Haloarchaea

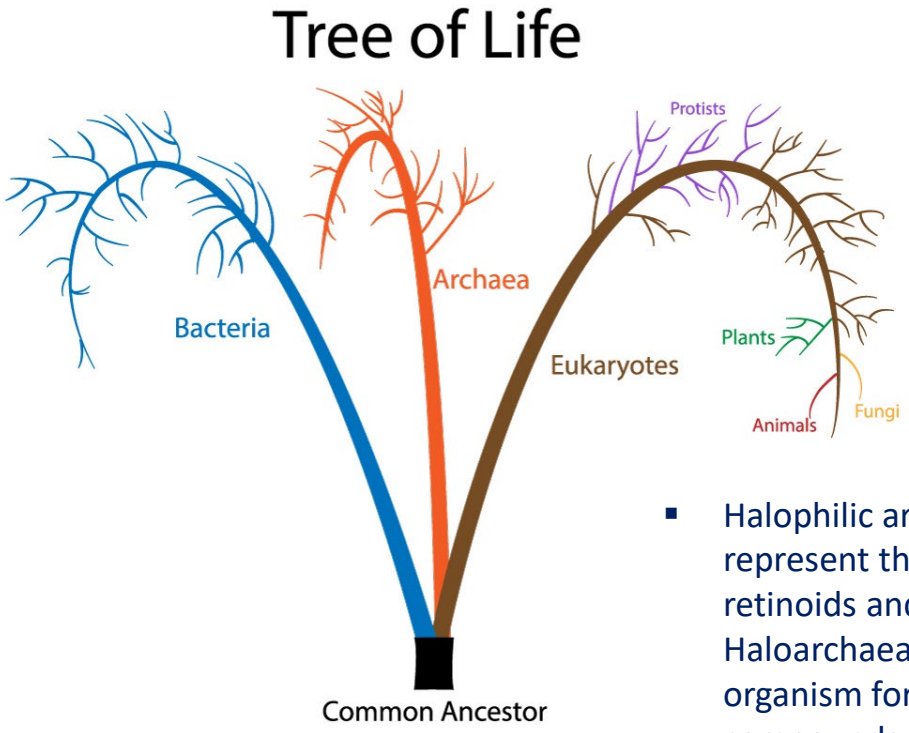
Retinaturel & Retinal O5

ADEKA
Add Goodness

ADEKA Europe GmbH

ADEKA: Origin of the Haloarchaea

- **The Archaea was recognized as a third domain of life 40 years ago. Molecular evidence soon suggested that the Eukarya represented a sister group to the Archaea or that eukaryotes descended from archaea.**

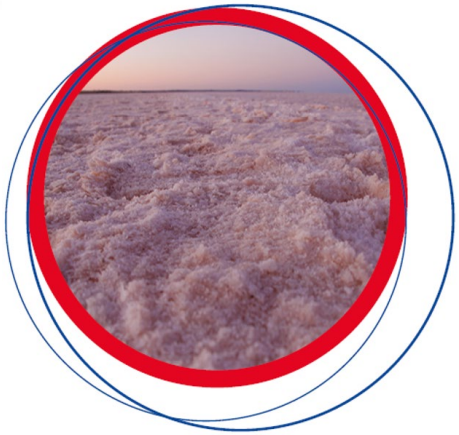


- Most biotechnology derived products are made from bacteria and yeast and fungi

- Halophilic archaea produce highly functional compounds and represent therefore a biotechnological source for carotenoids, retinoids and many more. The best characterized strain among Haloarchaea is called Halobacterium salinarum. This strain is an ideal organism for use in biotechnology as it can produce several different compounds in one process without any genetic modification.

ADEKA: Origin of the Haloarchaea & Benefits

- Haloarchaea : *Halobacterium salinarum*



- **Haloarchaea produces biomaterials to protect cells against extreme environmental factors**

RED-COLORED SALT LAKE
20 - 30 % salt content

High **UV light**

HALOARCHAEA ARE RESISTENT AGAINST STRONG UV LIGHT AND HEAT AND HIGH SALT CONCENTRATION

High **heat**

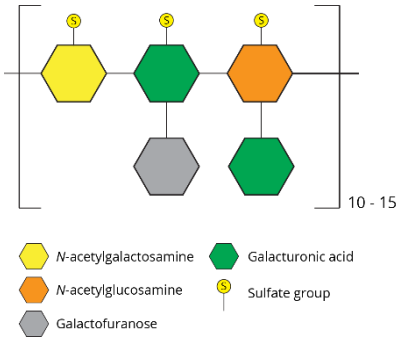
HALOARCHAEA LOVE SALT

High **salt concentration**

- *Halophilic bacteria and archaea are microorganisms that need high salt concentrations for their growth and found in saline waters and soils where other organisms cannot thrive. Interestingly, some of their products are more stable and show different properties in comparison to their non-halophilic counterparts, so it is not surprising that they have been drawing attentions towards them. Actually, halophiles provide a new natural source to manufacture ingredients with new functions and features for personal care products.*

ADEKA: Ingredients derived from Haloarchaea

N-GlycanS

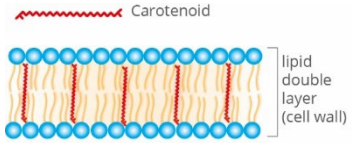


Sulfated sugar polymers

HALOCARE

Healthy skin, age defense

Carotenoids

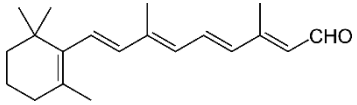


Nature's most effective Antioxidant for cell and DNA protection

HALORUBIN

Anti pollution, antioxidant DNA protection

Retinal

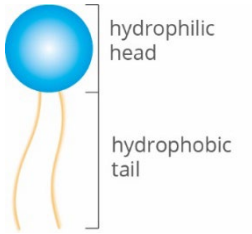


Natural Retinal (Vitamin A)

RETINATUREL & RETINAL O5

Age defense. Skin conditionning. Anti-acne, vitamin A

Lipids



Natural highly stable Phospho- and Glycolipids

Liposomes

Liporetine , Liporetine 05, Liporubin

Stable Liposomes, Support skin barrier

Expected launch 2023

COSME CERT COSMOS APPROVED

100 % Natural

VEGAN

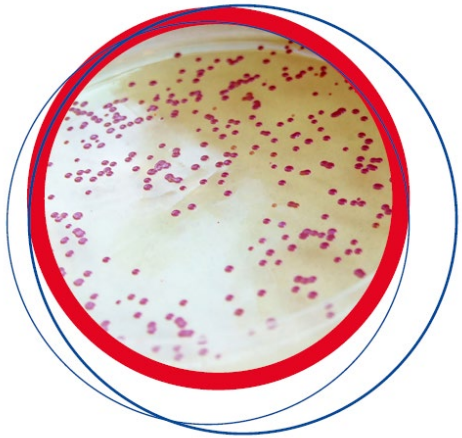
Non GMO

ADEKA: Retinaturel

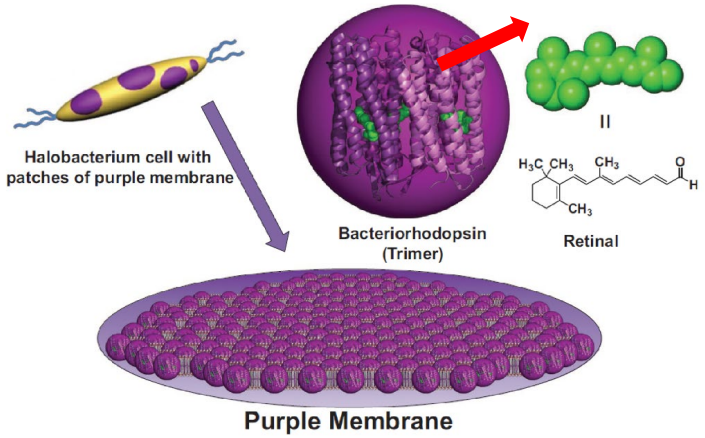
Retinaturel

ADEKA: What is Retinaturel

Halobacterium salinarum produce membrane-bound patches called Purple Membrane. Cells appear purple after incorporation of patches into the cell membrane.



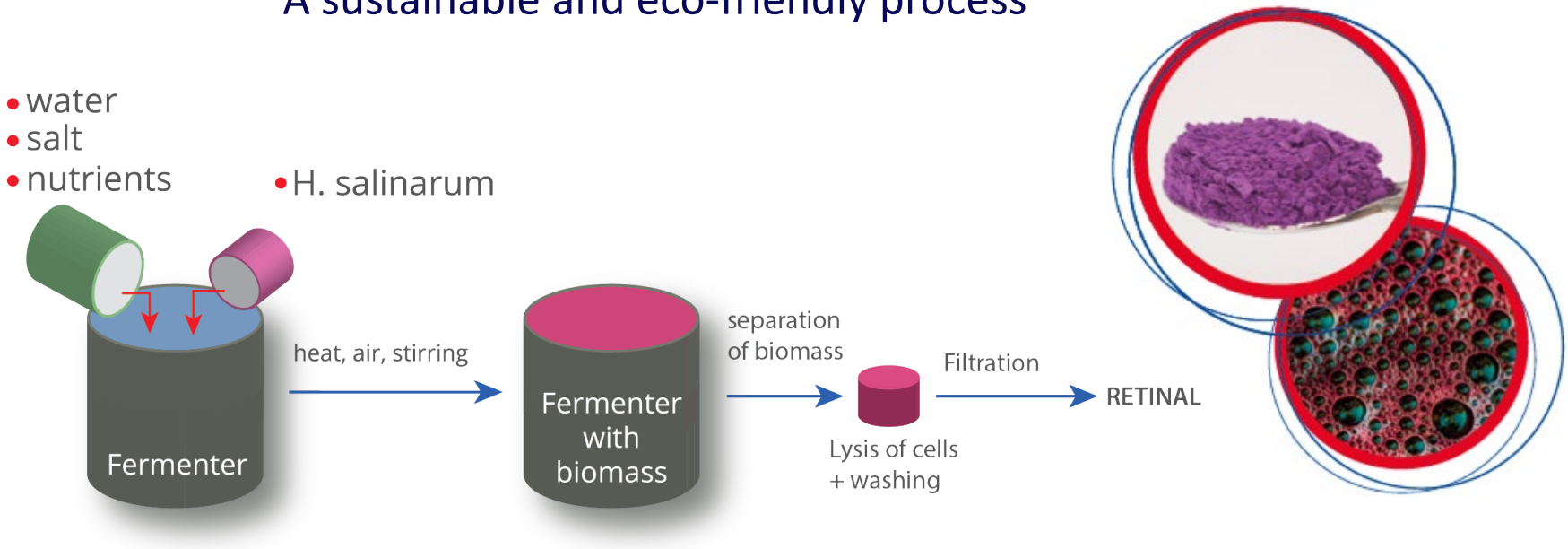
- *Halobacterium salinarum* produces "**Purple Membrane**"
- Purple Membrane one protein : **Bacteriorhodopsin**
- **Retinal is bound to Bacteriorhodopsin**



- Retinal is bound to Bacteriorhodopsin and can be isolated In a highly pure and stable form (< 98%).

ADEKA: Production of Retinaturel

A sustainable and eco-friendly process



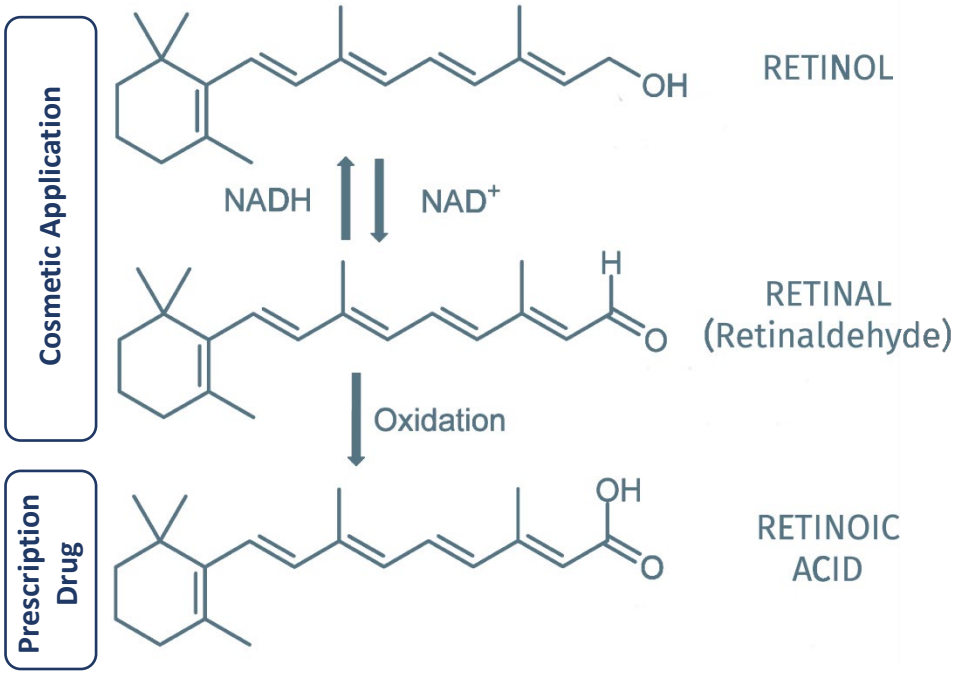
❑ Advantages of bioprocess Halobacterium Salinarium are:

- ➢ Non GMO production & eco-friendly
- ➢ Sustainable process (up to 50%re-used of growth medium)
- ➢ Suitable for Vegan
- ➢ Cosmos approved, Natural ISO16128
- ➢ Complete manufactured in Germany (low CO_2 Foot Print)

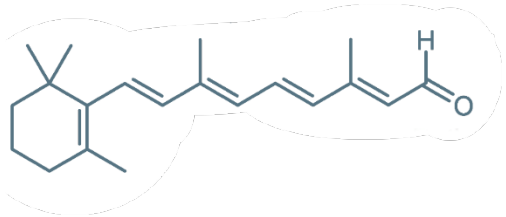
ADEKA: Pathway Retinal

The common chemical name Retinal is a retinoic acid precursor, which is formed as an intermediate metabolite in the transformation of retinol to retinoic acid in human keratinocytes. In the skin retinal is metabolized to retinoic acid (which is a well known anti-aging agent) as well as to retinol and retinylesters (which generally get depleted during photoaging),indicating its use in the treatment of photoaging.

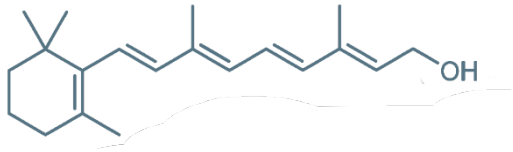
Moreover, metabolism of retinal to retinoic acid occurs only by keratinocytes at a pertinent stage of differentiation, leading to a more controlled delivery of retinoic acid and weaker retinoid associated adverse effects as compared to tretinoin and other synthetic retinoids



ADEKA: Retinal vs Retinol



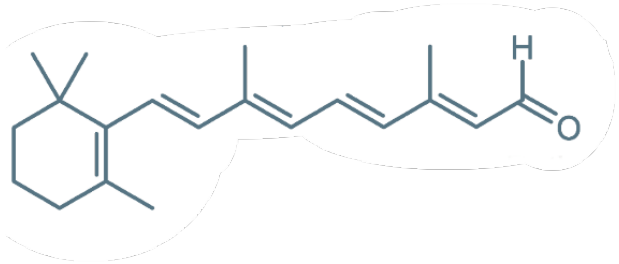
Retinal



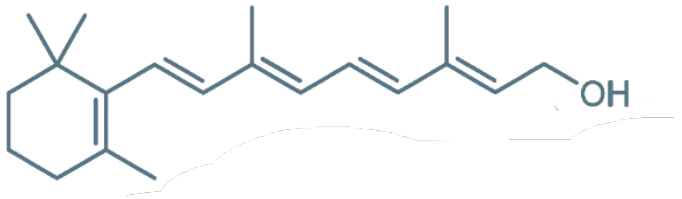
Retinol

- Key differences between Retin**al** and Retin**ol**
  - Retinal has antibacterial properties, making it perfect for oily or blemish-prone complexions
  - Retinol is 2 steps away from retinoic acid, whereas retinal is just the one
  - Retinal is as gentle on the skin as retinol
  - Both improve skin texture and tone
- ✓**Their main difference is the better tolerance profile among available retinoids**

ADEKA: Benefits of Retinal



Retinal



Retinol

Research has proven that Retinal is a useful topical agent for the treatment of aged and photoaged skin and in the treatment of acne and mild Rosacea.

It has been shown that it :

- ✓ increased skin elasticity
- ✓ protecting against free radical damage
- ✓ increase dermal thickness
- ✓ reduce the appearance of wrinkles and fine lines
- ✓ alleviate skin roughness
- ✓ decrease the level of skin hyperpigmentation
- ✓ reduce the occurrence of acne and improve signs of vascularization

ADEKA: Stability Retinaturel vs Retinol

The stability of Retinoids (15S Retinol, RETINATUREL) over a period of 12 months in a closed containment under elevated temperature were measured. Both products were stored in alumunium containers in the the dark.

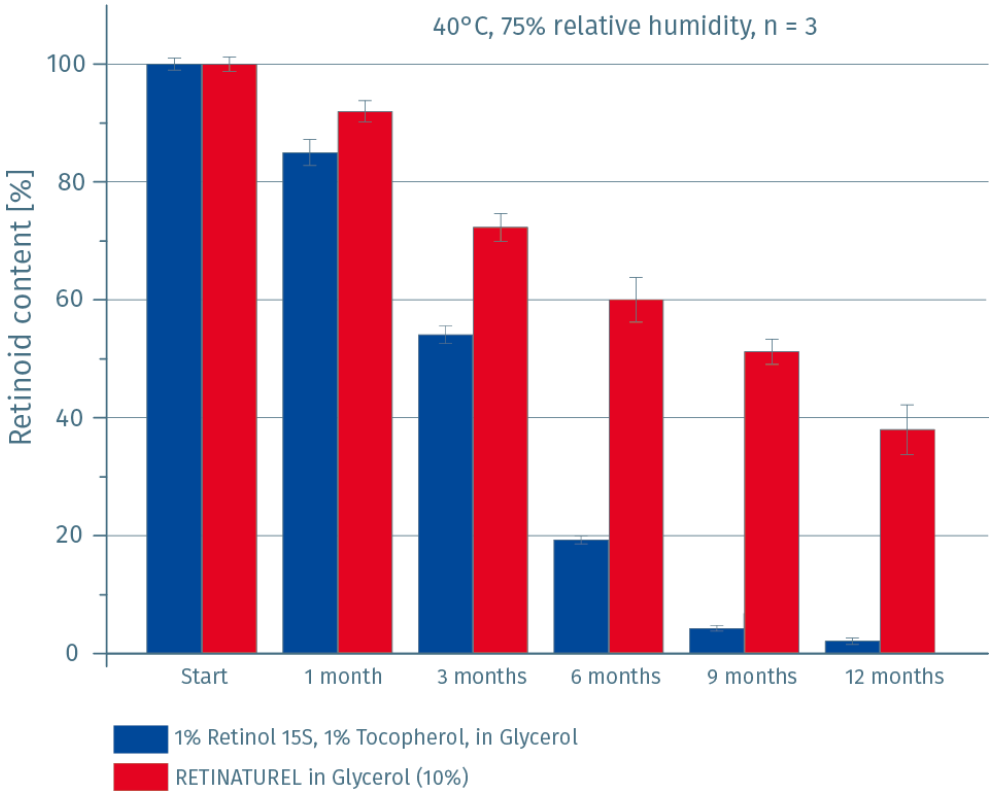
Measurement method :

Retinoid contents in the tested products at each time point were measured by a validated HPLC UV method using an Agilent 1100/1200 Series instrument (Agilent Technologies, Santa Clara, California, USA) equipped with a UV VIS detector and ChemStation data acquisition system.

Results :

After 12 months 38 % remaining Retinal could be detected. In contrast, only 2,1 % of Retinol 15S were still detected under the given experimental storage conditions.

ADEKA: Stability Retinaturel vs Retinol



Conclusion:

- **Natural produced Retinal shows increased stability compared to Retinol under elevated temperatures**

ADEKA: Skin Aging Physical properties clinical study

Background:

The natural precursor of retinoic acid, i.e. retinal, has been proven to exert retinoid activities.

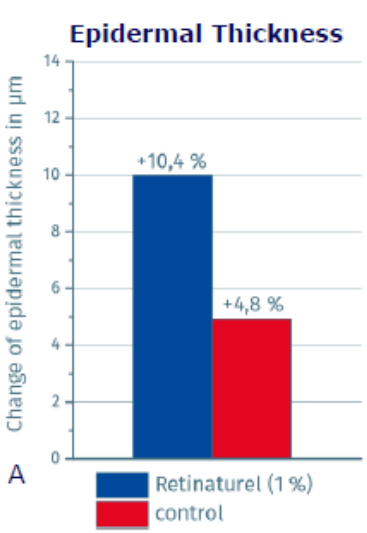
Aim and Methods:

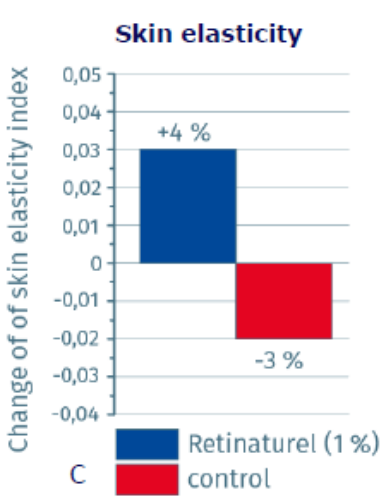
The aim of this prospective instrument study was to determine the effect of topical Retinaturel (1%) on the physical properties of aging skin. This was performed using two devices, namely a high resolution (70-80 µm) ultrasound scanner, which visualizes the thickness of both the epidermis and the dermis, and an echorheometer, which assesses the stiffness and elasticity of the skin by suction. In a 1-year study, 21 patients applied Retinaturel cream 1% on the face, while another group of 19 volunteers were only treated with an emollient (control group). Epidermal and dermal thicknesses, stiffness and elasticity were measured on the forehead. All the instrumental parameters were assessed at baseline and at the end of treatment.

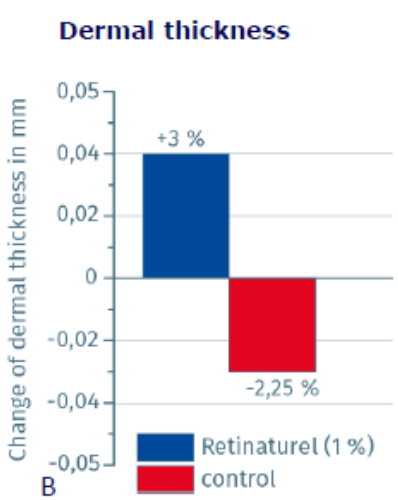
Results:

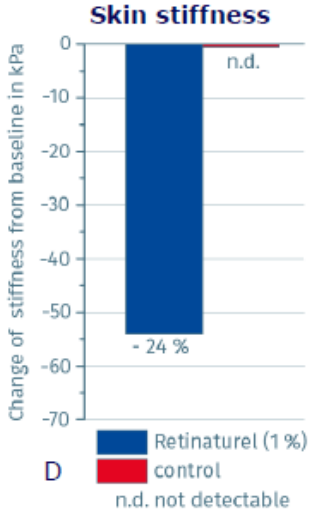
Compared to the control group, Retinaturel treatment induced a significant increase in epidermal Thickness (A) of the forehead area , as well as dermal
thickness (B). Similarly , Retinaturel treatment tended to increase cutaneous Elasticity (C) and reduce cutaneous stiffness (D).

ADEKA: Skin Aging Physical properties clinical study









Conclusion:

- **Taken together, the results further suggest that Retinaturel has counteracting effects on skin aging**

ADEKA: Photoaging Part I - Clinical study

Background:

Although topical retinoic acid effectively restores photoaged skin, the associated irritation limits the utility of the material. Retinal is the natural precursor of retinoic acid and can also be used to treat photoaged skin; the safety profile is good to evaluate the efficacy and safety of new anti-aging creams containing Retinaturel at 2% and 1% used to treat photoaged skin.

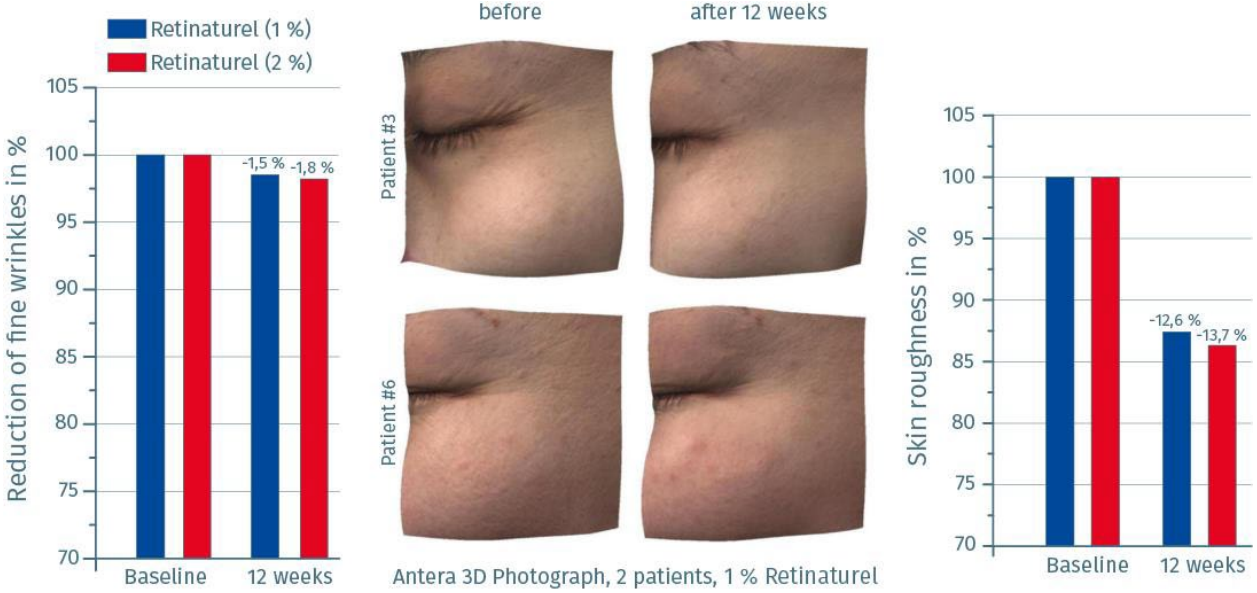
Method:

Study with 40 female Korean volunteers who applied Retinaturel 2% or Retinaturel 1% creams twice daily for 3 months. Wrinkles on, and the textures of, both crow's feet were quantitatively assessed using the Antera 3D system. Transepidermal water loss (TEWL), skin hydration. Overall improvement was assessed using a five-point scale by both the patients and the dermatologists.

Results:

The 3-months application improved overall photoaging in both Retunaturel 2% and Retinaturel 1%. After 12 weeks a recognizable reduction of wrinkles could be detected (by Photograph). Both Retinaturel 2% and Retinaturel 1% afforded significant textural improvements in skin roughness (13.7% and 12.6%, respectively), reduced the TEWL (14.5%, 17.9%), and increased hydration (10.2%, 6.0%).

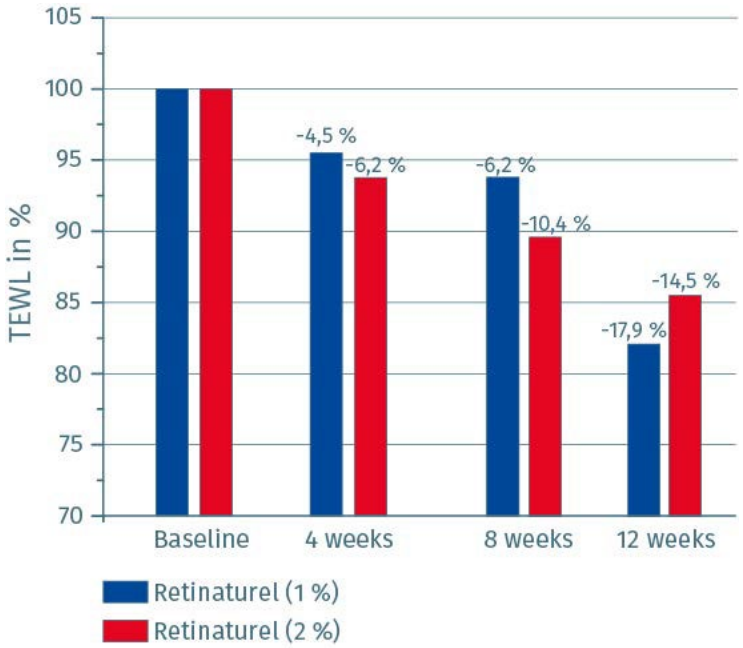
ADEKA: Photoaging Part I - Clinical study

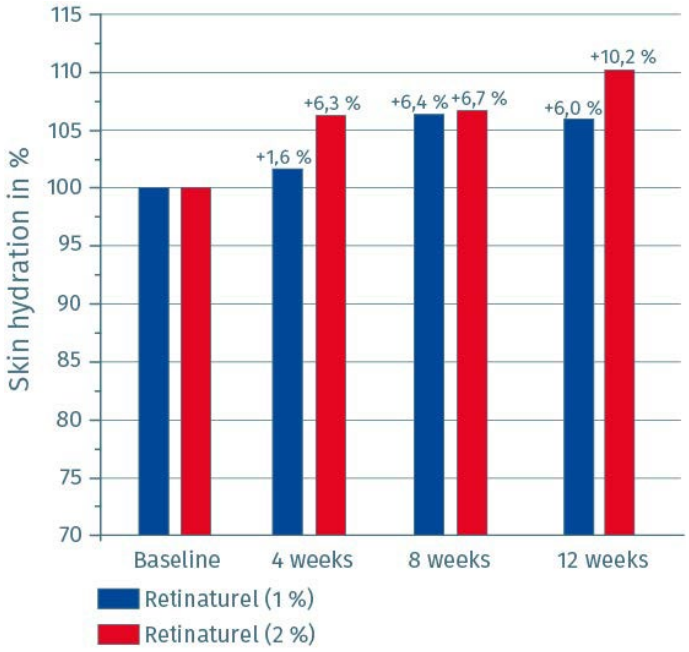


Conclusion:

- **Both Retinaturel 2% and Retinaturel 1% creams were well tolerated and improved skin hydration and texture.**

ADEKA: Photoaging Part II - Clinical study





Conclusion:

- **Both Retinaturel 2% and Retinaturel 1% creams were well tolerated and improved skin hydration and texture.**

ADEKA: Treatment of Rosacea (in vitro)

Background:

Vascular endothelial growth factor (VEGF), a potent angiogenic factor and vasodilator, is strongly expressed by epidermal keratinocytes in many angiogenesis dependent skin disorders. Retinoids may modulate VEGF in skin, and this may be related to an effect on rosacea.

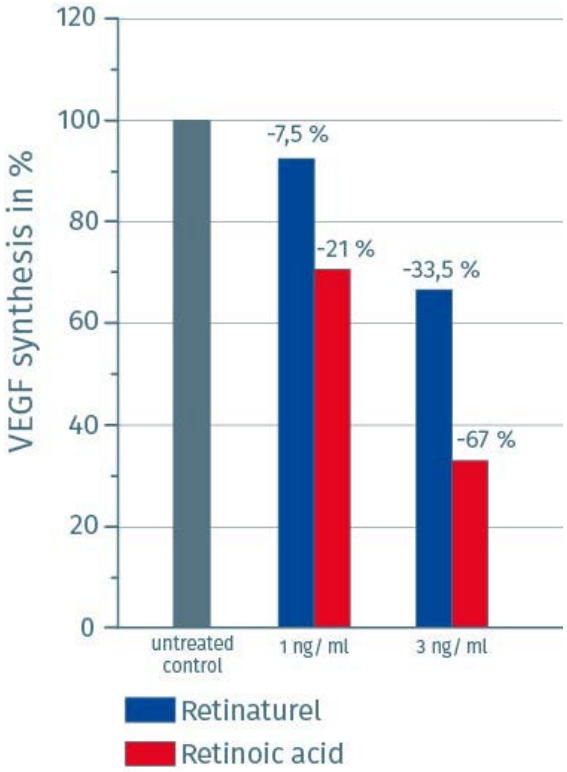
Method:

The effects of different concentrations of retinoids Retinaturel and retinoic acid) on VEGF production by cultured human skin keratinocytes were determined. Expression of VEGF was analyzed by enzyme linked immunosorbent assay (ELISA).

Results:

The amount of VEGF strongly decreased with retinoid concentration (e.g. 33,5 %, 67 % inhibition at 3 ng/ml Retinaturel and retinoic acid, respectively).

ADEKA: Treatment of Rosacea (in vitro)



Conclusion:

- **The decrease in VEGF expression by keratinocytes on contact with retinoids may prevent skin neoangiogenesis in certain skin diseases like rosacea.**

ADEKA: Alleviates Rosacea Clinical study In Vivo

Background:

Anecdotal observations suggest that retinoic acid may be effective in mild rosacea. The aim was to investigate, by an exploratory clinical and instrumental study, the effects of a topical formulation with the retinoic acid precursor retinal, in patients with vascular signs of facial rosacea.

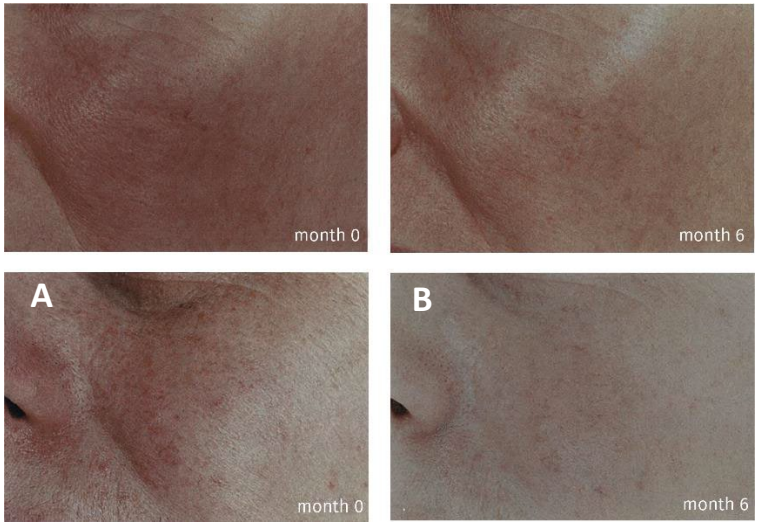
Method:

Female patients were treated with a 1% Retinaturel cream that was applied once daily for 6 months. Clinical assessments of persistent erythema and telangiectasia were performed every month, using a 4-points severity score (absent to severe). The clinical response for each parameter was defined as a decrease of at least 1 grade in the severity score.

Results:

The amount of VEGF strongly decreased with retinoid concentration (e.g. 33,5 %, 67 % inhibition at 3 ng/ml Retinaturel and retinoic acid, respectively).

ADEKA: Alleviates Rosacea Clinical study In Vivo



Two examples of clinical response to Retinaturel 1% topical treatment at the end of treatment. A, B Patient with persistent erythema and telangiectasia. C, D Patient with isolated telangiectasia. Month 0 = Baseline; month 6 = end of treatment.

Distribution of the number of responders non-responders with erythema and telangiectasia in the study population, at each assessment point.

	Baseline	1 month	2 months	3 months	5 months	6 months
Erythema (n=20)	0/20	4/16	12/8	10/10	15/5*	14/6*
Telangiectasia (n=13)	0/13	1/12	2/11	5/8	8/5	6/7

Responders were defined as patients with a reduction of at least 1 grade in the 4-point severity scale (absent to severe). *p< 0.05.

Conclusion:

- **This study indicates that Retinaturel has beneficial effects on the vascular component of rosacea.**

ADEKA: Antibacterial activity of Retinal for treatment of acne In vivo

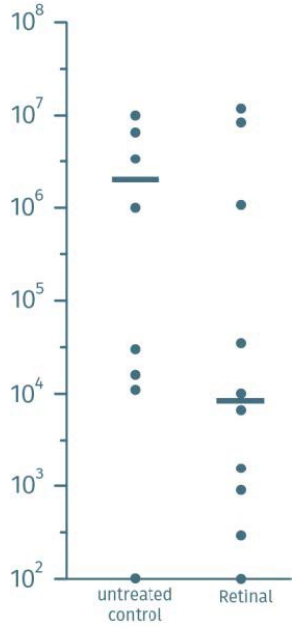
Background:
Retinal has been shown to exert antibacterial activity in vitro. This study evaluates the effect of Retinaturel on *Propionibacterium acnes* both in vivo and in vitro.

Method:
Microbial minimal inhibitory concentrations (MICs) of retinal and retinoic acid were determined on reference strains of *P. acnes*. In vivo activity of daily topical application of 1% Retinaturel on the P. acnes density was evaluated after application in a single blind randomized study.

Results:
MICs of retinal were 4 mg/l for *P. acnes* n° CIP179 and CIP53119 and 8 mg/l for *P. acnes* n°CIP53117. In contrast, the MICs of retinoic acid were superior to 128 mg/l for these three strains. In vivo, Retinaturel treated areas displayed a significant decrease in counts of viable *P. acnes* as compared with the untreated areas with a median decrease of 102 log *P. acnes*/cm^2 after 2 weeks of daily application. Vehicle alone had no effect.

ADEKA: Antibacterial activity of Retinal for treatment of acne In vivo

P. Acnes density after daily topical application of Retinaturel 1% for 2 weeks. (Horizontal bars indicate the median values)



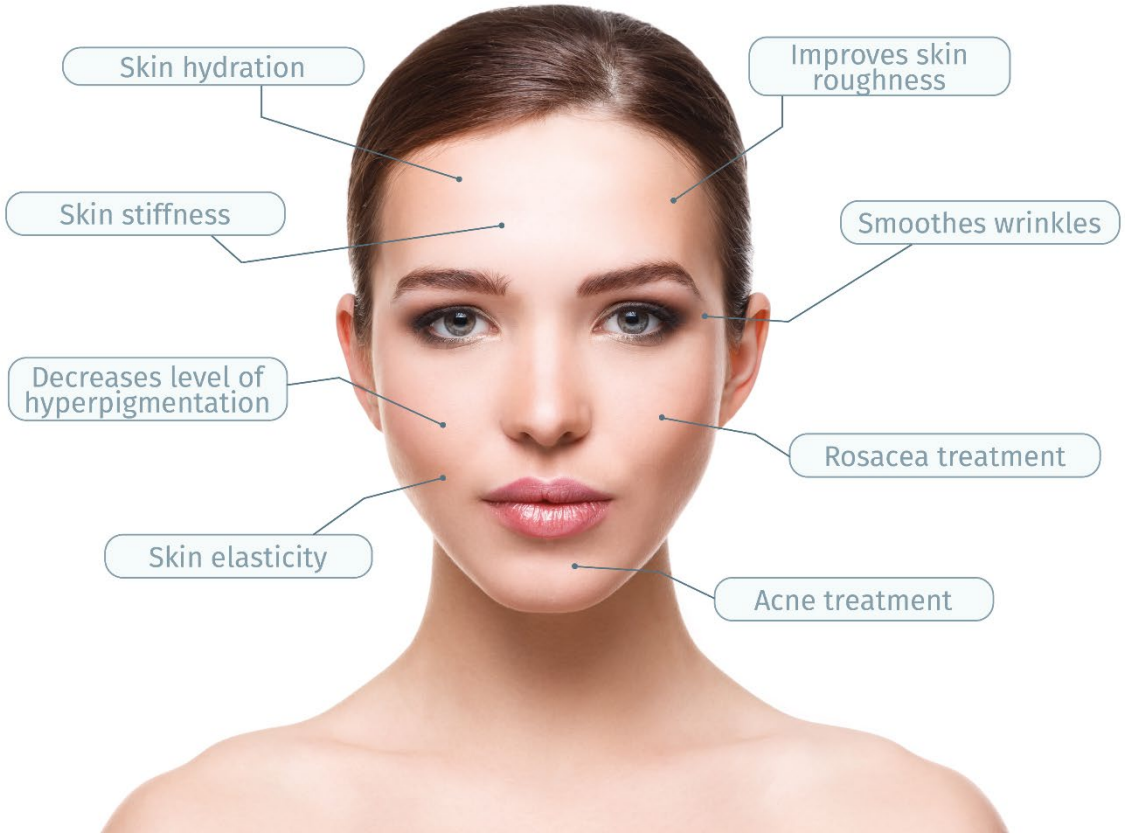
MICs (mg/l) of Retinaturel and retinoic acid against reference strains.

Strain	No.	Retinaturel	Retinoic acid
Propionibacterium acnes	CIP 179	4	>128
Propionibacterium acnes	CIP 53119	4	>128
Propionibacterium acnes	CIP 53117	8	>128

Conclusion:

- **The MIC of Retinaturel against *P. acnes* suggests a direct antibacterial activity. Daily topical application of 1% Retinaturel is associated with a clear reduction of the *P. acnes* density.**

ADEKA: Benefits of Retinaturel



➢**8 benefits with 1 product**

ADEKA Add Goodness

ADEKA: Summary

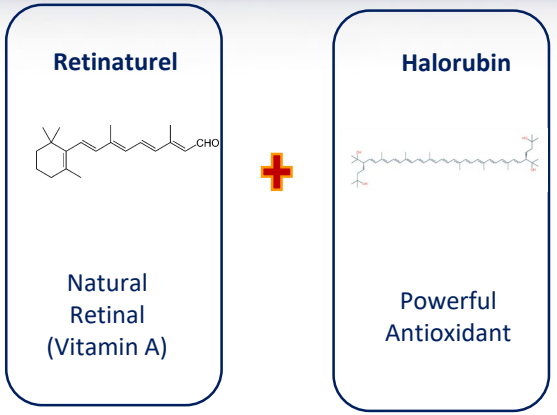
INCI: GLYCERIN, RETINAL
Active matter : 5% (Extract – 1.5 to 2.5 ppm pure natural Retinal)
Recommended dosage: 1-4%
Description: Natural retinal from *Halobacterium salinarum* stabilized in glycerol
Regulatory compliance : EU; US; CHINA; CANADA; AUSTRALIA
Microbiology: yeast and mould: <10 cfu/ml
aerobic microbial count: <10 cfu/ml
Solubility: partially in water
Shelf life: 12 months
Antioxidant/Stabilizer: none
Preservative: none
Biodegrability: biodegradable

ADEKA: Retinal ^{O5}

Retinal ^{05}

ADEKA: What is Retinal ^{05}

Retinal O^5 is a powerful blend with Retinaturel and Halorubin
99 % Retinaturel + 1 % Halorubin



The benefits:

- ✓ Combines safe protective activity of Halorubin with anti-aging benefits of retinal
- ✓ Protects against blue light and provide anti photo ageing activity
- ✓ Cell protective booster
- ✓ Boost hydration of skin

COSME CERT
COSMOS APPROVED

➢ **The genius of two single-ingredients combined in one unique and powerful product**

ADEKA: Summary

Trade name: RETINAL O[5]
INCI: GLYCERIN, RETINAL, XANTHOPHYLLS
Active matter : 4% (Retinal extract -1.2 to 2.2 ppm)
Microbiology: yeast and mould: <10 cfu/ml
aerobic microbial count: <10 cfu/ml
Solubility: partially in water & oil
Shelf life: 12 months
Recommended dosage: 1-4%
Antioxydant/Stabilizer: HALORUBIN 1%
Preservative: none
Biodegrability: biodegradable
Description: Natural retinal extract from *Halobacterium salinarum* stabilized in glycerol, blended with 1% HALORUBIN
Regulatory compliance : EU; US; CHINA; CANADA; AUSTRALIA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