



SYSTEMIC HYDRA-RESTORATION

SKIN HOLOBIONT INVIGORATOR

HOLOBIOSYS®



SKIN ISSUE STUDIED BY GREENTECH



DRY/DEHYDRATED SKIN & SLOWED-DOWN SKIN HOLOBIONT

HOLOBIOSYS® is the latest achievement of more than 30 years of Greentech research. Thirty robust years of expertise in various fields: biotechnologies, metabolically oriented fermentation, phytochemistry, green extraction, biomimeticism and microbiota.

Today, **our extensive scientific approach allows to unveil a new generation of active ingredients** for cosmetics. Utilizing an innovative **metaproteomic study** which focuses on the specific function of each cellular protein, A major advance in cosmetics! Our systemic method treats the skin as a whole and repairs conditions of dry and dehydrated skin via a boost of hyaluronic acid and skin lipids synthesis.

We are convinced that ecosystems must be studied as a whole, focusing on the interconnections between their various components rather than on the individual parts. **Taking it a step further than a simple microbiota study** comparing one side and the skin to the other, **the study of the holobiont** provides a comprehensive view of the interactions between the skin and its microbial ecosystem.

With age and loss of hydration, our research shows that these interactions evolve and tend to decrease over time. By focusing on the host/microbiota interactions, **HOLOBIOSYS® is able to contribute to a more harmonized holobiont, allowing a deep hydration-restructuring action** and reinvigorated, healthier skin.

Understanding and mastering the holobiont is a scientific achievement for Greentech. An innovation that **moves science forward** and provides a **next generation of skin care actives**: more specific, more sustainable and ever more effective.

ACTIONS

DEEPLY HYDRATES

HYDRA-
RESTRUCTURES SKIN

PROTECTS/RESTORES

HYDROLIPIDIC
FILM

SMOOTHES

WRINKLES &
FINE LINES

INVIGORATES

SKIN
HOLOBIONT

A NEXT-GENERATION MOISTURIZER

MOLECULES

- PHOSPHOLIPIDS
- AMINO ACIDS (INCLUDING GLUTAMIC ACID) - KNOWN FOR ITS HYDRATING PROPERTIES
- LOGANIC ACID - ANTIOXIDANT PROPERTIES

SOURCING *Inspiration from nature's defenses*

A LOCAL AND RESISTANT MOUNTAIN PLANT

- **ORGANIC WILD YELLOW GENTIAN ROOTS**
SUSTAINABLY HARVESTED IN FRANCE BY GENTIAN-PICKERS
TRAINED IN GOOD HARVESTING PRACTICES

A RARE AND RESISTANT BACTERIA

- **SPHINGOMONAS FAENI**
A COLD-TOLERANT BACTERIA ISOLATED
FROM FRENCH AEROBIOME ABLE TO RESIST
A DESICCATED ENVIRONMENT



COSMETIC USES

- DRY SKIN CARE PRODUCTS
- MOISTURIZING CARE PRODUCTS
- SKIN HOLOBIONT INVIGORATING PRODUCTS
- HYDRATING MAKE-UP PRODUCTS

GREENTECH INNOVATION

SYSTEMIC HYDRA-RESTORATION

FROM DERMIS TO SKIN SURFACE

SKIN HOLOBIONT INVIGORATOR

STIMULATED SKIN HOST-MICROBIOTA INTERACTIONS - METAPROTEOMIC ANALYSIS

UPCYCLED FERMENTATION PROCESS

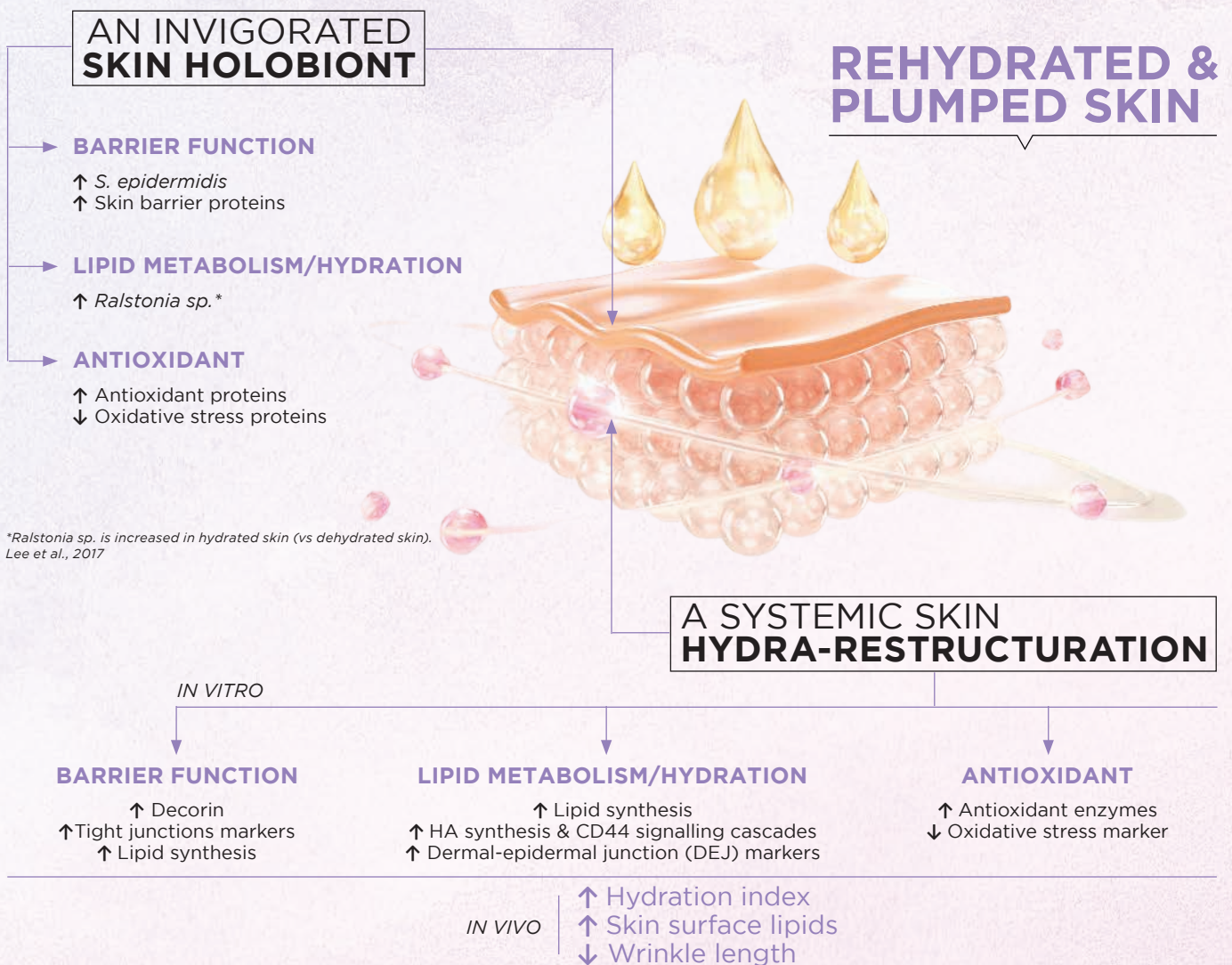
WILD YELLOW GENTIAN EXTRACT ENHANCED BY FERMENTATION
WITH A RARE BACTERIA FROM AEROBIOME

SYSTEMIC APPROACH FOR A NEXT-GENERATION MOISTURIZER

Holobiont is an assemblage of a host organism and its microbial ecosystem.

With age and dehydration, some **interactions between skin host/microbiota** are slowed-down (Greentech studies).

So **beyond simply studying the sum of the parts**, with host studies on one hand and microbiota studies on the other, **the next-generation active ingredients have to study the skin as a whole**, to understand and master skin host/microbiota protein interactions and provide ever more innovative and effective products, targeting the skin holobiont.

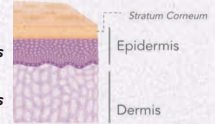


PROVEN EFFICACY

IN VITRO ANALYSIS

NHEK: Normal human epidermal **keratinocytes**

NHDF: Normal human dermal **fibroblasts**



1. SYSTEMIC HYALURONIC ACID (HA) BOOSTER

1.1. UPREGULATES HA SYNTHESIS

NHDF or NHEK, ± HOLOBIOSYS® 0.5% (NHEK or NHDF). Dosage by ELISA.

BY KERATINOCYTES **+62%*****

BY FIBROBLASTS **+32%***

*p<0.05; ***p<0.001 vs control

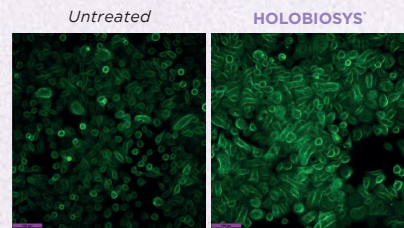
HOLOBIOSYS® UPREGULATES HA SYNTHESIS BY KERATINOCYTES & FIBROBLASTS REINFORCING SKIN MOISTURE AND PARTICIPATING TO SKIN PLUMPING AND FIRMNESS

1.2. BOOSTS HA RECEPTOR CD44

NHEK, ± HOLOBIOSYS® at 0.5%. CD44 immunostaining (green).



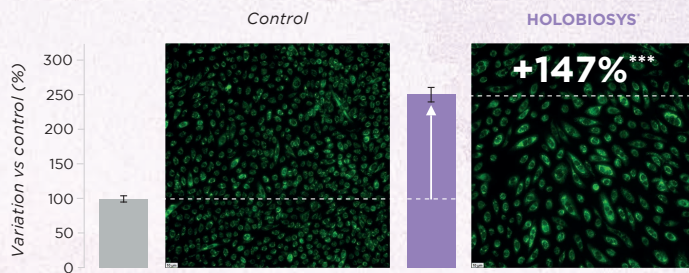
**p<0.01 vs control



HOLOBIOSYS® UPREGULATES CD44 SYNTHESIS PARTICIPATING TO HA SIGNALING CASCADES AND SKIN MOISTURE

2. LIPID SYNTHESIS BOOSTER

NHEK, ± HOLOBIOSYS® at 0.5%. Neutral lipid staining (green).

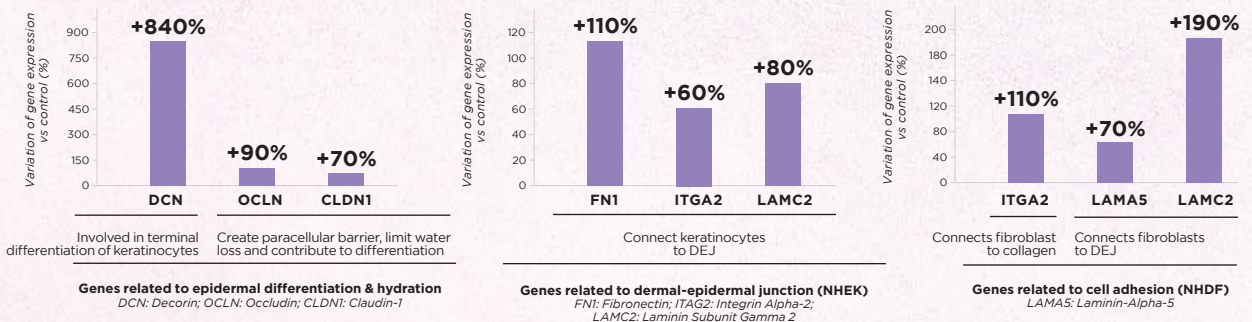


HOLOBIOSYS® UPREGULATES LIPID SYNTHESIS PARTICIPATING TO LIPID BARRIER REINFORCEMENT AND SKIN MOISTURE

***p<0.001 vs control

3. STRENGTHENING EFFECT FROM EPIDERMIS TO DERMIS

NHDF or NHEK, ± HOLOBIOSYS® at 1%. Gene expression by RT-qPCR.



HOLOBIOSYS® UPREGULATES GENES CODING FOR EPIDERMAL DIFFERENTIATION & CELL COHESION TO REINFORCE SKIN BARRIER FOR CELL-MATRIX/DEJ ADHESION REQUIRED FOR PROPER HALURONIC ACID DIFFUSION

4. SYSTEMIC ANTIOXIDANT CELL RESPONSES BOOSTER

Glutathione-dependant redox enzyme	Oxidative stress resistant enzymes		Oxidative stress marker	Glutathione-dep redox enzyme	Detoxifying enzymes		Antioxidant enzymes	
GLRX	SIRT3	SIRT7	PPIA	GLRX	MGST1	TXN	HMOX1	PRDX1
+130%	+90%	+70%	-40%	+120%	+90%	+90%	+80%	+160%

NHEK: Genes related to antioxidant defenses

GLRX: Glutaredoxin - SIRT3: Sirtuin 3
SIRT7: Sirtuin 7 - PPIA: Peptidylpropyl isomérase 3

NHDF: Genes related to antioxidant defenses

MGST1: Glutathione S Transferase 1 - TXN: Thioredoxin
HMOX1: Heme Oxygenase 1 - PRDX1: Peroxiredoxin 1

HOLOBIOSYS® ACTIVATES GENES CODING FOR CELL RESPONSES AGAINST OXIDATIVE STRESS, FROM DERMIS TO EPIDERMIS, TO PROTECT HA FROM DEGRADATION

PROVEN EFFICACY

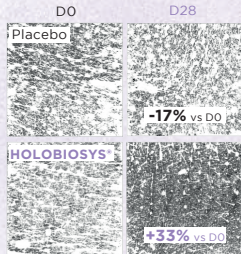
CLINICAL STUDY 1 IN VIVO - EVALUATION OF SKIN CONDITION

- **20 volunteers**, 42-54 yo (mean: 48 yo), 100% women. **Dehydrated to very dehydrated facial skin, visible crow's feet wrinkles skin on face.**
 - Sub-Panel: sebum-deficient skin: sebum $\leq 100 \mu\text{g}/\text{cm}^2$ on forehead.
- **HOLOBIOSYS® 1%** versus Placebo (gel). Randomized **Split-face application 2x/day, 28 days.**
- **Measurements at D0 and D28:** Skin hydration on forehead by MoistureMap®, skin surface lipids by Sebumeter®, wrinkle length by Primos® Lite.

HYDRA-RESTRUCTURING EFFECT

At D28
+7.3%*
Hydration

+12.5%** for the Sebum-deficient sub panel



* $p < 0.05$; ** $p < 0.01$ vs placebo

PROTECTIVE EFFECT ON HYDROLIPIDIC FILM

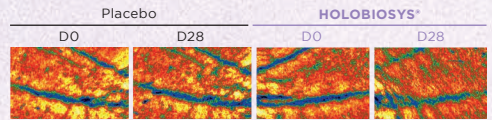
At D28
+27%**
Lipids

+43%* for the Sebum-deficient sub panel

* $p < 0.05$; ** $p = 0.01$ vs placebo



SMOOTHING EFFECT ON WRINKLES



At D28
-5%
Wrinkle length

$p = 0.08$ vs placebo

A HYDRA-PUMPLING ACTIVE INGREDIENT

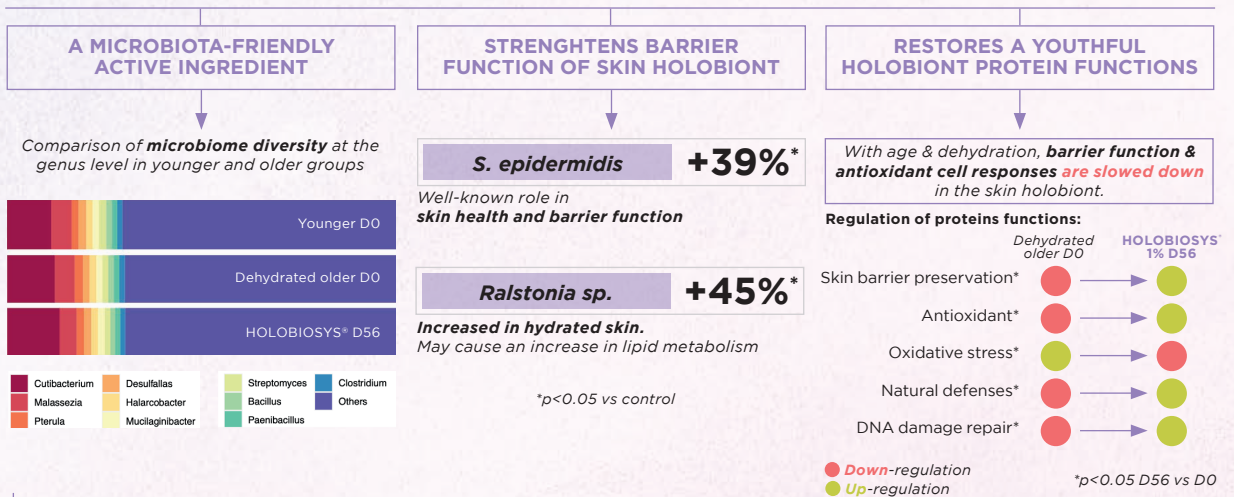
CLINICAL STUDY 2 IN VIVO - EVALUATION OF SKIN METAPROTEOME

- **40 volunteers in 2 groups, 1 dehydrated older and 1 younger.**
 - Group 1: same than clinical study 1.
 - Group 2: 20 volunteers, 25-35 yo (mean: 30 yo), 100% women. No treatment. All skin types.
- **HOLOBIOSYS® 1%** versus Placebo (gel). Randomized **Split-face application 2x/day, 56 days.**
- **Measurements at D0 and D56:**
 - D0 only for younger group (group 2), D0 and D56 for dehydrated older group (group 1).
 - Skin surface sampling (cheek) - Metaproteomic analysis

THE WHOLE IS BETTER THAN THE SUM OF ITS PARTS

Holobiont (host-microbiota complex functional interactions) can be studied thanks to an innovative and emerging advanced technology : the **METAPROTEOMIC ANALYSIS**

HOLOBIOSYS®



AN INVIGORATED SKIN HOLOBIONT & A REHYDRATED SKIN

HOLOBIOSYS®

TECHNICAL INFORMATION

FORMULATION

Concentration for use: 1%

pH for use: 4.0 - 6.0

Caution for use:

Add at any time for cold processes and during cooling (30-40°C) for hot processes (possible to heat at 70°C during 20min, time for emulsion).

TECHNICAL DATA

Characteristics

Organoleptic	Appearance: liquid Color: Amber yellow to brown
Solubility	Soluble in water, in glycols

Storage

Keep in a dark place, in the original packaging, at an ambient temperature between 15° and 25 °C.

Tests of tolerance

- Cutaneous irritation (at 5%) : Very good skin compatibility (Patch test)
- Sensitization (at 5%) : Very good skin compatibility (HRIPT)
- Eye irritation (at 5%) : Practically non irritant (HETCAM)
- Phototoxicity : Not phototoxic (in vivo test)
- Mutagenicity test : Not mutagenic (AMES test)

Formulation guidelines and stability studies available on demand.

- **INCI name:** Propanediol, Aqua/Water, Gentiana Lutea Root Extract, Sphingomonas Ferment Extract
- **Preservative:** None
- **Authorized:** China
- **Certified:** COSMOS
- **Naturality (ISO 16128) :** 100% natural origin content



Organic certified by ECOCERT GREENLIFE, according to COSMOS Standard

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