

# RETYL®

**A promising marine active to boost retinol metabolism**

**A powerhouse of outstanding anti-ageing benefits**



**BLUE INGENUITY**

GELYMA has developed a seaweed alternative to retinol named RETYL® based on the stimulation of retinol metabolism at several levels, leading to remarkable performances against ageing effects.

RETYL® can provide the same positive results against skin ageing than those obtained with retinoids but without the disadvantages.

## What is RETYL® ?

RETYL® combines 1,3 propanediol (COSMOS grade) with a selective fraction, carefully calibrated of the brown alga *Padina pavonica*, sustainable sourced in Natura 2000 areas of the Mediterranean Sea.

## How does RETYL® work to bring skin benefits?

The skin requires an appropriate supply of retinoid acid to support normal structure and function, with intracellular levels tightly regulated through numerous signaling pathways.

RETYL® upregulates significantly numerous retinoid binding and metabolizing genes at both level cytosol and nucleus, exhibiting a similar activity of retinol and bakuchiol on certain key genes, especially the major actor CRABP2, the enzyme CYP 1 and two important nuclear receptors RARB and RARG.

RETYL® also vitalizes the functionality of the epidermis at different levels (desquamation, keratinization and keratinocyte differentiation) to fortify normal epidermal development and barrier function. It improves cell proliferation that encourages new cell renewal for a plumpness skin.

Clinical evaluation has been performed on 19 Caucasian female aged 40-70 years with healthy skin and visible signs of ageing. Volunteers applied on face a cream with 3% RETYL once daily at night for a period of 60 day. After this trial, the results showed significant Improvements of skin firmness and elasticity, increase of dermis density, reduction of wrinkle depth and clearing up of skin tone.

Although the chemical structure of RETYL® bears zero resemblance to retinol and bakuchiol, a similar multidirectional mode of activity is applied to minimize the signs of facial ageing and revitalize the skin for a younger looking skin.

## Why to choose RETYL®?

- A marine natural retinol alternative.
- Algal sustainable sourced from the Mediterranean Sea.
- Smart mechanisms of action to boost several steps of retinol metabolism at levels cytosol and nucleus like bakuchiol.
- Multi-targeted anti-ageing advantages.
- Stability to UVA/UVB and temperature exposures as well as in cosmetic formulation, therefore bringing the benefits of retinoids without the applications disadvantages.
- Suitable for all kinds of skin.

RETYL® allows new opportunity for retinol alternative skin care to improve skin anti-ageing qualities without the drawbacks.

# EFFICACY POTENCY : transcriptomic and *ex vivo* studies

## RETYL® ACTIVATES RESPONSIVE EPIDERMAL GENES RELEVANT TO RETINOL FUNCTIONALITY

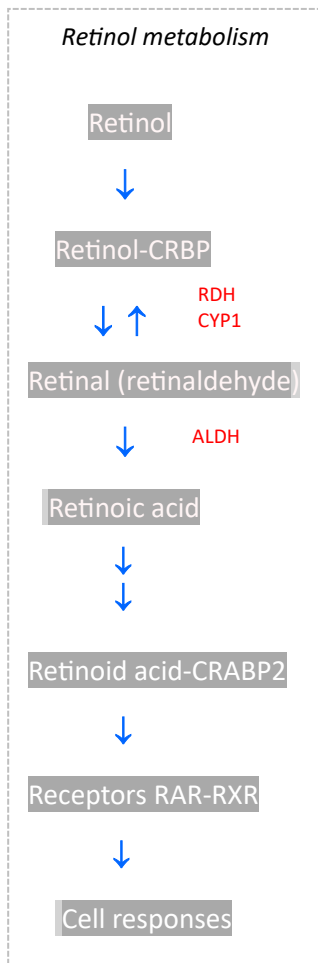
### 1 a- Stimulation of key markers linked to retinol metabolism

#### Method

Transcriptomic study of skin markers on normal human keratinocytes. Tested dose: 3%. Significant values with \*P<0.05 - \*\* p < 0.01 - \*\*\* p<0.001.

#### Results

RETYL® activates key genes involved in the retinol metabolism, at both levels cytosol and nucleus.



#### Cytosol level

Major enzymes of retinoic acid metabolism			
Gene	FC	Comparisons FC *	
RDH16	1.73 ***		
ALDH1A3	3.50 ***		
ALDH3B2	3.07 ***		
CYP1A1	4.03 ***	Retinol :4.0	Bakuchiol :4.9
CYP1B1	2.29 ***		
CYP1A2	1.33 *	Retinol :3.6	Bakuchiol :6.7
Major actor			
CRABP2	21.45 ***	Retinol :NS	Bakuchiol :4.1

RETYL® increases significantly the expression of numerous retinoid binding and metabolizing genes, in particular:

- ▶ several enzymes implicated in the oxidative conversion of retinol to retinaldehyde (RDH- ALDH- CYP1),
- ▶ le major actor CRABP2 indispensable to deliver retinoic acid to nuclear receptors,
- ▶ specific nuclear receptors RARs essential to mediate cell responses for fighting and reversing signs of ageing.

#### Nucleus level

Retinoic acid receptors			
Gene	FC	Retinol	Bakuchiol
RARG	1,97 ***	:1.8	:NS
RAET1L	1,93 ***		
RARRES3	1,60 ***		
RORA	1,60 **		
RORC	1,50 ***		
RBP2	1,47 **		
NCOA7	1.41 **		
RARRES2	1,35 *		
RARB	1,27 *	Retinol :5.6	Bakuchiol :NS

RETYL® exhibits a similar activity of retinol and bakuchiol on certain key genes: the major actor CRBP2, the enzyme CYP 1 and two important nuclear receptors RARB, RARG.

\* From Chaudhuri RK, Bojanowski K. Bakuchiol 2014 *Int J Cosmet Sci.* 36(3):221-230.

### 1 b- Immunolabelling of CRABP2 in aged human skin explants

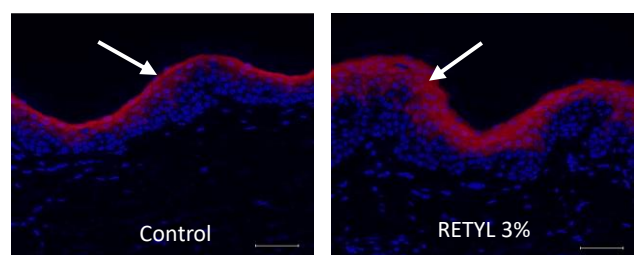
The expression of CRABP2 is reduced in human epidermis when ageing. (Bielli A. *et al.* (2019 AGING, Vol. 11, No. 6).

#### Method

Immunofluorescence labelling of CRABP2 on aged human skin explants . Tested dose : 3% .Treatment for 7 days.

#### Results

RETYL® at 3% enhances the expression of CRABP2 in aged human explants compared to untreated control, therefore RETYL® helps to fight skin ageing.



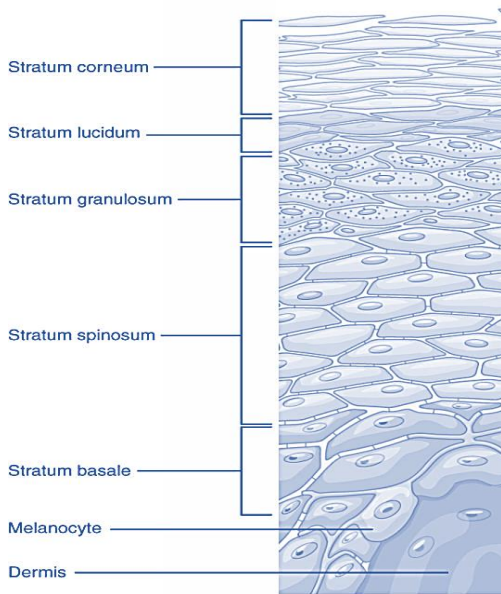
# RETYL® REVITALIZES THE FUNCTIONALITY OF THE EPIDERMIS

RETYL® can increase and enhance the epidermal functionality at different levels (desquamation- keratinization- keratinocyte differentiation, cell proliferation) for maintaining healthy and youthful skin.

## Method

Transcriptomic study of skin markers on normal human keratinocytes. Tested dose: 3% . Significant values with \*P <0.05 - \*\* p < 0.01 - \*\*\* p<0.001.

## Results



### ACTIONS OF RETYL®

Desquamation ↑

By controlling the shedding of corneocytes, RETYL® maintains the ability of the epidermis to constantly renew itself and support homeostatic healthy skin.

Keratinization ↑

By tightly regulating keratin synthesis, RETYL® strengthens the mechanical stability and integrity of the epidermis. It also fights against cutaneous tissue fragility.

Keratinocyte differentiation ↑

RETYL® modulates keratinocyte differentiation, essential to provide normal epidermal development and efficient barrier function.

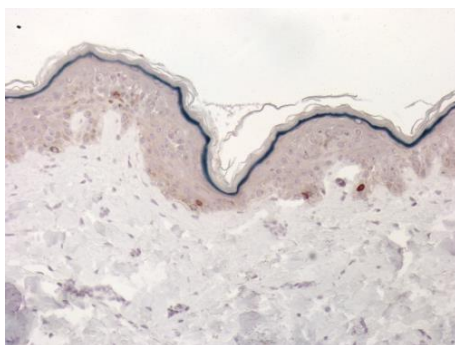
Cell proliferation ↑

## Methods

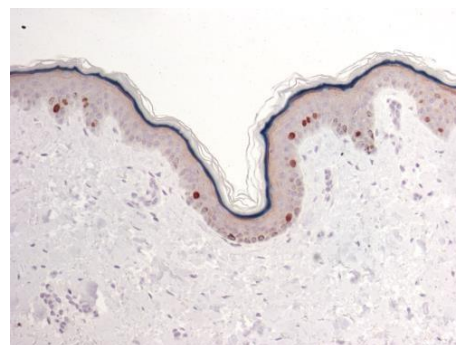
KI 67 staining on UV aged human explants Tested dose : 3%.

## Results

RETYL® at 3% increases by 67% the number of epidermal proliferating cells in photoaged human explants, therefore RETYL® supports cell renewal and repair processes like retinol.



Control UV



UV+ RETYL® 3%

X200

As retinoids, RETYL® helps to encourage new epidermal turnover, rejuvenate skin cells and restore thickness that has become thinner over time. As a result, the skin appears smoother and plumpness.

## CLINICAL EVALUATION

Clinical evaluation enrolled 19 female patients aged 40-70 years with healthy skin (40% dry, 5% normal and 55% mixte skin) and visible signs of ageing. Volunteers applied a cream with 3% RETYL® once daily at night for a period of 60 days. Observations done at D0 and D60 under dermatologist control.

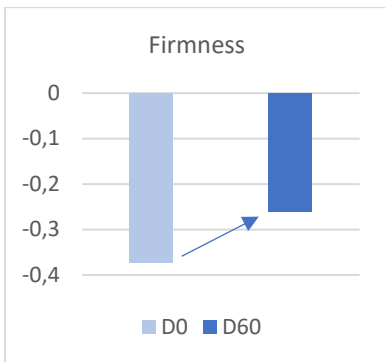
### RETYL® IMPROVES SKIN FIRMNESS AND ELASTICITY

As we age, skin becomes thinner and less elastic, leading to sagging and wrinkled appearance.

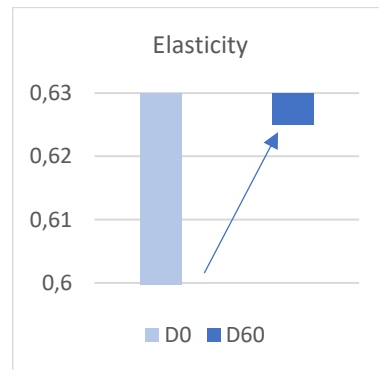
#### Method

Cutometry MPA 580, dual 2mm probe.

#### Results



↑ +30 %  
\*\*\*  
Increased firmness



↑ +11 %  
\*\*\*  
Increased elasticity

RETYL® raises significantly skin firmness and elasticity after a 60 days trial with a cream at 3% active. As a result, the skin appears firmer and more elastic with a smoother skin texture.

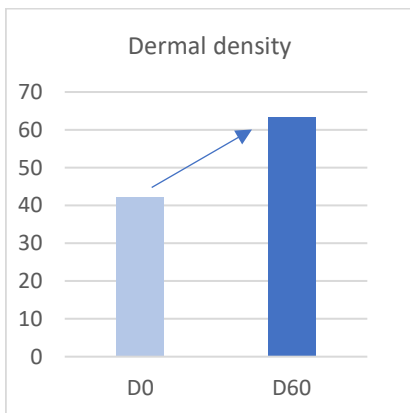
### RETYL® INCREASES DERMIS DENSITY

Dermis density is regarded as an important parameter to monitor skin regeneration.

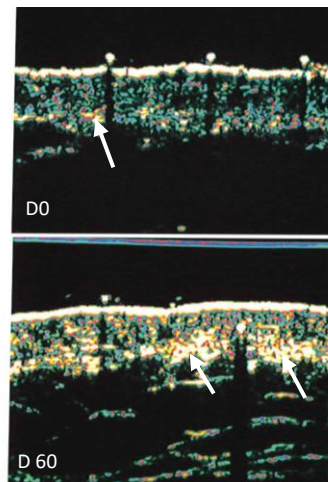
#### Method

Echography with sonde 2D.

#### Results



↑ +51 %  
\*\*\*  
Increased dermis density



Note the remarkable abundance of white dense structures in the dermis after a 60 days trial with 3% RETYL®

RETYL® increases dermis density by +51% after 60 days treatment, therefore RETYL® reinforces the extracellular matrix structure and firmness to safeguard the skin from further wrinkle development.

## RETYL® REDUCES THE CROW'S FEET WRINKLES

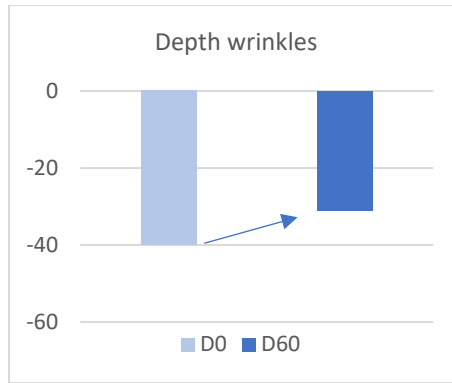
Wrinkles are a primary sign of skin ageing. They occur when the structural skin integrity is compromised.

### Method

Fringe projection and ID imaging.

### Results

↓ - 24 %  
\*\*\*  
Decreased wrinkles depth



RETYL® combats the appearance of fine lines at the crow's feet areas for a younger appearance.

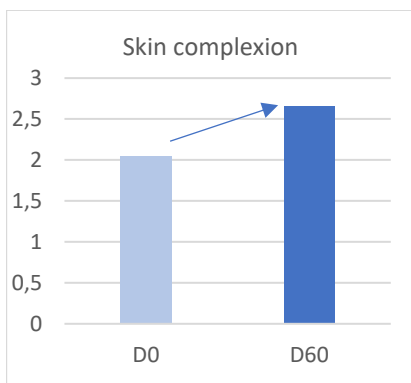
## RETYL® BRIGHTENS SKIN TONE AND REDUCES HYPERPIGMENTATION

Facial skin tone and luminosity are key indicators to the age perception of people past their maturity.

### Method

Evaluation of GREDECO scores by dermatologist.

### Results

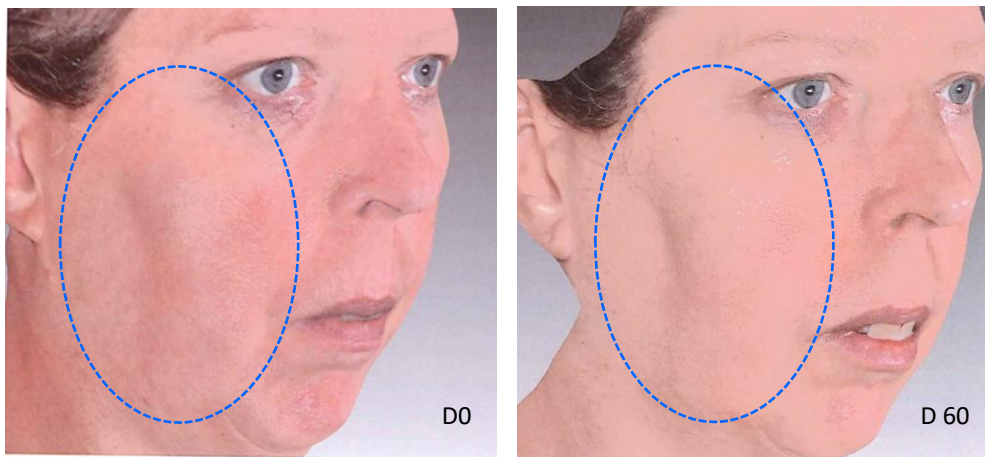


↑ +29 %  
\*\*\*  
Increased tone homogeneity

Age spots are caused mostly by over exposure to UV rays and become more evident in ageing skin.



RETYL® at 3% reduces visibly the size and color spots at the nose and the temple after a trial of 60 days, leading to improved skin tone.



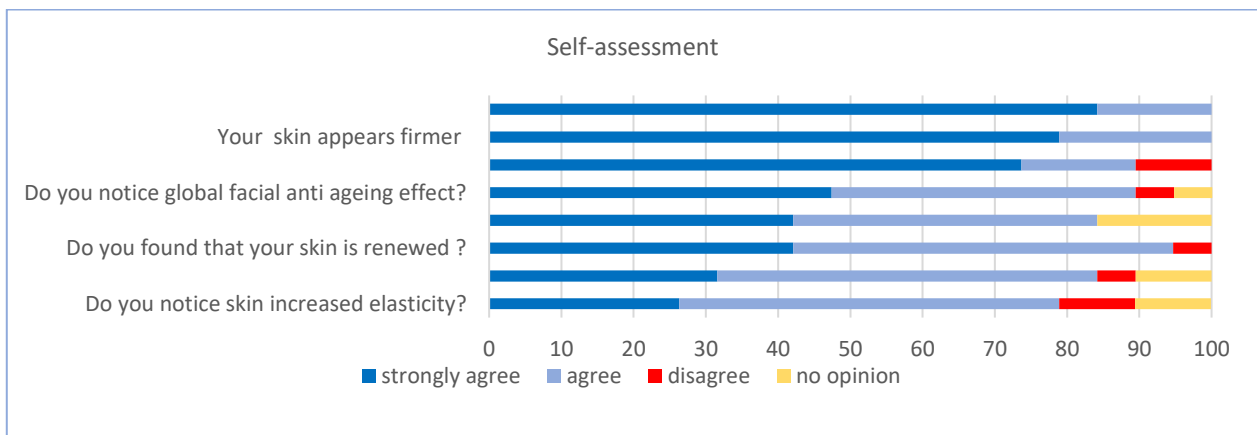
RETYL® at 3% enhances visibly skin complexion in reducing skin redness and skin irritation after a trial of 60 days.

With RETYL® dermatologically tested at 3%, overall skin clarity and appearance are enhanced for a healthier complexion. Unwanted or excess of hyperpigmentation and skin imperfections are reduced for a more even skin tone leading to a brighter complexion.

### CONSUMER ASSESSMENT

The volunteers confirmed these clinical results by their own assessment of the product effectiveness.

RETYL® offers retinol-like qualities without the harsh side effects such as sensitivity, irritation and dryness.



### Satisfaction rate

100% of volunteers agreed with a firmer and improved skin tone

## CONCLUSION AND COSMETIC BENEFITS

The cosmetics benefits of RETYL<sup>®</sup> has been revealed by gene expression profiling, *ex vivo* studies and clinically evaluation under dermatologist control.

These studies provide evidence that RETYL<sup>®</sup>, that having no structural resemblance to retinoids, can act as a functional analogue of retinol.

### RETYL<sup>®</sup>

- ▶ boosts and controls retinol metabolism to enhance and regulate the intracellular level of retinoic acid, by stimulating influential enzymes and the major actor CRABP2 as well as specific nuclear receptors in order to directly influence cell responses to anti-ageing processes,
- ▶ regulates epidermal functionality to reinforce the barrier function and stimulates cell proliferation (+ 67%) to support the process of skin cell turnover for a smoother skin,
- ▶ minimizes the signs of skin ageing, demonstrated in a 60 days trial, one application per day on face at night:



Skin firmness (+ 30%)  
Skin elasticity (+ 11%)



Dermis density  
(+ 51%)



Reduction of wrinkles  
depth (- 24%)



Clearing up of  
skin tone (+ 28%)



Taken together, these studies demonstrate the high potential of RETYL<sup>®</sup> to revitalize and rejuvenate aged skin for a more youthful appearance.

Due to its excellent stability profile to UV rays and temperature exposures as well as in cosmetic formulations, RETYL<sup>®</sup> provides natural exceptional opportunities to deliver the powerful anti-ageing properties, boosting all the good qualities of retinol without causing adverse effects, such as irritation, dryness and redness.

## CONCLUSION AND COSMETIC BENEFITS

RETYL<sup>®</sup> is safe and suitable for all skin types for face and body care for :

- advanced anti-ageing products
- skin firming products
- specific care for mature skins.

Recommended use levels : 3%

INCI : water (and) *Padina pavonica* thallus extract (and) propanediol.

Compliance



Morphology of *Padina pavonica*

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