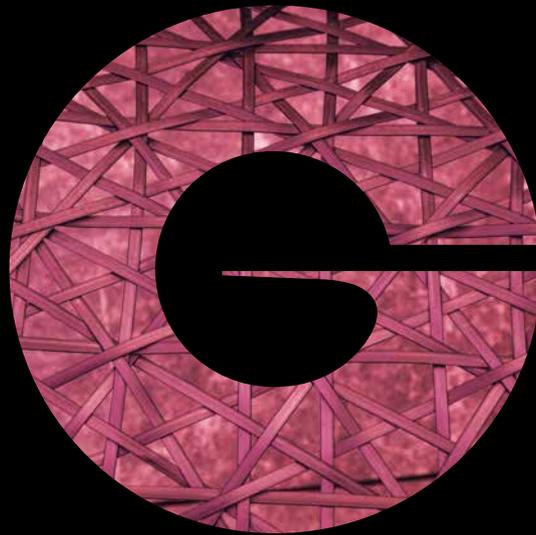


Active Beauty
Rubixyl[®]
Anti stress-ageing peptide

Crafted by synthesis



Focus on the product

The skin barrier function

The most crucial part of the skin barrier functions is the *stratum corneum*. The *stratum corneum* consists of corneocytes surrounded by a neutral lipid-enriched extracellular matrix.

The mechanical strength of the skin is provided in the corneocytes, which are encased by a cornified cell envelope. The hydrophobic extracellular lipid matrix provides a barrier against the movement of water and electrolytes.

Finally, the *stratum corneum* is involved in the regulation of water release from the organism into the atmosphere, known as transepidermal water loss (TEWL).

Stress and consequences on skin

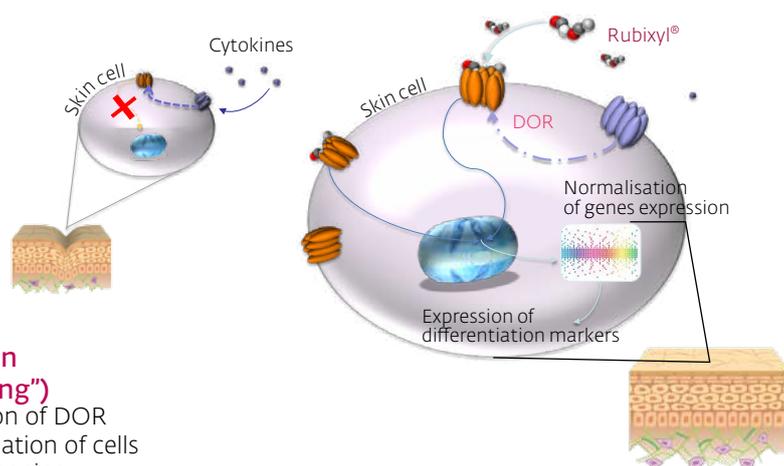
Psychological stress and chemical stress (pollution, smoke of cigarettes, chemical agents, oxidative stress, etc.) are known to have a negative effect on skin leading to epidermal permeability and skin barrier deficiencies. These skin issues, leading to an acceleration of skin ageing called "stress-ageing", are always associated with production of inflammatory molecules such as cytokines.

At the cellular level, delta opioid receptors (DOR) are essential in the maintenance of proper epidermis differentiation. Stress-ageing leads to a decrease of DOR expression due to their internalisation. As a consequence of DOR internalisation, the epidermis differentiation process and the skin barrier function are disrupted therefore accelerating the classical ageing process further.

Rubixyl®: the unique anti-stress peptide acting on DOR

Rubixyl® is a naturally derived neuro-calming peptide acting on opioid receptors, which was discovered from the hydrolysis of plant proteins. This unique bio-peptide upholds DOR to maintain their level of expression in skin cells, which enables reactivation of skin cell differentiation markers, and thus reverses signs of stress-ageing.

Rubixyl® shows high clinical efficiency within 2 to 8 weeks: a visible reduction of deep wrinkles and an improvement of skin smoothness on both smokers and non-smokers.



Ageing situation ("inflamm-aging")

- ▶ Lower expression of DOR
- ▶ Lower differentiation of cells
- ▶ Visible signs of ageing

Reverse ageing situation

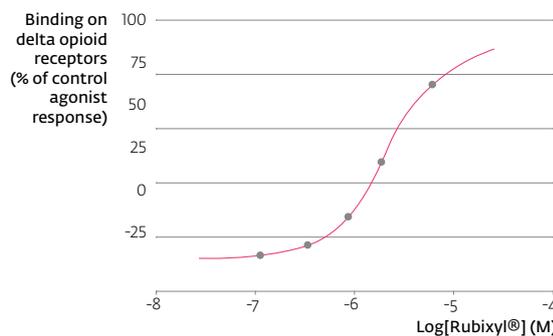
- Rubixyl® upholds DOR
- ▶ Higher level of skin cells differentiation markers
- ▶ Reinforcement of skin barrier and reduction of wrinkles

Biological activity

Dose dependent increase of fibroblasts viability (*in vitro* tests)

Rubixyl® was tested on specific cells expressing DOR, in order to confirm the agonist potential of the peptide. Rubixyl® was also tested on other cells expressing other types of receptors to check the specificity of the agonist effect of the peptide.

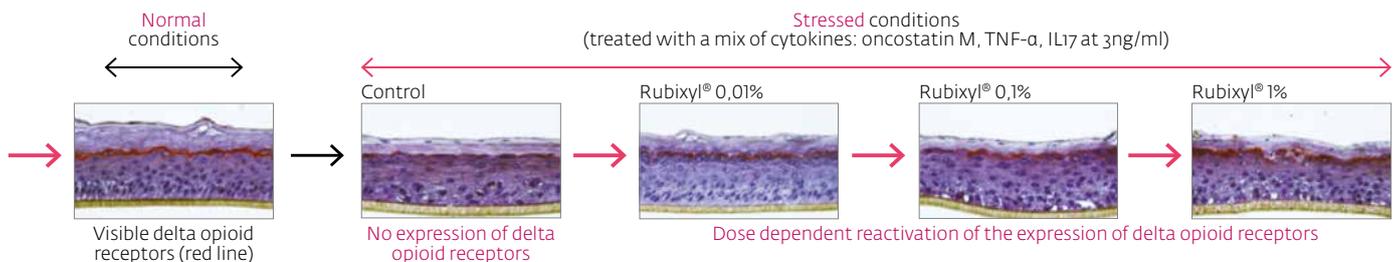
Results: Rubixyl® is a DOR agonist and is specific.



Receptor type	Agonist Effect
4 melanocortin receptors	Non agonist
5 adrenergic receptors	Non agonist
2 dopaminergic receptors	Non agonist
2 histamin receptors	Non agonist
5 muscarinic receptors	Non agonist
1 tachykinin receptors	Non agonist
7 serotonergic receptors	Non agonist
K and M opioid receptors	Non agonist

Reactivation of DOR (*ex vivo* tests)

The action of Rubixyl® on DOR was evaluated on reconstructed human epidermis (RHE), placed in simulated stress-ageing conditions (incubation with a mix of interleukin-17, TNF-α and oncostatin M to stimulate micro-inflammation). DOR receptors were detected by immuno-labelling (red color near the arrow).

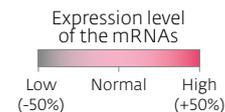


Results: Rubixyl® counteracts the effect of stress and restores an efficient expression of DOR in human epidermis.

Regulation of skin differentiation markers under stress (*ex vivo* tests)

The level of mRNA expression of 39 genes of human skin was measured by qRT-PCR on RHE treated with cytokines to stimulate a stress-ageing environment, with or without 0.1% of Rubixyl®. The same experiment was performed on reconstructed human epidermis with 1% of Rubixyl® on a set of key specific skin differentiation protein markers by immuno-labelling.

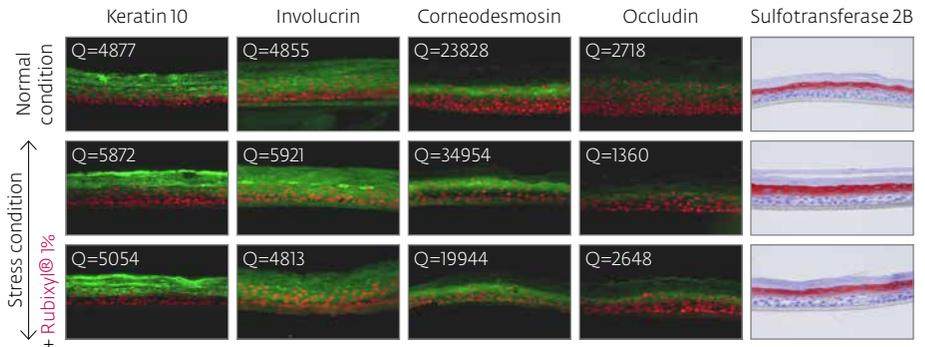
Results: Rubixyl® acts as an equaliser of the stress-ageing processes. It normalises 100% of the unbalanced genes that are age de-regulated under the influence of cytokines.



Stress condition mRNA expression profile							Stress condition + Rubixyl® 0.1% mRNA expression profile						
1	8	15	22	29	36	1	8	15	22	29	36		
2	9	16	23	30	37	2	9	16	23	30	37		
3	10	17	24	31	38	3	10	17	24	31	38		
4	11	18	25	32	39	4	11	18	25	32	39		
5	12	19	26	33		5	12	19	26	33			
6	13	20	27	34		6	13	20	27	34			
7	14	21	28	35		7	14	21	28	35			

Biological activity

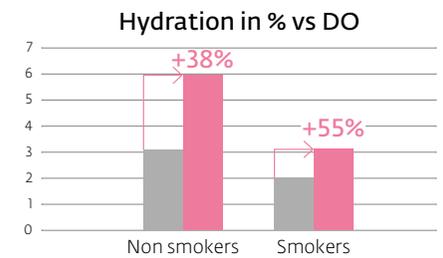
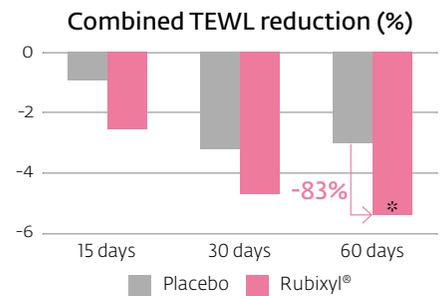
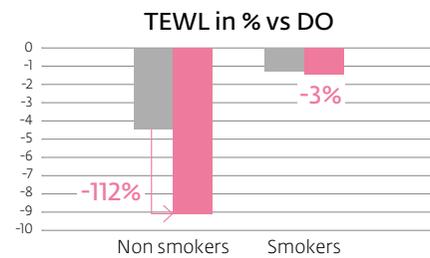
Results: Rubixyl® at 1% gives outstanding results at equalising 5 key proteins expression (involved in epidermis integrity) under stress conditions.



Significant improvement of skin barrier function on smokers / non smokers (clinical)

The efficiency of Rubixyl® was evaluated during a double-blind clinical trial versus a placebo. 20 urban women aged between 40-65 participated in the study. Of the participants, 50% of them were smokers. Twice a day, a placebo cream was applied on one side of the face and a cream containing 1% Rubixyl® was applied on the other side of the face. This clinical study was performed under the control of a dermatologist. Trans-epidermal water loss (TEWL) was measured by a Tewameter® and hydration by using a corneometer, both after 15 days, 30 days and 60 days.

Results: Rubixyl® improves the TEWL within 15 days with an 82% reduction of dehydration in 60 days: -112% for non smokers. Hydration is increased by +38% for non smokers and by +55% for smokers after two months.



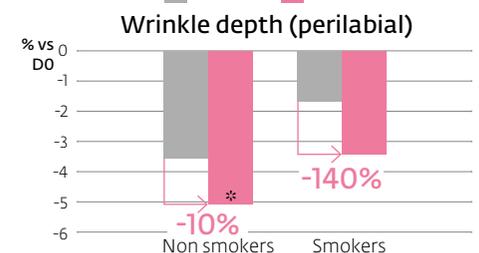
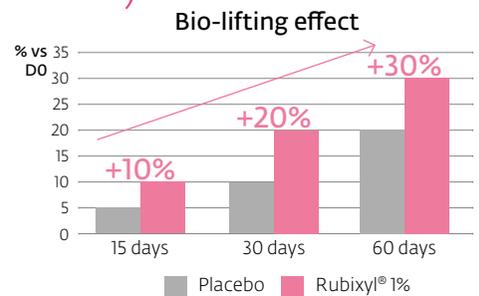
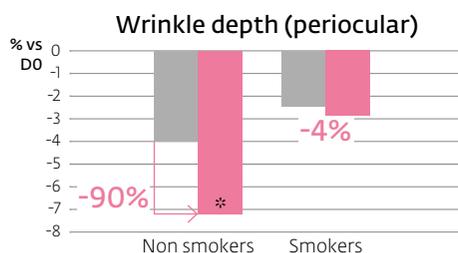
After 2 months

*p<0.05 Student's t Test

Smokers / non-smokers wrinkles reduction (clinical)

Wrinkles depth around the eyes and lips was quantitatively assessed on volunteers by Primos 3D after 15 days, 30 days and 60 days of treatment with Rubixyl® at 1% versus placebo on both smokers and non smokers. In parallel, a clinical evaluation was done by a dermatologist according to a standardised clinical scoring table.

Results: The use of Rubixyl(tm) at 1% results in a visible reduction of wrinkles within 60 days. The dermatological evaluation revealed a continuous bio-lifting effect.



After 2 months

*p<0.05 Student's t Test

Summary

Technical information

INCI:	Water (and) Glycerin (and) Hexapeptide 48 HCL
Origin:	Organic synthesis
Preservation:	Preservative free
Appearance:	Clear solution
Solubility:	Water soluble
Dosage:	0.1-2%
Storage:	Store at room temperature under 25°C.
Processing:	Can be added at the end of the formulation process under stirring or homogenising. Can be heated for a limited period of time. Formulate at pH 3.0 to 7.0 and temperature below 45°C.

Claims

Claims:	Protects from stress, Normalises skin barrier, restructures mature skins, smoothes skin surface, refills deep wrinkles.
Applications:	Anti-stress products, eye care products, products for the treatment of expression lines, anti-ageing products, face care products for mature skins, neck care products, restructuring body care, protection from daily aggressions.

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