



Lipowheat™

NATURAL VEGETABLE CERAMIDES

Lipowheat™ hydrates skin; stimulates healthy skin and follicular fibroblasts



Wheat Ceramides in human skin and hair biology

1. Definition of wheat ceramides, distinction from wheat germ oil, and role in skin biology.
2. Stability and safety of ceramides for human use.
3. Preclinical studies of ceramides in fibroblast culture protecting cells against action of free radicals & increasing their functionality, e.g. collagen production.
4. Three clinical studies for oral use of ceramides in skin hydration.
5. Preclinical studies of ceramides improving nourishment of hair follicles by stimulating proliferation of specialized cells, follicular fibroblasts.

Fibroblast... The Skin Treasure Cell™

Fibroblast is most versatile and multi-tasking cell in human skin.

It manufactures the extra-cellular matrix (collagen, elastin) and participates in regeneration, healing and immune defense of the skin.



What are ceramides ?

Ceramides belong to a family of lipid molecules composed of sphingosine and fatty acids. [1]

Ceramides are components of skin protective barrier against entry of environmental allergens, exposure to UV light, and chemical, physical and biological skin irritants. [2]

Ceramides are integral part of skin cell membranes. [3]

Ceramides provide a protective layer of hair fiber and function as signaling molecules; e.g., signaling stress, whether physical, chemical or biological in nature. [3,4]

[1] <http://lipidlibrary.aocs.org/Lipids/ceramide/index.htm>

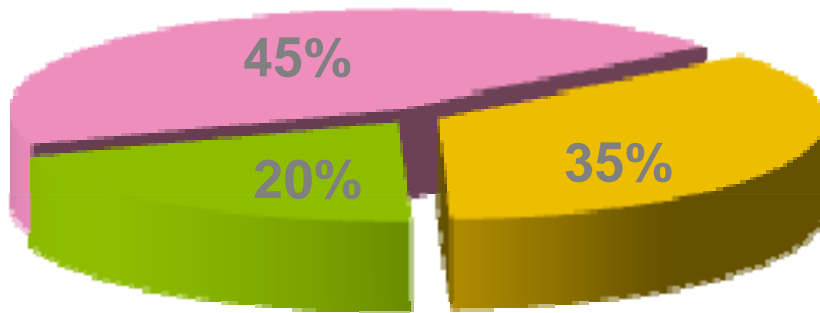
[2] Rogers J « Stratum corneum lipids : the effect of ageing and seasons", Arch Dermatol Res, 1996, 288:765-70.

[3] Mazière JC " Histophysiology of skin and cutaneous lipids layers of the epidermis and metabolism of lipids in relation to the hydric barrier function of the skin" *Oléagineux Corps gras, lipides*, 1997, vol 4, n°4, 258-265.

[4] MASUKAWA Y. "Characterization of the lipid composition at the proximal root regions of human hair" International Journal of Cosmetic Science 2005, 27, 191-192.

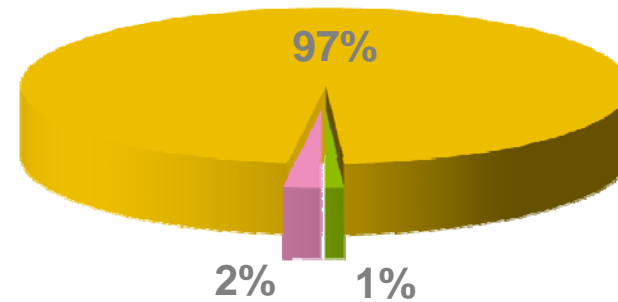
Comparison between LIPOWHEAT and wheat germ oil

LIPOWHEAT composition [1]



- POLAR LIPIDS
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ceramides, glycosylceramides,
phospholipids, glycolipids
- FATTY ACIDS
- OTHERS

Wheat germ oil composition [2]

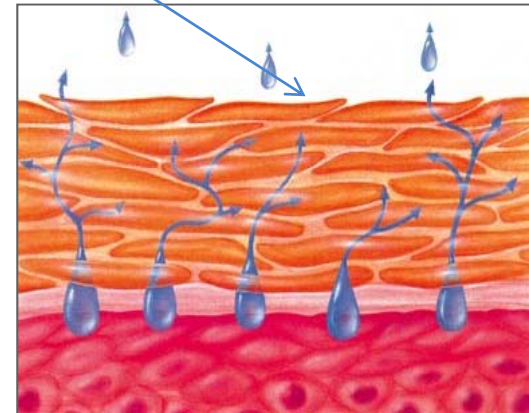


[1] ITERG report, 2006

[2] VIOGERM - Hochdorf nutrition AG

Focus on ceramide functions

- A part of the sphingolipid family, ubiquitous in the whole body
- Naturally present in animals and plants
- Major constituent of **skin intercellular cement** [1]
- Key role in healthy **skin barrier** [1,2,3,4,5]



[1] Maziere JC « Histophysiology of skin and cutaneous lipids layers of the epidermis and metabolism of lipids in relation to the hydric barrier function of the skin » *Oléagineux Corps gras, lipides*, 1997, vol 4, n°4, 258-265.

[2] Claudy A « Les lipides cutanés : de la physiologie à la clinique », *Pathologie Biologie*, 2003, 51, 260-263.

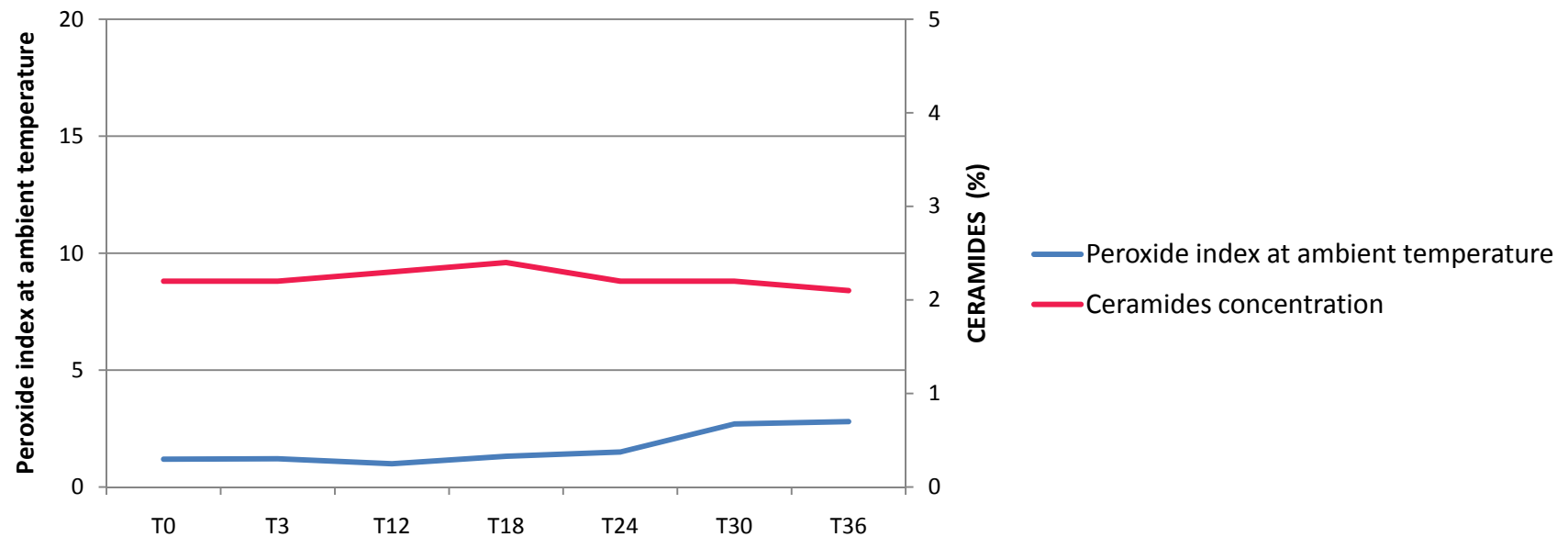
[3] Wertz PW. "Glycolipids in mammalian epidermis: structure and function in the water barrier." *Science*, 1982, 217 : 1261-2.

[4] Menon GK « Lamellar bodies as delivery systems of hydrolytic enzymes : implications for normal and abnormal desquamation » *Br. J. Dermatol.*, 1992, 126:337-345.

[5] Marilyn A. Lampe « Human stratum corneum lipids : characterization and regional variations » *J Lipid Res.* 1983 Feb;24(2):120-30.

LIPOWHEAT: Stability data

LIPOWHEAT oil is very stable: [1]



After 3 years at room temperature:

- $I_p < 3$
- No change in ceramide concentration

[1] Stability data, HITEX 2006-2009 - Vannes, France

SAFETY

Non-allergen

- Non allergen: gluten < 20 ppm - ELISA Test [1]
- In compliance with Codex Alimentarius definition for gluten free products

Safety tests

- No mutagenicity potential - Ames [2]
- LD 50 > 5000 mg/kg for Lipowheat oil and Lipowheat WS powder [3]

[1] ELISA TEST, done on each batch of Lipowheat, IDAC Nantes, France

[2] AMES TEST, Chrysalis 1998 - L'Arbresle, France

[3] LD 50, Physcher 2009 - Cestas, France

LIPOWHEAT: NDI

SAFETY AND APPLICATION: THE FDA NDI DOSSIER

NDI obtained from the FDA without objection in March 2010

Claim « *Helps maintain healthy skin hydration* » [1]

Non allergen: gluten < 20 ppm, conform to the Codex Alimentarius definition for gluten free products [2]



[1] FDA LETTER, 11th of March, 2010.

[2] ELISA TEST, done on each batch of Lipowheat, IDAC Nantes, France

SUMMARY OF LIPOWHEAT *IN VITRO* STUDIES

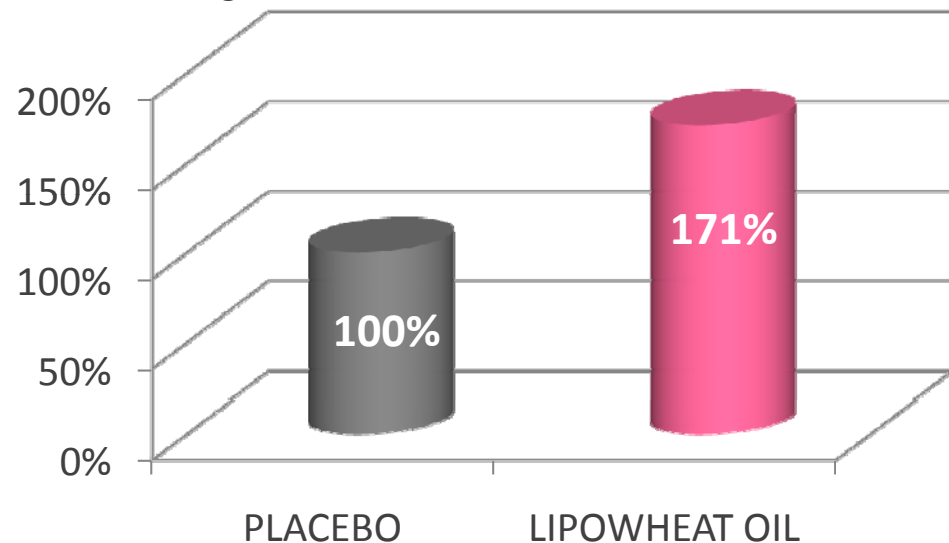
- 1- Lipowheat stimulates collagen synthesis
- 2- Protection of the cultured human fibroblasts against xanthine/xanthine oxidase free-radical damage
- 3- Protection against elastase activity
- 4- Restoration of skin barrier (human skin tissue model) dehydrated and damaged with acetone

1- Lipowheat stimulates collagen synthesis

Lipowheat oil (50µg/ml) was incubated during 48 hours with normal human fibroblasts.

Incorporated radioactivity in the synthesized collagen was measured.

% of incorporation of L-[3H]proline in synthesized collagen

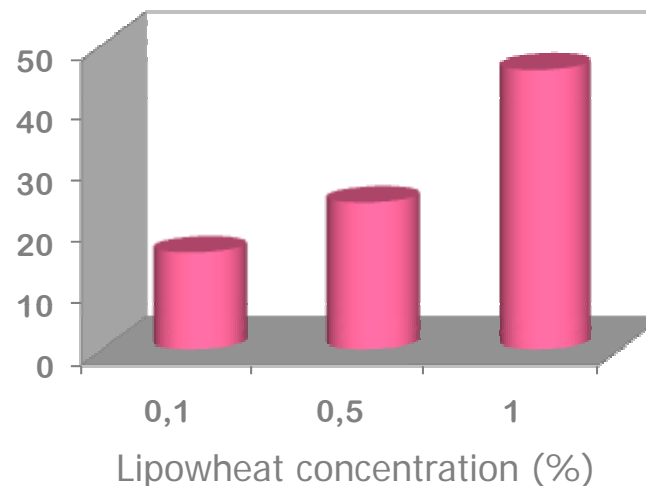


2- Protection of the cultured human fibroblasts against xanthine/xanthine oxidase free-radical damage

On fibroblasts after generating free radicals by Xanthine-Xanthine oxidase system.

Results are expressed in a protection percentage compared to control fibroblasts.

Radical protection %

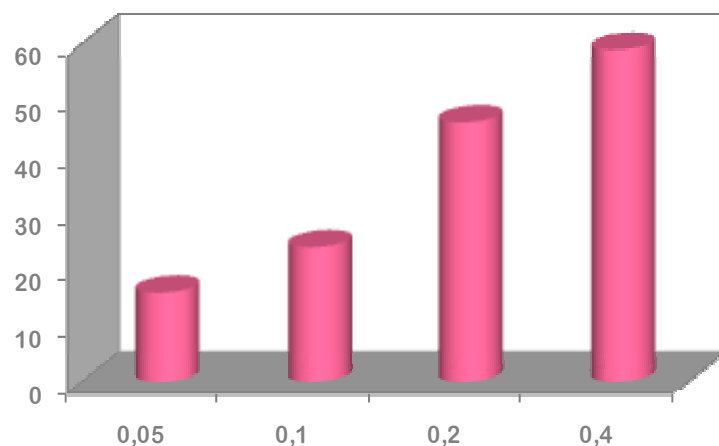


	Control	Xanthine oxidase	Lipowheat 0.1%	Lipowheat 0.5%	Lipowheat 1%
Optical density 470 nm	0.292	0.152	0.177	0.188	0.222
Protection percentage			16%	24%	47%

3- Protection against elastase activity

The HLE (Human Leucocyte Elastase) activity is measured at 37°C in polystyrene tanks. The enzymes have been pre-incubated for 1 hour with a ceramide concentration of 0.4%, 0.6%, 0.7% and 1%. A synthetic substratum is added to the buffer and the hydrolysis reaction runs at 37°C for 2 hours.

HLE inhibition %



Lipowheat concentration (%)

Results are expressed in anti-elastase activity

	HLE	Lipowheat concentration µg/ml						
		20	50	250	500	1000	2000	4000
Optical density	0.526	0.509	0.482	0.446	0.441	0.428	0.278	0.215
Protection %	0%	3%	8%	15%	16%	25%	47%	59%

Lipowheat induced a dose-dependent inhibition of HLE. This inhibition is < 15% from the 20 to 500 µg concentrations, and is very strong for 1 000 to 4 000 µg concentrations with more than a 50% inhibition.

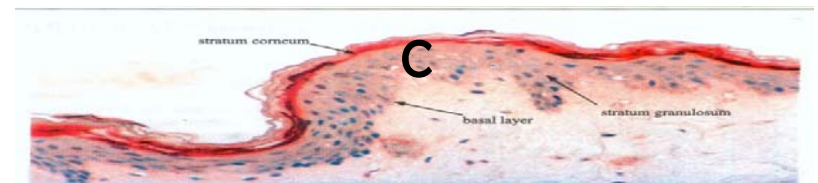
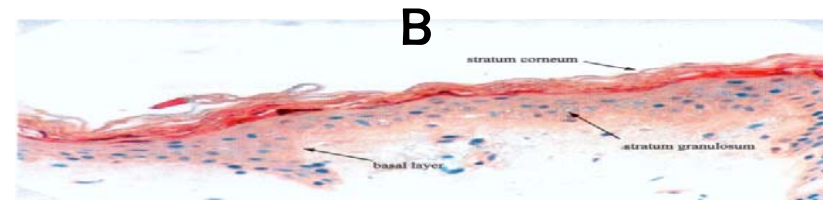
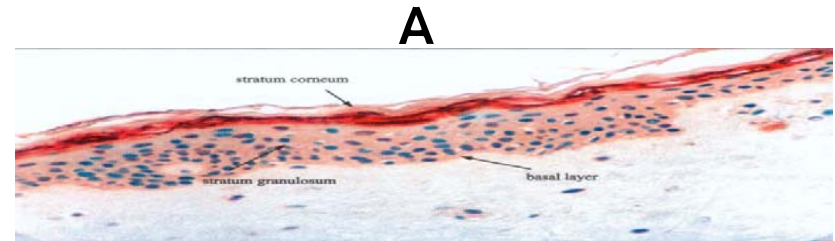
4- Restoration of skin barrier (human skin tissue model) dehydrated and damaged with acetone

Restructuring properties

- Human skins (ex-vivo methods).
- Immunohistochemical method using antifilaggrin (antikeratin) antibodies.

Results:

- After acetone treatment : destructured skin barrier.
- With Lipowheat (1%) : restores the barrier function of irritated skin.
- With placebo : no change.



A: control

B: after acetone treatment

C: after Lipowheat application

SUMMARY OF LIPOWHEAT ORAL INGESTION CLINICAL STUDIES

- Hydrates dry and very dry skin
- Decreases itching sensations
- Decreases squames
- Bring softness and wellness to skin
- Excellent compliance and tolerance

ONLY 350 mg/day of LIPOWHEAT oil
Very easy to formulate and take !

CLINICAL STUDY #1

Pilot study 2003 - Dermexpert

- Testing product: Lipowheat powder / Placebo
- Dose: 80 mg / day (tablets)
- Including: 40 women from 30 to 55 years old, phototypes II to IV, with dry skin on legs
- During: 1 month

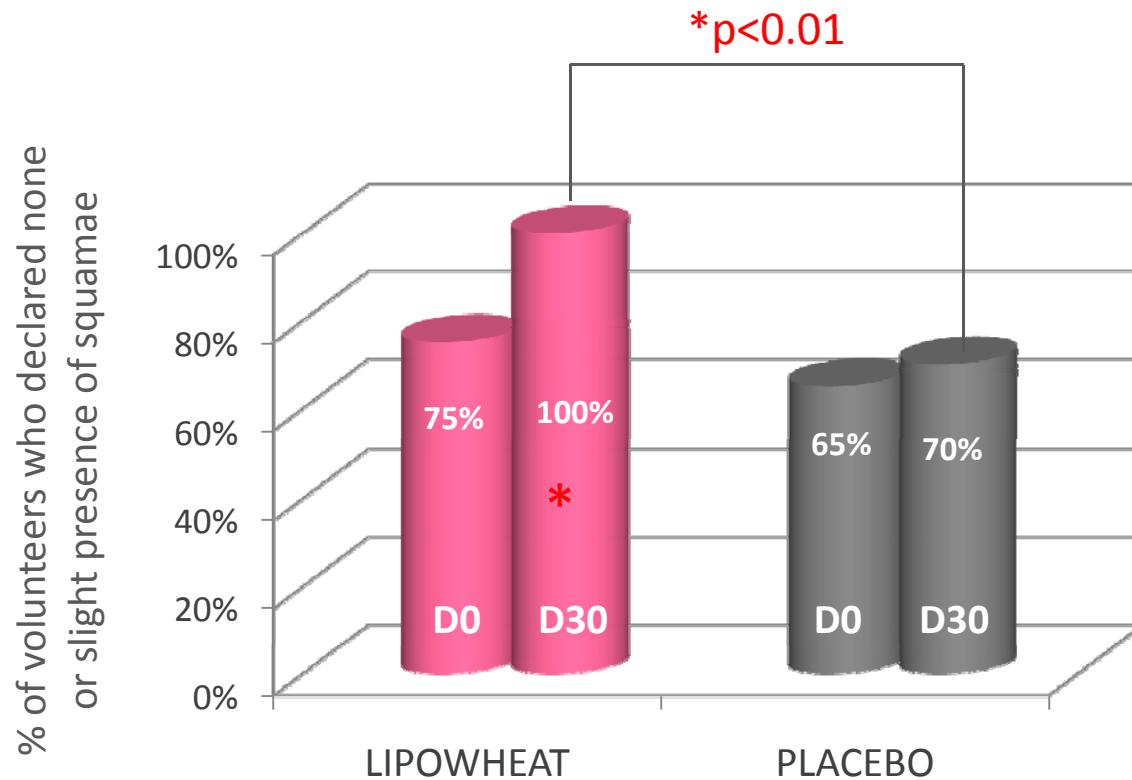
Clinical evaluation

Hydration measurement
Corneometry

Self assessment

CLINICAL STUDY #1

SQUAMES PRESENCE: percentage of volunteers who declared none or slight presence of squamae between D0 and D30



CLINICAL STUDY #2

Clinical study 2005 - Gredeco

- Testing products: Lipowheat powder / placebo
- Dose: 200 mg / day (tablets)
- Including: 45 women aged from 23 to 60 years old, phototypes II to V, with dry or very dry skin on legs
- During: 3 months

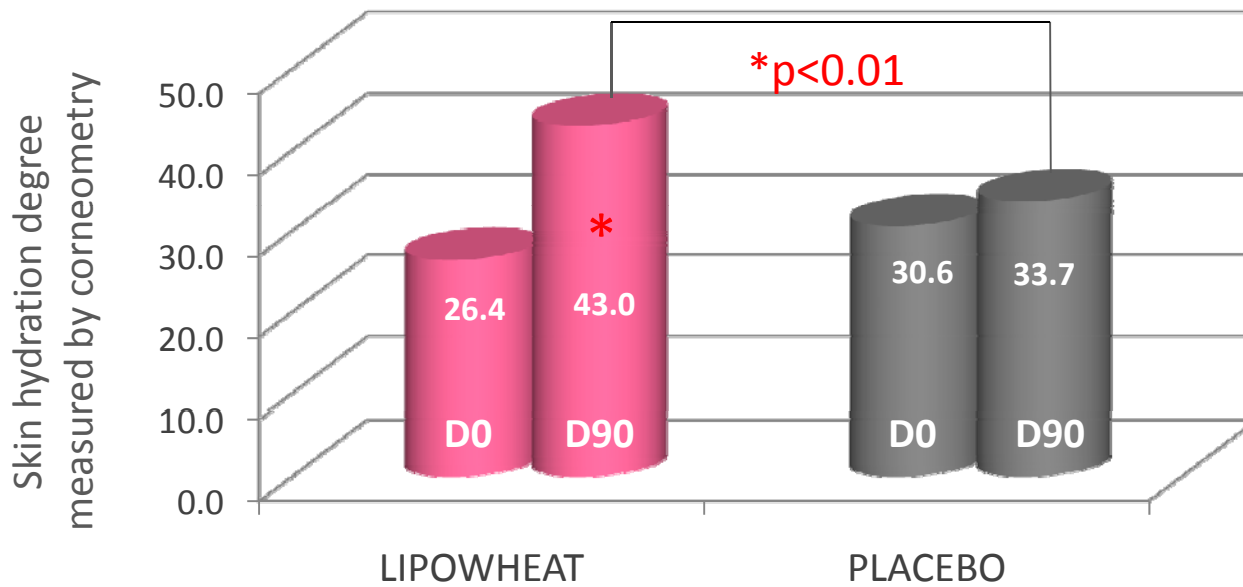
Clinical evaluation

Hydration measurement
Corneometry

Self assessment

CLINICAL STUDY #2

Skin hydration measures on legs - corneometry



CLINICAL STUDY #3

Clinical study 2007 - Proclaim

- Testing products: Lipowheat oil/placebo
- Dose: 350 mg/day (capsules)
- Including: 50 women aged from 20 to 65 years old, with dry to very dry skin on legs
- During: 3 months

Clinical evaluation

Hydration measurement
Corneometry

Self assessment

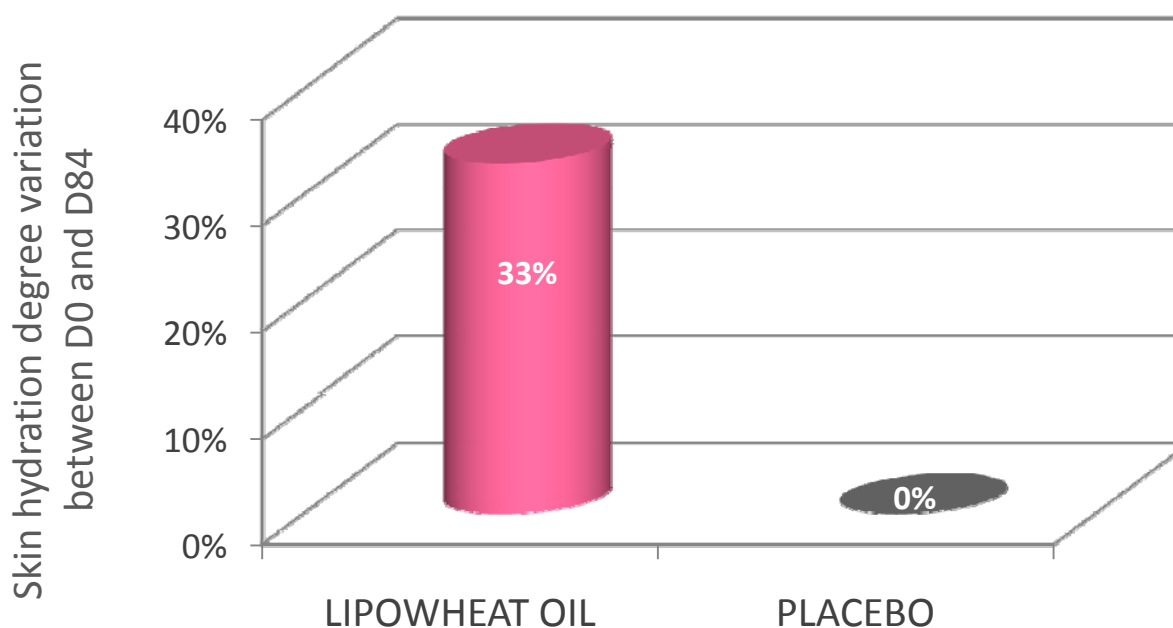
Guillou S et al. « The moisturizing effect of wheat oil food supplement on women skin: a randomized double-blind placebo-controlled trial », 2010, International Journal of Cosmetic Science.

Proclaim 2007 - Saint-Grégoire, France

CLINICAL STUDY #3

Hydration measurement

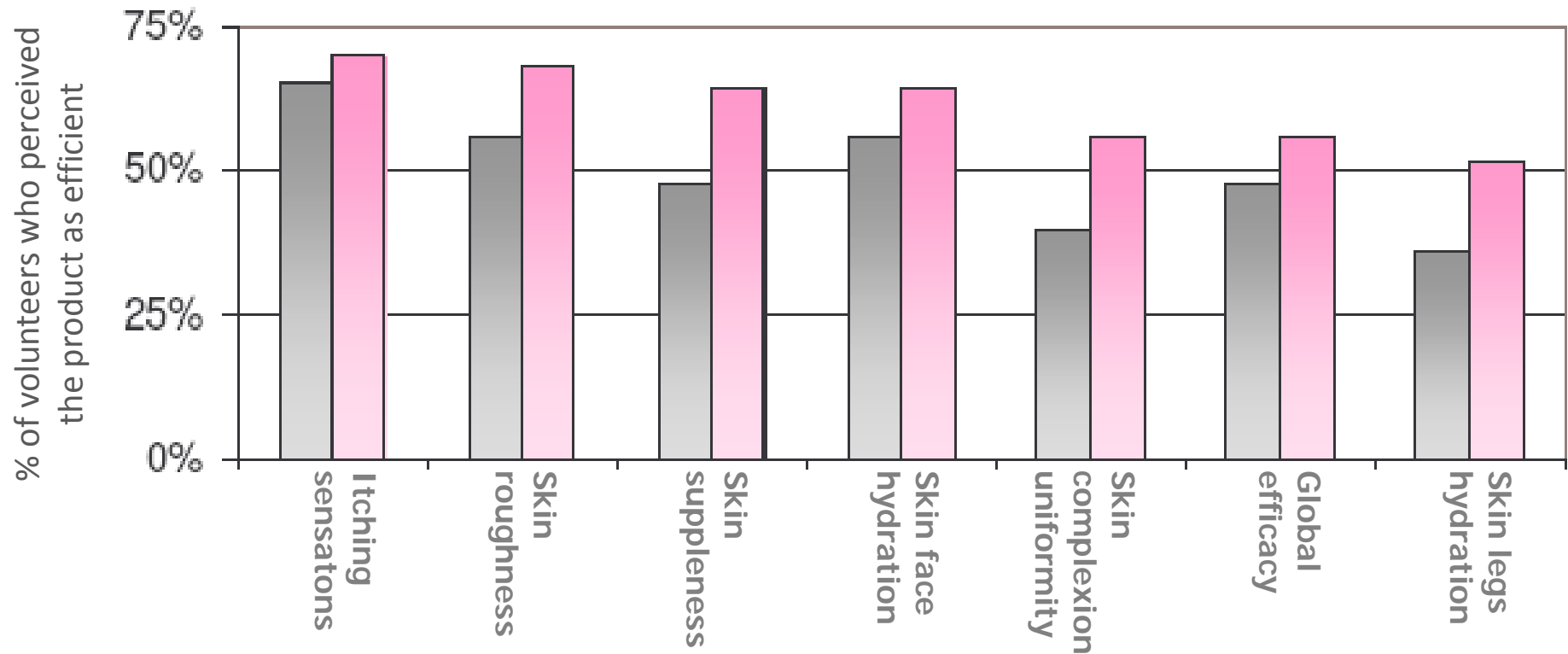
Hydration degree variation on arms between D0 and D84



Guillou S et al. « The moisturizing effect of wheat oil food supplement on women skin: a randomized double-blind placebo-controlled trial », 2010, International Journal of Cosmetic Science.

RESULTS - Self-assessment

Perceived efficacy at D84: Placebo vs. Lipowheat



Guillou S et al. « The moisturizing effect of wheat oil food supplement on women skin: a randomized double-blind placebo-controlled trial », 2010, International Journal of Cosmetic Science.

SUMMARY OF PRE-CLINICAL STUDIES OF LIPOWHEAT IN HAIR CARE

Telogen effluvium is an abnormal loss of hair due to alteration of the normal hair cycle. It is usually linked with a stress and affects middle-aged women.

The telogen effluvium evolution is fluctuating, shedding are diffuse, sudden and recurrent. But the hair renewal and hair density are correct between two events. The pull test is usually positive for the whole scalp.

Telogen effluvium is characterized by an abnormal shedding of hairs which can be explained by a quick passage of numerous hairs into the telogen phase. Normally, 10 to 15% of scalp hairs are in the telogen phase and 85 to 90% are in the anagen phase. The telogen effluvium is diagnosed if more than 20% of hairs are in the telogen phase (EEMCO Guidance, 2004).

LIPOWHEAT PRE-CLINICAL STUDY #1

Purpose

Mitotic index: measure of the proliferation status of a cell population.

Evaluate the mitotic index after an application of Lipowheat.

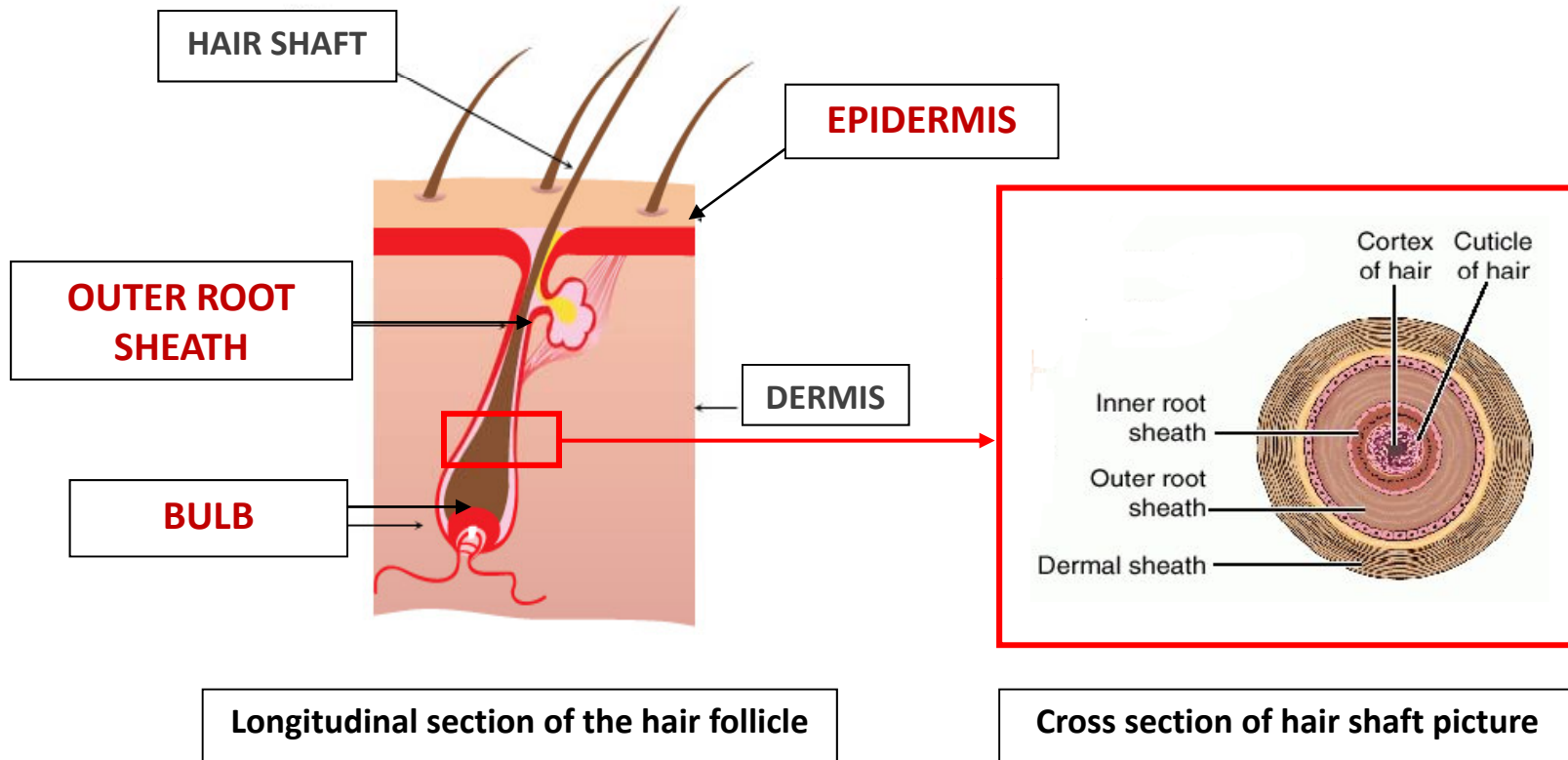
Material & Method

- Experimental model of hair culture obtained from face-lift residues of 8 different donors
- LIPOWHEAT: 33.3 µg/ml of Lipowheat WS powder (6.66 µg/ml of Lipowheat oil)
- CONTROL : culture medium

The mitotic index evolution was measured by the quantification of cells in mitosis (Ki67) - colored in red.

LIPOWHEAT PRE-CLINICAL STUDY #1

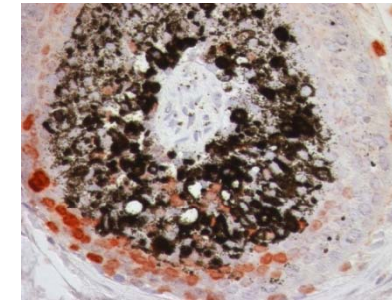
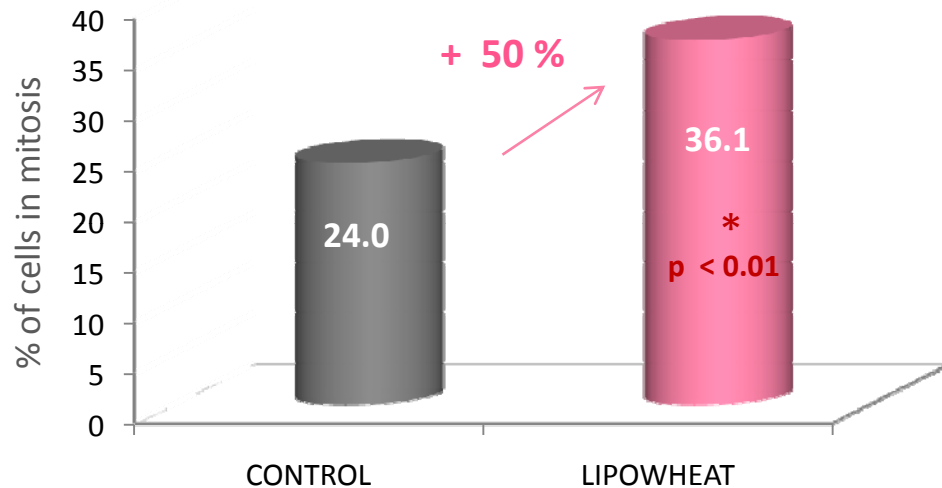
Cell proliferation is measured in : BULB, EPIDERMIS and OUTER ROOT SHEATH.



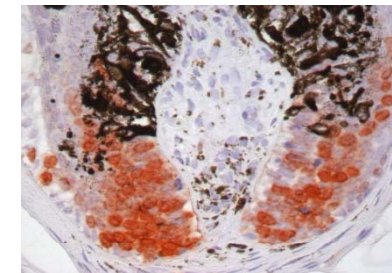
PRE-CLINICAL STUDY #1

LIPOWHEAT & CELL PROLIFERATION IN HAIR BULB

% OF CELLS IN PROLIFERATION IN HAIR BULB



CONTROL

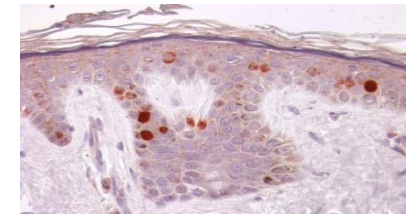
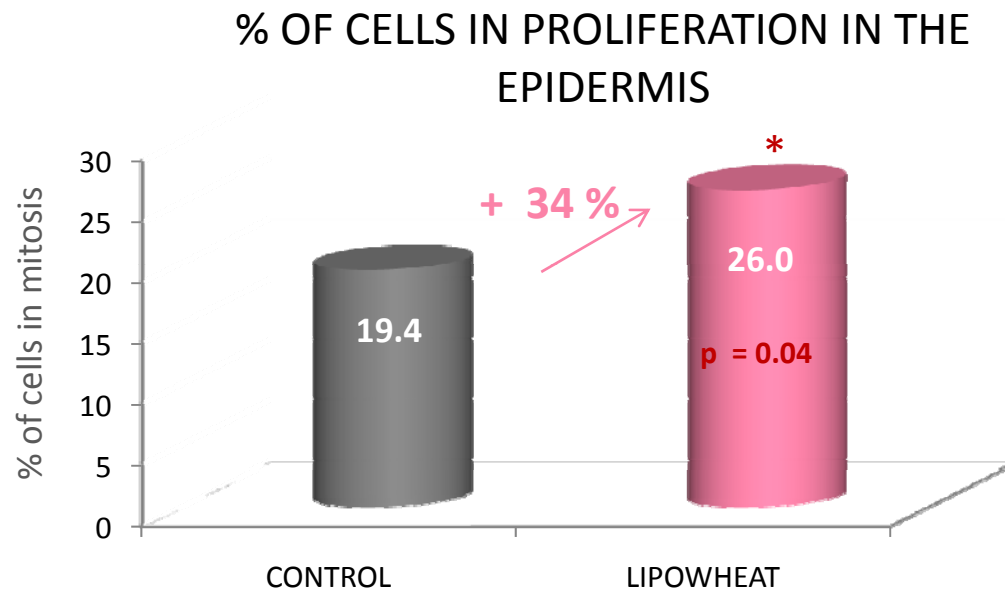


LIPOWHEAT

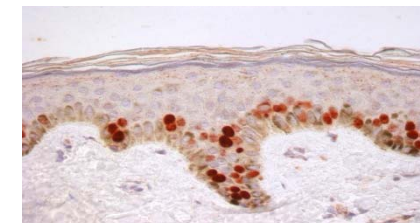
Cross-section of the bulb

With LIPOWHEAT, the number of cells in mitosis was about **36.1%** compared to **24%** for the control scalp (**p < 0.01**). LIPOWHEAT increases of about **50%** the hair bulb cells proliferation.

LIPOWHEAT & CELL PROLIFERATION IN EPIDERMIS



CONTROL

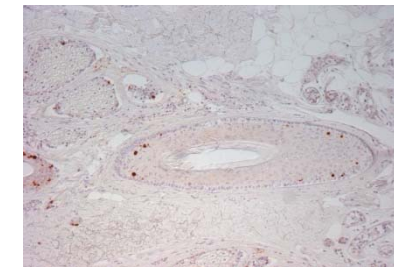
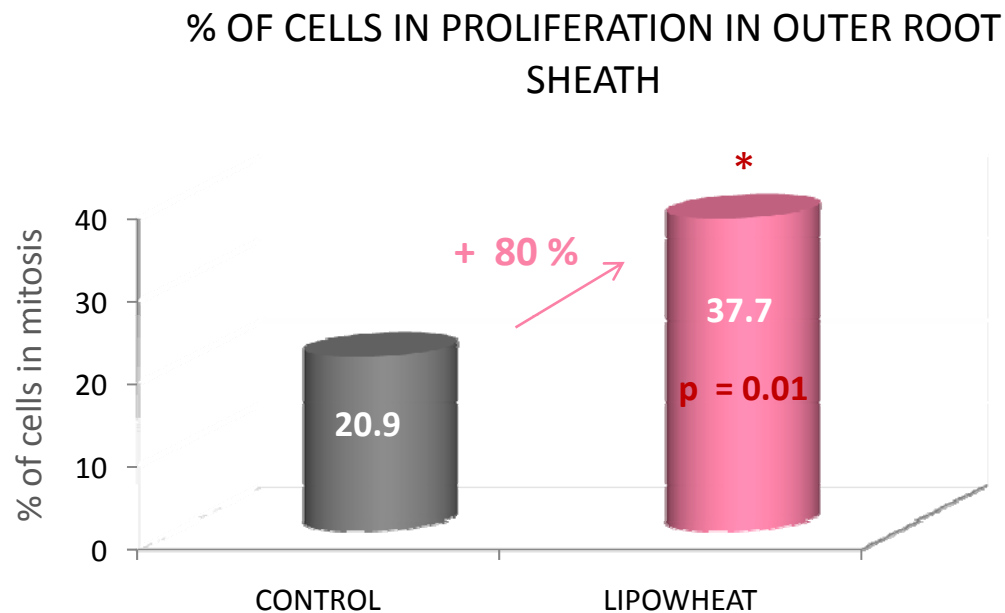


LIPOWHEAT

Cross-section of the epidermis

With LIPOWHEAT, the number of cells in mitosis was about **26.0%** compared to **19.4%** for the control scalp (**p= 0.04**). LIPOWHEAT increases of about **34%** the epidermis cells proliferation.

LIPOWHEAT & CELL PROLIFERATION IN OUTER ROOT SHEATH



CONTROL



LIPOWHEAT

Cross-section of the outer root sheath

With LIPOWHEAT, the number of cells in mitosis was about **37.7%** compared to **20.9%** for the control scalp (**p= 0.01**). LIPOWHEAT increases of about **80%** the Outer Root Sheath cells proliferation.

LIPOWHEAT SUMMARY

Ceramides are essential for healthy skin

Deficiency of ceramides in protective skin layer may lead to a disturbed skin barrier, and may contribute to pathogenesis of contact dermatitis, ichthyosis, psoriasis, and atopic dermatitis

Preclinical studies of Lipowheat show broad protective effect including protection of skin fibroblasts or “treasure cells”

Oral ingestion Clinical studies of Lipowheat show its obvious efficacy in skin hydration and improvement of associated skin health parameters

Lipowheat is safe for both topical and food use



Thank you for your attention!

For more information, please contact

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