

Active Beauty

Rubixyl®

The answer to stress: acting on beauty receptors

Crafted by synthesis



Givaudan

engage your senses

Stress

A daily problem for our skin

"Stress": an organism's response to a stressor such as an environmental condition or a stimulus. Stress can be positive.

Examples of skin's daily direct stresses

- ❖ Pollution
- ❖ Cigarettes smoke
- ❖ UV irradiation
- ❖ Mechanical, temperature variations
- ❖ Bacterial contaminations
- ❖ Chemicals

Indirect stresses

- ❖ Hormonal changes
- ❖ Daily stress (indirect action from the brain)
- ❖ Lower detox capabilities
- ❖ Chronological aging



High stress consequences

- ❖ Depression
- ❖ Heart attack
- ❖ Burn out
- ❖ Premature aging

Without stress ...

Cells are communicating

- ❖ Skin cells are constantly **exchanging information**
- ❖ They set up a **network** that enables them to be aware of the global physiological processes happening in our skin and to react.
- ❖ To **communicate**, they use emitters (small molecules) and receptors.



What happens In stress conditions ?

Upon **stress (or ageing)**, the efficiency of cells **communication network slows down** and even has major breakdowns

Why?

Because **stress induces the disappearance of some cellular receptors**: cells become deaf and isolated

One category of specific receptors is impacted by stress: the DOR (Delta Opioid Receptors)



Delta Opioid Receptors disappear In stress conditions

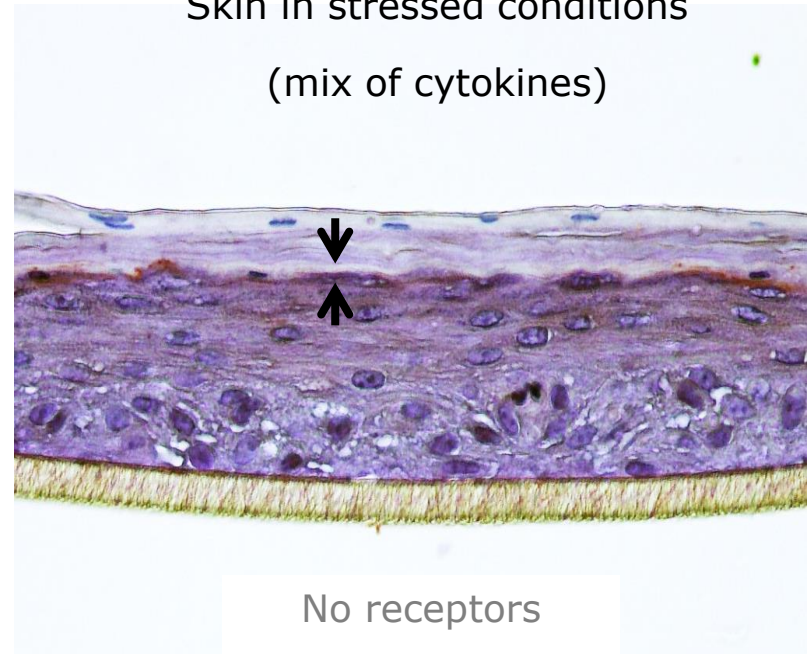
Visualisation of Delta Opioid Receptors in Skin

Skin in normal conditions



Visible receptors (D.O.R) (**red line**)

Skin in stressed conditions
(mix of cytokines)

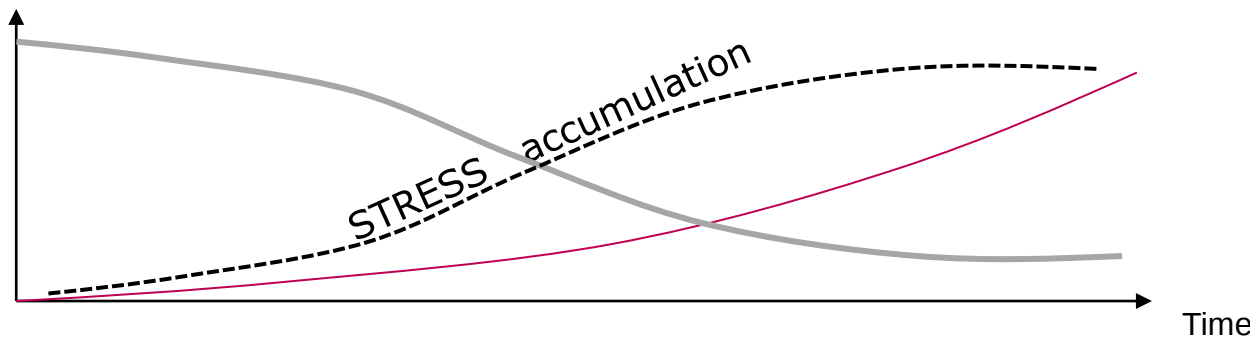


No receptors

DOR are important For the beauty of the skin

Delta opioid receptors, so called “Beauty Receptors” have been shown to directly control the beauty of our skin*.

These receptors are needed to maintain the normal differentiation process in skin.



VISIBLE SIGNS OF AGEING



LOWER AMOUNT OF
“BEAUTY RECEPTORS”

(*) Bigliardi et al. 2006.

Stress



“Beauty Receptors” Disappearance



Premature Ageing

We control stress by
maintaining the “Beauty
Receptors” in stress
conditions

Rubixyl®

The first molecule acting on “Beauty Receptors”

A **revolutionary active molecule** inspired from **nature**.

Rubixyl®, can act on these receptors to **reverse signs of stress induced ageing**.



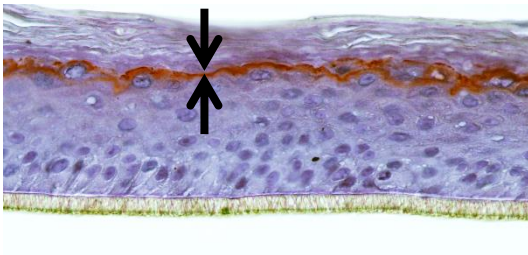
- ❖ Several years of **fundamental research**
- ❖ A **big bang** in the anti-ageing world
- ❖ A discovery arising **from pharma researches**
- ❖ A **worldwide patented** discovery

Rubixyl®

Efficient even in stressed conditions

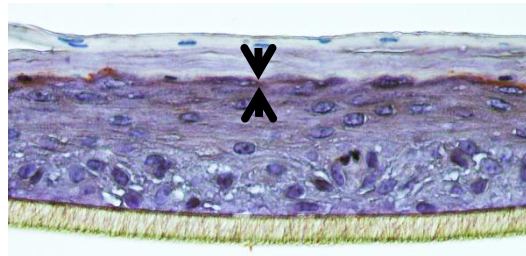
Visualisation of skin Beauty Receptors

Skin in **normal** conditions



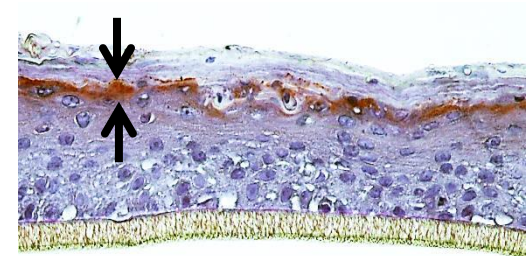
Beauty receptors (**red line**)

Skin in **ageing** conditions



No Beauty receptors

Skin in **stressed** conditions with Rubixyl®



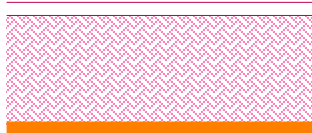
Beauty receptors again

Genetic profiling on stressed skin

Gene array profiling protocol

Reconstructing epidermis

Normal conditions



24H in culture medium

24H in culture medium

Stressed (ageing) conditions



24H in culture medium

24H induction with **cytokines**

(IL-17 + OSM + TNF-α) at 3 ng/ml

Stressed conditions + Rubixyl®



24H in culture medium + 0.1% Rubixyl®

24H induction with **cytokines**

(IL-17 + OSM + TNF-α) at 3 ng/ml

mRNA extraction

&

q-RT-PCR

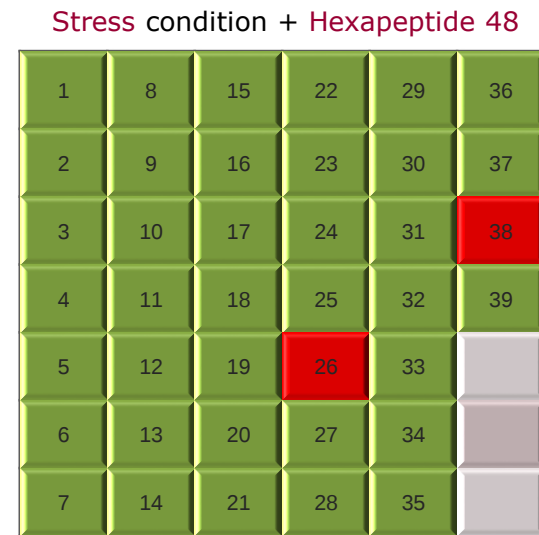


Calculation of the expression **level of each gene** versus reference genes and control conditions



Normalises genes in stressed skin

mRNA expression of 39 genes of human skin measured by q-RT-PCR on RHE treated with cytokines to simulate “inflamm-ageing”, with or without 0.1% of Rubixyl®



EXPRESSION LEVEL OF THE mRNAs

Low

Normal

High

(-50%)

(+50%)

Rubixyl® normalizes unbalanced genes in stressed skins

Evaluation on proteins expression in stressed skin

Protocol for the **immuno-detection of proteins** in skin

Reconstructing epidermis

Normal conditions



24H in culture medium

24H in culture medium

Stressed (ageing) conditions



24H in culture medium

24H induction with **cytokines**

(IL-17 + OSM + TNF-α) at 3 ng/ml

Stressed conditions + Rubixyl®



24H in culture medium + 0.1% Rubixyl®

24H induction with **cytokines**

(IL-17 + OSM + TNF-α) at 3 ng/ml

**Immunolabelling of
proteins**

and image analysis



Calculation of the expression **level of each PROTEIN** versus
reference conditions



Rubixyl®

Normalises key proteins for skin differentiation

Images of reconstructed human epidermis with or without Rubixyl®

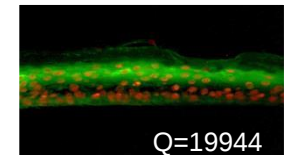
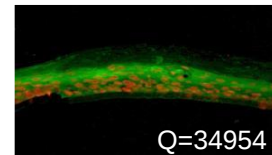
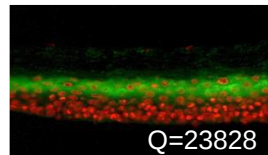
Normal conditions

Stressed with cytokine

Stress with cytokine
+ 1% Rubixyl®

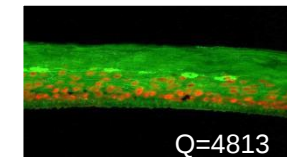
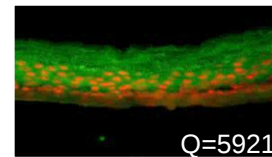
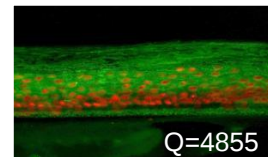
CORNEODESMOSIN

(green color)



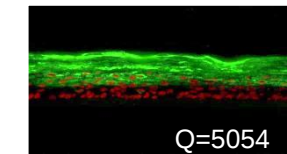
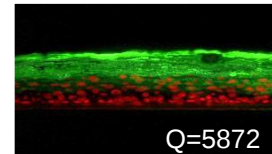
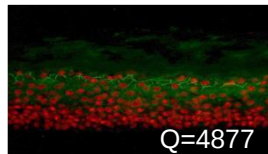
INVOLUCRIN

(green color)



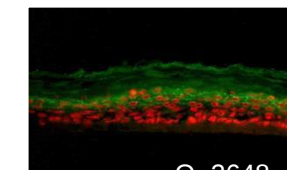
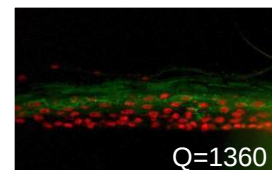
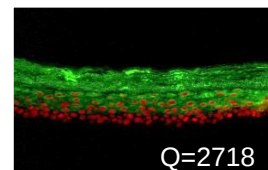
KERATIN-10

(green color)



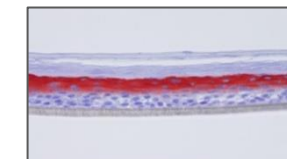
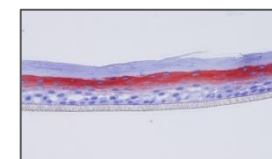
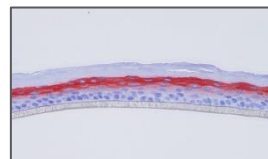
OCCLUDIN

(green color)



SULFOTRANSFERASE 2B

(red color)



Acts on key proteins for skin differentiation

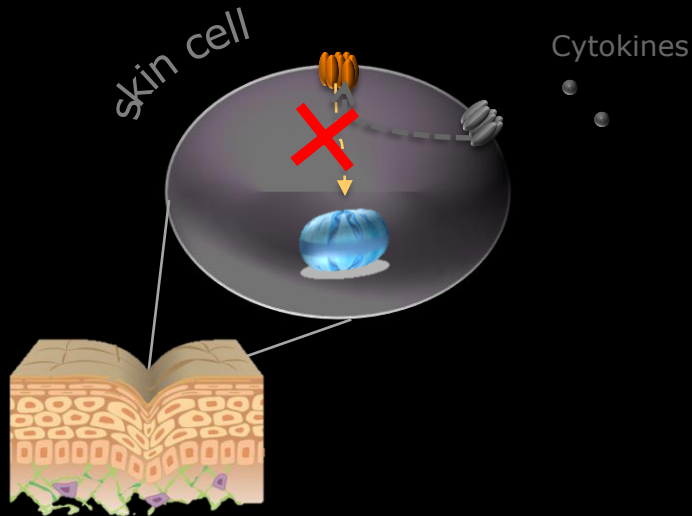
Protein expression quantification measured by **immunolabelling** on RHE treated with cytokines to simulate “inflamm-ageing”, with or without 1% of **Rubixyl®**

Proteins expression level in human epidermis (RHE)				
		Normal conditions	Stimulated conditions with cytokines	
Protein	Role in skin		No Rubixyl®	1% Rubixyl®
Corneodesmosin	Barrier function (adh. Junc. & corneocytes)	100%	147 % 	84 %
Involucrin	Barrier function (kerat. Diff. & cornified envelope)	100%	122 % 	99 %
Occludin	Homeostasis (tight junctions)	100%	50 % 	97 %
Keratin 10	Robustness (kerat. Diff. & epidermis integrity)	100%	120 % 	104 %
Sulfotransferase 2B	Lipids synthesis (cholesterol sulfate)	100%	200 % 	100 %

Rubixyl® equalises the expression level of key proteins in stressed skin

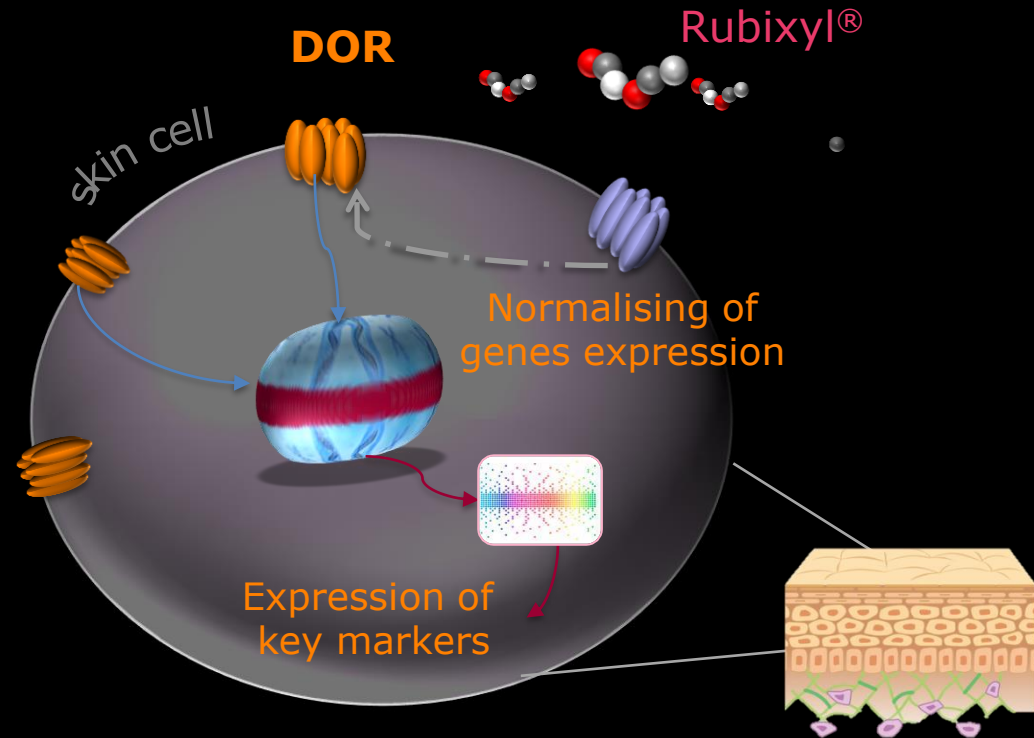
Rubixyl®

Suggested mode of action



Stressed situation ("Stress-ageing")

- Increased level of cytokines
- Lower expression of DOR
- Lower differentiation of cells
- Visible signs of ageing



Reverse stress situation

Rubixyl® upholds DOR

- Higher level of skin cells differentiation markers
- Reinforcement of skin barrier
- Reduction of signs of ageing

Clinical assessment



Rubixyl®

Clinical study #1

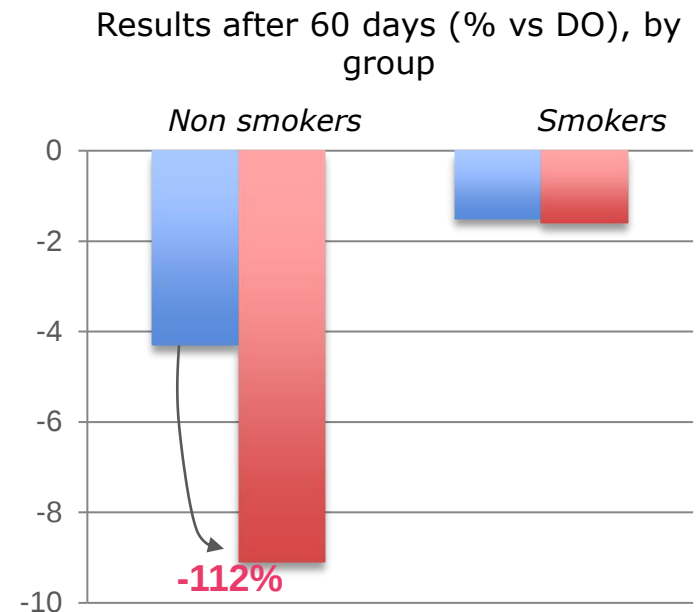
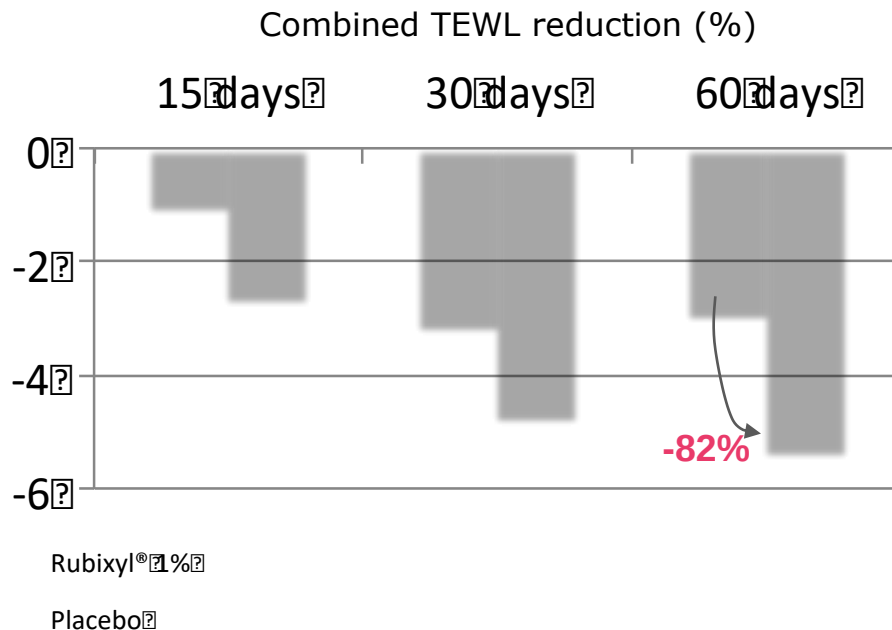
Protocol:

- ❖ **Double blind clinical trial** versus a placebo
- ❖ 20 urban **women aged between 40-65**
- ❖ **50%** of them **being smokers** (stressed skin)
- ❖ Applied twice a day either a placebo cream on one side of their face or a **cream containing 1% of Rubixyl®** on the other side.
- ❖ Clinical study was performed under the **control of a dermatologist.**



Reduces TEWL in mature and stressed skins

Trans-epidermal water loss (TEWL) was measured by Tewameter® after 15 days, 30 days and 60 days of use of the creams.



❖ **Improvement of TEWL** within 15 days

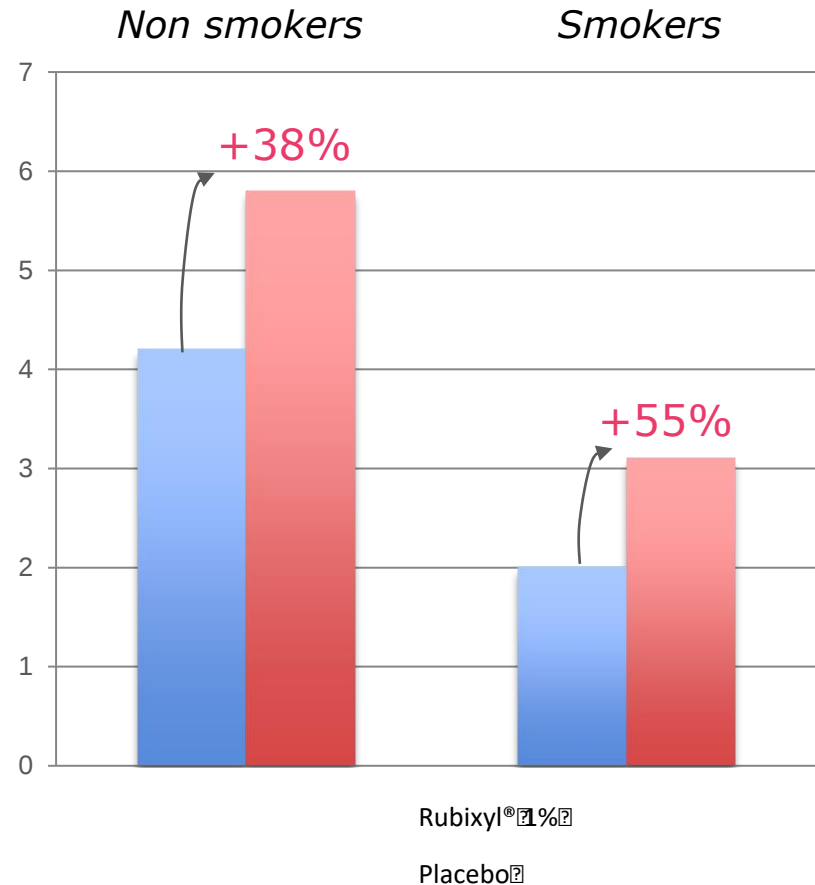
❖ **82% reduction of dehydration** in 60 days: -112% for non smokers

Rubixyl®

Increases hydration in mature and stressed skins

Hydration was measured by Corneometry **after 60 days of use** of the creams.

❖ **Hydration is increased by +38%** for non smokers and by **+55%** for smokers



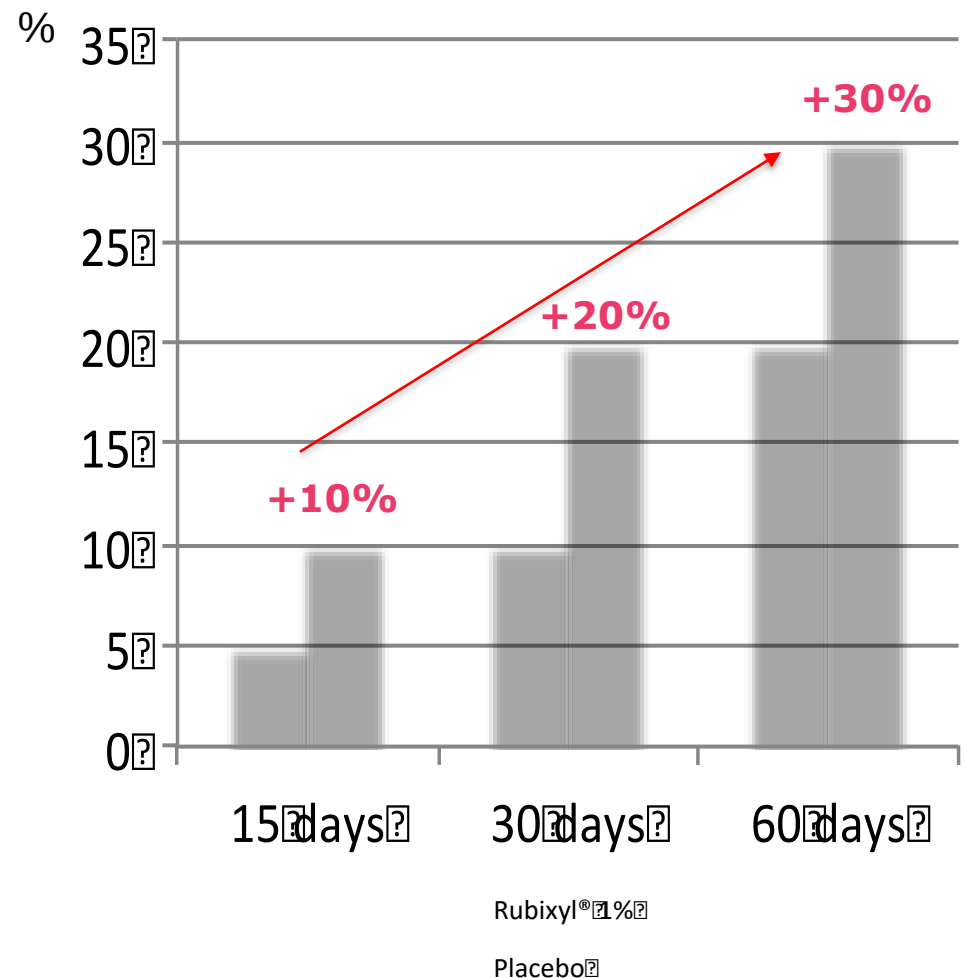
Rubixyl®

Improves skin smoothness (“bio-lifting” effect)

Clinical evaluation by dermatologist of **skin wrinkledness** after 15 days, 30 days and 60 days of use of the creams.

❖ **Visible improvement** of skin within 15 days

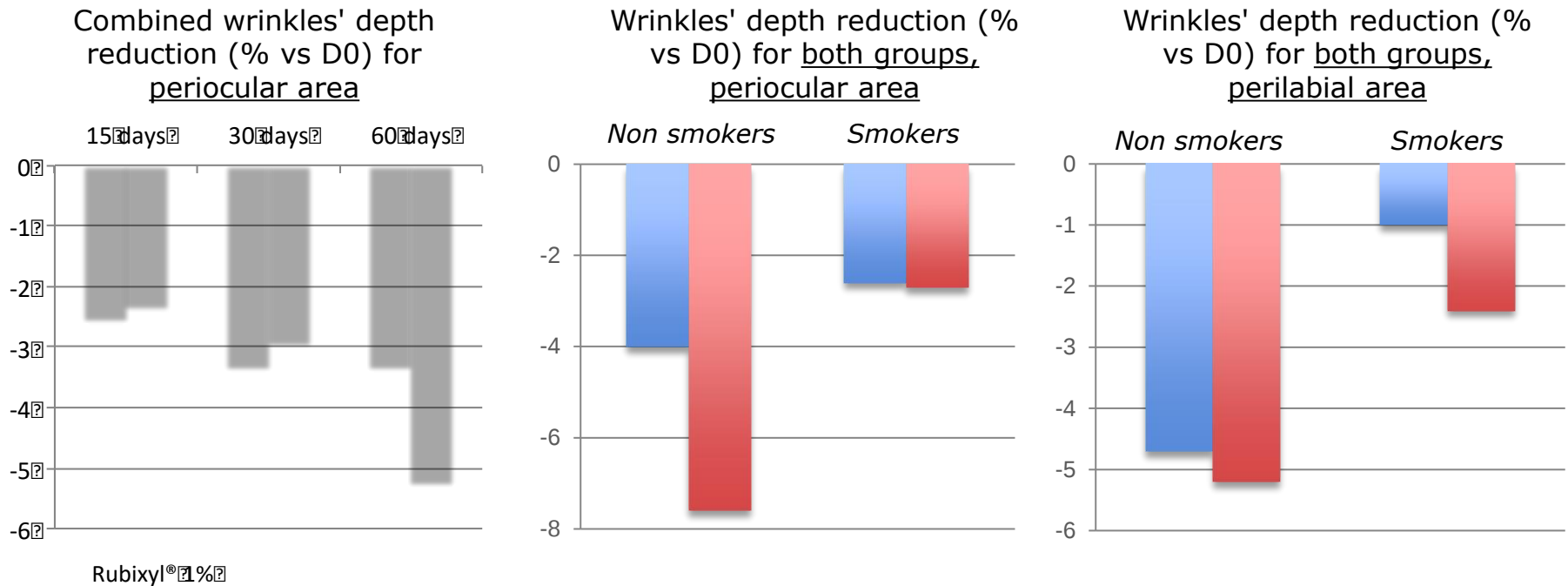
❖ **30% increase of smoothness** in 60 days



Rubixyl®

Shows a cumulative effect to refill deep wrinkles

Wrinkles depth assessed on volunteers by Primos 3D after 15 days, 30 days and 60 days of treatment with Rubixyl® or a placebo.



Rubixyl® 71%

Placebo

❖ **58% reduction of wrinkles depth** in 60 days

❖ **90% reduction** for non smokers on the periocular area
and **-140%** for smokers on the perilabial area

Rubixyl®

Reduces crows' feet wrinkles

Crows' feet pictures on a 56 years old woman after 60 days of treatment with **Rubixyl®** or a placebo

❖ **Reduction of fine lines, deep wrinkles and texture**

❖ **No visible effect of placebo** on Crows' feet

Day 0



After 60 days



Placebo day 0



Placebo after 60 days



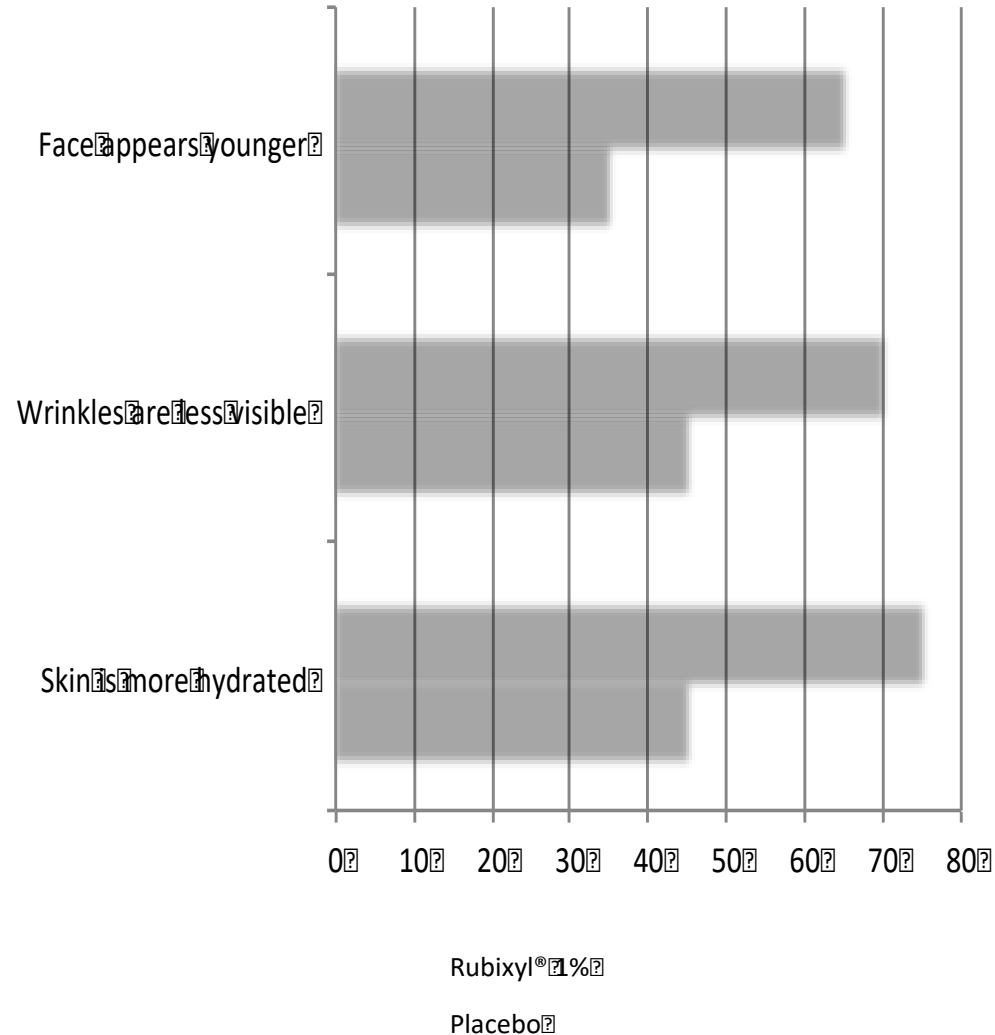
Rubixyl®

Self assessment by volunteers

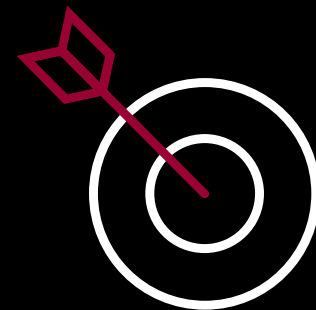
Auto evaluation by volunteers after 60 days of treatment with Rubixyl® or a placebo.

❖ **Volunteers see the difference** within 2 months

❖ **Placebo cream remains far behind**



Summary



Rubixyl®

Acts like a Beauty Equaliser

Rubixyl® turns back the noise of ageing into the melody of youth

- ❖ It equalises **back to a normal level 80% of genes** that are unbalanced upon stress
- ❖ **It stimulates** the overall **activity of cells**
- ❖ **It reactivates the normal evolution process of skin** as it happens in a young skin



A Scientific Breakthrough with Visible Clinical Results

Stress is no more a matter of concern : you can reactivate the molecular key of your beauty

- ❖ Deep wrinkles disappear: **-58% of wrinkles depth** reduction
- ❖ Skin looks younger: **+30% improvement of skin smoothness** in 2 months, with visible results in 2 week
- ❖ Skin is more hydrated: **+42% after 2 months**, and already **+20% after 15 days**



Rubixyl®

Main claims

1. Beauty Equaliser
2. Youth Active Philosophy
3. Constant Beauty
4. Beauty control
5. Stressless Beauty



Technical information

INCI

Water (and) Glycerin (and)
Hexapeptide 48-HCL

Origin

Synthesis

Preservation

Preservative free

Appearance

Clear, transparent liquid

Solubility

Water soluble

Dosage

0.1% to 2%

Processing

Can be incorporated in any formula in
liquid form at pH between 5 and 8 and
temperature below 45°C

Compliance

Thank you

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