance exfoliation of the skin.
- A more progressive supply of AHA which is therefore less aggressive for the skin.

LWG technology should provide similar performance than free AHAs but with much less aggressiveness. Two parameters which define the Performance Index of an AHA treatment.
PERFORMANCE INDEX
THE PERFORMANCE INDEX
DEFINITION AND CALCULATION METHOD

AHAs are characterized by two major properties.
- Exfoliation
- Inflammation

It is important to maintain a balance between both effects. Indeed, a cocktail of AHAs cannot be used for powerful exfoliation if it is going to generate severe irritation or even burns.

The Performance Index (PI) defined by our laboratories is inspired by the therapeutic index previously developed by Dr Smith in 1994. The PI of an AHA or combination of AHAs is the ratio of its exfoliating performance to the inflammation it generates.

The Performance Index PI

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% exfoliation</td>
<td></td>
</tr>
<tr>
<td>% inflammatory mediator</td>
<td></td>
</tr>
</tbody>
</table>

A PI greater than 1 is characteristic of a good exfoliation with a minimum of inflammation.

SKINPERF LWG

PERFORMANCE INDEX

The PI of a formulation containing 2% SKINPERF LWG was calculated and compared to formulations containing 8% and 15% AHA. The exfoliating action of the three formulations was evaluated by stripping and counting scale while the level of inflammation was evaluated by assaying the inflammation mediator COX2.

Only SKINPERF LWG has a PI > 1, characteristic of a good exfoliation without irritation.

The lack of inflammation is explained by a very low concentration of AHA in the SKINPERF LWG formulation. Nevertheless the following studies show that even though its AHA concentration is lower, its exfoliating properties are as effective as the 8% and 15% AHA formulations.

The progressive and continuous diffusion generated by LWG technology means that lower AHA concentrations can be used leading to less inflammation while maintaining an effective level of skin renewal.
SKINPERF LWG
EVALUATION OF DESQUAMATING EFFECT

Protocol
Human skin explants (39 year old donor). Application of preparations at D0, D1 and D2. Analysis of desquamating effectiveness at D5 by stripping and counting of scales obtained on the strip.

2 PARAMETERS ARE ANALYSED
- The number of scales (% variation versus untreated explant).
- The heterogeneity index of the scales: treatment which is too aggressive causes deep desquamation and eliminates a clump of epidermal cells. This phenomenon is visible on the strips with the AHA 8 and 15 creams. The exfoliation then damages the cohesion of the skin below the stratum corneum and may be accompanied by burns.

Only SKINPERF LWG provides both significant and uniform exfoliation which means its action is less aggressive than the AHA 8 and AHA 15 formulations.
SKINPERF LWG

EVALUATION OF INFLAMMATION LEVEL

Protocol
Human skin explants (39 year old donor). Application of preparations at D0, D1 and D2 after stripping. Analysis of inflammation-inducing effect by quantification of COX2 (purple-pink) by immunohistochemistry.

The quantification of the enzyme COX2 (green band), responsible for the production of Prostaglandin mediators, is first performed in the epidermis.

An additional analysis showed that the 8% and 15% AHA formulations also caused significant inflammation of the dermis. The data is characteristic of an aggressive action.

While SKINPERF LWG does not generate any significant inflammation, the AHA 8 and 15 formulations activate a significant and high inflammatory response of more than 60%. These results correlate with the aggressiveness of their previously observed exfoliating action.

**CREAM SKINPERF 2% (0.56% AHA)**
Good epidermal cohesion.
15% inflammation

**CREAM AHA-8 (8% AHA)**
Damaged cohesion
68%***inflammation

**CREAM AHA-15 (15% AHA)**
Damaged cohesion
82%***inflammation

*** p<0.001 Student t Test
## SkinPerf LWG

### Exfoliation Benefit / Inflammation

<table>
<thead>
<tr>
<th>CREAM</th>
<th>Exfoliating Performance</th>
<th>Inflammation Level</th>
<th>Performance Index</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>LWG 2% (0.56% AHA)</td>
<td>+50%* of scales Heterogeneity Index 487 (vs 503 for untreated skin)</td>
<td>15% Non Aggressive Inflammation</td>
<td>3.33</td>
<td>**p&lt;0.05; ***p&lt;0.001 Student t Test</td>
</tr>
<tr>
<td>AHA-8 (8% AHA)</td>
<td>+59% of scales Heterogeneity Index 956</td>
<td>68%*** Aggressive Inflammation</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>AHA-15 (15% AHA)</td>
<td>+75%* of scales Heterogeneity Index 1181</td>
<td>82%*** Aggressive Inflammation</td>
<td>0.91</td>
<td></td>
</tr>
</tbody>
</table>
IN-VIVO BENEFITS
**IN-VIVO TEST**

**PROTOCOL**

**EPIDERMAL EXFOLIATION**
Cream containing SKINPERF LWG at 2%
Twice daily applications on the forearm for 14 days
17 volunteers aged 21 to 50.

**Analytical Method:** On D0, skin is colored with DHA. Skin pigmentation is then measured using chromametry. Skin depigmentation is directly linked to the rate of cellular exfoliation.

**SKIN IMPERFECTIONS**
Cream containing SKINPERF LWG at 2%
Twice daily applications for 28 days on the whole face.
24 volunteers aged 34 to 64.

**Analytical Method**
- Scarring blemishes: clinician scorage on a structured scale of 0 to 10.
- Blackheads: counted by a clinician
- Skin bright: sensory evaluation by a 5 person jury on a non-structured scale of 0 to 15.
- Irritation: sensory evaluation by the volunteers on a structured scale of 1 to 10.
IN-VIVO TEST

SKINPERF LWG BOOSTS SKIN EXFOLIATION

After 3 days use, the exfoliation level obtained with SKINPERF LWG is significantly 3 TIMES HIGHER than the exfoliation obtained on untreated skin.

Due to its exfoliating performance SKINPERF LWG leads to total cellular exfoliation in less than 2 weeks.

*** p<0.001 Student t Test
IN-VIVO TEST
SKINPERF LWG IMPROVES SKIN COMPLEXION WITHIN 14 DAYS

The action of SKINPERF LWG on cellular renewal leads to a visible improvement in skin quality.

- Skin grain more velvety: +20%*** on average
- More luminous skin tone: +31%*** on average
- More uniform skin tone: +15%*** on average

SKINPERF LWG provides a resurfacing effect on the skin within 2 weeks.

*** p<0.001 Student t Test
IN-VIVO TEST
SKINPERF LWG DIMINISHES BLEMISHES AFTER 28 DAYS

The action of SKINPERF LWG on cellular renewal is also accompanied by a significant reduction in cutaneous blemishes after 4 weeks treatment.

- Acne scars: -8%** on average
- Pigmentation spots: -11%** on average
- Number of blackheads: -43%*** on average

SKINPERF LWG removes cutaneous blemishes and refines skin grain.

**p<0.01 Student t Test  ***p<0.001 Student t Test
IN-VIVO TEST
VISUALISATION OF THE EFFECT OF SKINPERF LWG ON ACNE SCARS

D0

D14

D28
TOLERANCE OF SKINPERF LWG
IN-VIVO TEST

EFFECT OF SKINPERF LWG ON SKIN PH

Protocol

Immediately after application, creams formulated with 8 and 15% AHA decrease skin pH. 2H after a single application pH is still abnormally low.

SKINPERF LWG does not impact at all skin pH demonstrating the benefits of the LWG technology for the natural physiological barrier of the skin, and its absence of aggressiveness.

Effect of AHA formulations on skin pH

*Cream Skinperf 2%: 0.56% AHA*
*Cream AHA-8: 8% AHA*
*Cream AHA-15: 15% AHA*
IN-VIVO TEST

SENSORY EVALUATION OF IRRITANT EFFECTS

Protocol
Cream containing SKINPERF LWG at 2%
Twice daily applications for 28 days on the whole face.
24 volunteers aged 34 to 64.
Sensory evaluation by the volunteers on a structured scale of 1 to 10.

The cumulative evaluation of 3 irritation parameters reached a maximum score of 0.5 points on a scale of 0 to 10.

Use of SKINPERF LWG twice a day does not lead to redness or feelings of heating or stinging which are usually noted with classical AHA treatments.
SKINPERF LWG
AHA PERFORMANCE WITHOUT IRRITATIONS

LWG technology delivers a progressive and mastered diffusion of AHAs to the skin. It allows to work with lower % of AHA while maintaining an exfoliating performance similar to classical AHA treatments.

EX-VIVO BENEFITS
• Exfoliating action: +50%* versus 59%* with treatment AHA 8%
• Weak inflammation: 15% versus 68%*** with treatment AHA 8%
• Performance Index: 3.33 versus 0.86% with treatment AHA 8%

IN-VIVO BENEFITS
• 100% cellular exfoliation in less than 2 weeks***
• Skin velvety: +20%***
• Skin bright: +31%***
• Skin uniformity: +15%***
• Acne scars: -8%**
• Pigmentation spots: -11%***
• Number of blackheads: -43%***
• No impact on skin pH
• Irritation scorage: grade 0.5/10