LANCO®
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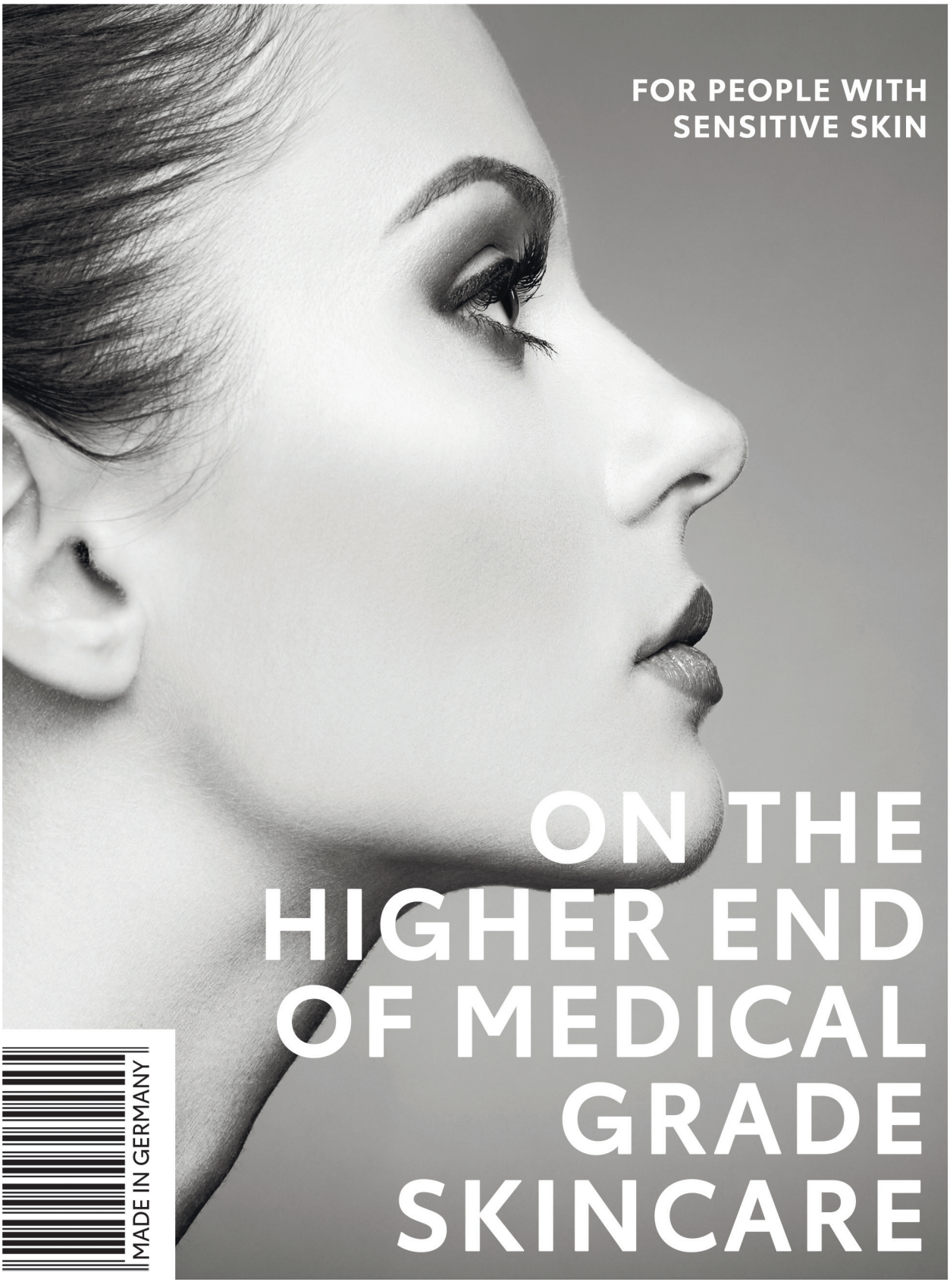


www.crevil.de

LABORATORIES GERMANY

EXFOLIATE 30% AHA & 2.0% BHA SOLUTION

- AHA 30% (Glycolic Acid, Malic Acid, Lactic Acid, Citric Acid)
- BHA 2% (Salicylic Acid)
- Daucus Carota Sativa Root Extract
- Tasmannia Lanceolata Fruit/Leaf Extract
- Ribes Nigrum Fruit Extract
- Ipomoea Batatas Root Extract
- Sodium Hyaluronate Crosspolymer

Exfoliation is a weekly skin treatment that helps to peel off the top layer of the skin. The Lancomed Exfoliate 30% AHA & 2.0% BHA solution is a highly effective solution that uses an AHA blend to exfoliate dead and dull skin to reveal fresher, smoother skin with refined tone and texture. BHA penetrates deep into pores to relieve clogging and prevent breakouts. Moreover, this exfoliating serum is enriched with fruit extracts to soothe and hydrate the skin.

- Leaves the skin looking smooth and more radiant
- Minimizes pores and diminishes the appearance of blemishes
- Gets rid of stubborn dead cells for a glowing finish
- This treatment is non-comedogenic
- Contains no allergic fragrances

AHA: Alpha Hydroxy Acids

Alpha-hydroxy acids (AHAs) include glycolic acid (GA), citric acid (CA), malic acid (MA), tartaric acid (TA), and lactic acid (LA), all of which are naturally-occurring organic acids present in many foods and milk sugars. They are carboxylic acids substituted with a hydroxyl group on the alpha carbon. Since 1992 there have been many products marketed as cosmetics designed to exfoliate the skin.

- AHAs reportedly function as exfoliants by reducing intercorneocyte cohesion and interfering with intercellular ionic bonding which causes an acceleration of cell turnover in the stratum corneum.
- AHAs are usually applied in the form of superficial and medium-depth peels such as those used to treat acne, scars, melasma, hyperpigmentation, roughness, age spots, and seborrhea.
- AHAs can improve wrinkled skin by increasing the synthesis of glycosaminoglycans and thickening skin.
- AHAs can prevent ultraviolet (UV)-induced skin tumor development.

- Malic Acid and Citric Acid are abundantly present in many fruits and their seeds, such as cocoa pods, grapes, and blackberries.
- Malic Acid and Citric Acid have been reported to function as pH adjusters and humectants (moisturizing agents) in cosmetic formulations.
- One study found that Citric Acid induced collagen I and procollagen II proliferation and Glycolic Acid improved the epidermis and dermis, thereby verifying the usefulness of AHAs for rejuvenating photo-damaged skin.
- Lactic Acid increases cell turnover and helps eliminate accumulated dead skin cells on the epidermis — the top layer of the skin
- Glycolic Acid may have an anti-inflammatory effect via epigenetic modifications at low concentrations, whereas GA at high concentrations had a synergistic phototoxic effect on HaCaT keratinocytes.
- Glycolic Acid at a low concentration (0.1 mM) has a significant photoprotective effect on human keratinocytes.

SAFETY OF USE

In the Federal Republic of Germany, on the basis of information available to the BGVV it has been recommended that:

- Glycolic acid may be used at a level of up to 4% and a pH ≥ 3.8.
- Lactic acid up to a maximum level of 2.5% and a pH ≥ 5.
- Malic Acid and Sodium Malate are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).
- Citric Acid: the CIR panel reported that citric acid was used at concentrations from 0.0000005 to 10% in cosmetic products, and concluded that citric acid was considered safe in the present practices of use.

BHA: Beta Hydroxy Acids

Beta Hydroxy Acids (BHAs), such as salicylic acid, are very similar to AHAs except for difference in their solubility, they are lipid-soluble in contrast to water solubility of AHAs.

- BHAs penetrate into the skin through sebaceous follicles, making it appropriate for patients with oily skin and open comedones due to their structure.
- BHA such as Salicylic Acid has anti-inflammatory effect and less skin irritancy effect than AHAs.
- Salicylic Acid has been used topically to treat various skin disorders for more than 2,000 years.
- Salicylic Acid is a lipid-soluble agent, and is therefore miscible with epidermal lipids and sebaceous gland lipids in hair follicles.
- Salicylic Acid removes intercellular lipids, which are linked covalently to the cornified envelope surrounding the surface epithelial cells.
- Salicylic Acid, being an organic acid, extracts desmosomal proteins including desmogleins. As a result of this action, the cohesion of epidermal cells is lost, leading to exfoliation.
- Salicylic Acid does not affect mitotic activity in human epidermal cells.
- Salicylic Acid peels are a good therapeutic option for comedonal acne, and can be a good adjunctive modality for treating open and closed comedones, post-acne erythema, and hyperpigmentation.

SAFETY OF USE

The SCCS (Scientific Committee on Consumer Safety) considers salicylic acid (CAS 69-72-7) safe when used for purposes other than preservative at a concentration up to 3.0 % for the cosmetic rinse-off hair products and up to 2.0 % for other products.

Daucus Carota Sativa Root Extract

CARROT EXTRACT

Daucus carota L. belongs to the Apiaceae family (Umbelliferae) and the term carrot is commonly used for both the plant and its edible part.

THE COMPOSITION OF CARROTS IS RICH AND VARIED

Cheminal composition of carrots (per 100 g)	
Proteins	1 g
Carbohydrates	5.2-7.3 g
Lipids	0.24 g
Fiber	2.9-3.4 g
Carotene	8.000-12.000 UI
Vitamin B1(thiamin)	0.06 mg
Vitamin B_2(riboflavin)	0.05 mg
Vitamin B_3(niacin)	0.6 mg
Vitamin B_6(pyridoxine)	0.10 mg
Vitamin E	0.6 mg
Vitamin C	8 mg
Vitamin K	80 µg
Folic acid	18 µg

Approximate composition of carrots (Alonso, J., 2004).

CAROTENOIDS

Carotenoids are multi-coloured compounds that occur naturally and are abundant as pigments in plants.

Carrots are rich in carotenoids, the main responsible for their color. The predominant carotenoids are β-carotene (45-80%), α-carotene (15-40%) and γ-carotene (2-10%).

ESSENTIAL OIL

α-pinene, camphene, β-pinene, myrcene, α-terpinene, p-cymene, limonene, γ-terpinene, terpinolene, caryophylene, β-bisabolene, γ-bisabolene, heptanol, octanol, nonanol, 2-nonenal, terpinen-4-ol, α-terpineol, bornyl acetate, 2,4-decadienal, dodecanal and falcarinol have been detected.

VITAMINS

Carrots contain many vitamins, including vitamin E (tocopherols family), which take different forms: α, β and δ (Carreras M., 2000). The antioxidant activity of tocopherols increases in the series α→δ. The opposite occurs with vitamin activity and with the rate of reaction with peroxide radicals (Belitz, H.D. & Grosch, W., 1997).

DETAILS THE MAIN MINERALS PRESENT IN CARROTS

Minerals	mg/100 g
Iron	2.1 mg
Calcium	37 mg
Magnesium	17 mg
Phosphorus	36 mg
Potassium	290 mg
Sodium	60 mg
Fluoride	0.04 mg

Minerals found in carrots (Alonso, J., 2004).

COSMETIC APPLICATION OF CARROT

Action	Active ingredient	Cosmetic application
Moisturizing and restoring activity of the barrier function	Carbohydrates	Emollient
	Proteins	Smoothing
	Fatty acids	Moisturizing
	Vitamins	
Regenerating and anti-aging activity	Carotenes	Anti-aging
	Vitamins	Hair and skin repairers
Sun	Carotenes	Tan accelerator and extender
	Vitamins	Facilitate tanning
		Photoprotective

BENEFIT OF CARROT

- **Moisturizing restoring activity of the barrier function:** this activity is mainly due to carbohydrate and protein content. Carbohydrates have the capacity to absorb and retain water under certain conditions. Some carbohydrates can remain on the stratum corneum surface, acting as humectant and filmogenic substances that considerably improve the biomechanical properties of skin. Low molecular weight proteins increase skin elasticity, while high molecular weight proteins, with the protective film they create, are good strengthening, firming and smoothing agents.
- **Regenerating and anti-aging activity:** Carrots are rich in carotenes, predominantly β-carotene, which is a known precursor of vitamin A. It has been confirmed that β-carotene also transforms into this vitamin when applied topically, as the enzymes and conditions required for its conversion to vitamin A are also found in the skin. When applied topically, vitamin A helps maintain normal skin conditions, promotes proper skin metabolism and improves healing and dryness, while significantly decreasing the effects of aging on skin condition. It has been observed that vitamin A increases skin cell regeneration by 30%, and there is a thickening of the epidermis when applied topically.
- **Sun application:** Smit, N. et al (2004) demonstrated that a fraction rich in plant carotenoids and vitamins C and E, as it is the case in carrots, increases the growth and pigmentation of melanocytes in monocultures, in addition to protecting against UVA radiation. α-tocopherol, or vitamin E, is the tocopherol type with the greatest biological activity in the body and it is highly important for skin.

Tasmannia Lanceolata Fruit/Leaf Extract

MOUNTAIN PEPPER OR ALPINE PEPPER

COMPOSITION

Polygodial: multifunctional natural active ingredient

- Anti-inflammatory property
- Broad antimicrobial activity
- Calms skin discomforts

Anthocyanins: protects your skin against free radicals

- Cyanidin 3-rutinoside, cyanidin 3-glucoside
- Powerful antioxidants

Rutin: helps to calm reactive skin

- Anti-inflammatory property
- Anti-allergic effects
- Strengthens capillaries

Essential minerals: nourish your skin!

- Magnesium: Stimulates cell regeneration & increases energy production
- Zinc: Helps decrease rash & alleviate inflammation associated with acne

Ribes Nigrum Fruit Extract

Blackcurrants (Ribes nigrum L., Grossulariaceae) contain high concentrations of flavonoids, a group of polyphenolic compounds that includes anthocyanins and flavonols.

- Polyphenolic substances in Blackcurrants have antioxidant, antimicrobial, antiviral, and antibacterial properties. The antioxidant, one could expect an effective protection of the membranes against oxidation-inducing agents.
- An antioxidant activity of the extracts were examined with spectrophotometric methods. The FTIR investigation showed that extracts modify the erythrocyte membrane and protect it against free radicals induced by UV radiation.
- The Antioxidant properties help to protect and nourish damaged skin, leaving the skin soft and healthy.

Ipomoea Batatas Root Extract

Ipomoea batatas (L.) Lam. from the family Convolvulaceae is the world's sixth largest food crop which is widely grown in tropical, subtropical and warm temperate regions. Orange-fleshed sweetpotato is also a rich source of beta-carotene, a precursor of bio-available vitamin A. The flesh may be white, yellow, orange or purple. The I. batatas plant has been used extensively in traditional medicines for various ailments

- The study showed that the peels of sweet potato possessed a definite pro-healing action.
- In the excision wound model, the extract of the peels and peel bandage of the Ipomoea batatas tubers showed significant increase in percentage closure of the wounds by enhanced epithelization. This enhanced epithelization may be due to the antioxidant effect of the peels, which augments collagen synthesis.
- The wound healing effect, which appears to be related to the free radical scavenging activity of the phytoconstituents, and their ability to inhibit lipid peroxidative processes.

Sodium Hyaluronate Crosspolymer

Sodium Hyaluronate Crosspolymer is a cross-linked hyaluronic acid. This cross-linked form is a unique delivery system for water.

- The gel forms a film on the skin and continuously delivers bound water.
- Five times the water binding capacity of hyaluronic acid.
- An infinite molecular weight HA.

IN VITRO TEST

In vitro assay: Inhibition of Superoxide radicals generated in vitro by xanthine oxidase metabolism of hypoxanthine. The free radicals reduce Cytochrome C which is quantified by measuring absorbance at 550 nm.

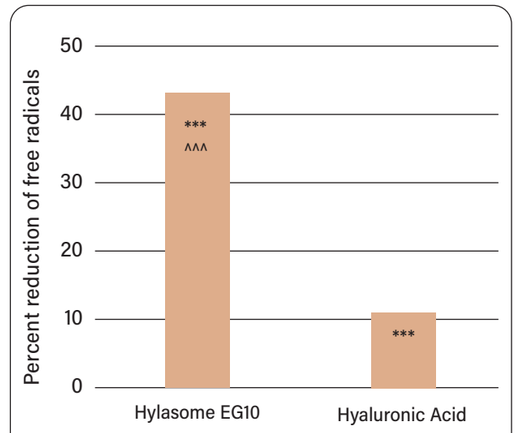
Positive control: Superoxide dismutase (SOD) known to block reduction of Cytochrome C.

Test products:

- Sodium Hyaluronate Crosspolymer (50 µlper 1.2 ml reaction volume; final HA conc 0.42 mg/ml).
- Soluble HA -1.1 X 106 daltons-(50 µlof 1% solution, per 1.2 ml reaction volume; final HA conc 0.42 mg/ml).

Measurement: Data normalized to the SOD value to calculate % reduction of free radicals (SOD= 100% reduction).

Assay Principle - free radicals increases absorbance which is reduced in presence of anti-oxidants.



*** statistically significant (p<0.001) vs untreated
^^^ statistically significant (p<0.001) vs HA

Sodium Hyaluronate Crosspolymer was found to reduce free radicals by 43% compared to untreated samples and 4X better than Hyaluronic acid.

EX-VIVO TEST

Surgically removed skin (with stratum corneum, viable epidermis and dermis).

Test material:

- Sodium Hyaluronate Crosspolymer at 0.1% polymer weight in D2O
- Hyaluronic Acid HA -1.1 X 106 daltonsat 0.1% polymer weight in D2O

Procedure:

- 5 µL D2O-based test material applied to 2x2 cm2 surgically removed skin.
- Held at 55% relative humidity (D2O) and room temp for 24 hrs.
- Placed in milled brass sample holder and covered with glass cover slip.
- D2O content in the skin measured by confocal Raman spectroscopy in the x and z axes.

Result:

After 24 hours at 55% RH, Sodium Hyaluronate Crosspolymer -treated skin contained 6x more moisture in the total sample.

After 24 hours at 55% RH, Sodium Hyaluronate Crosspolymer -treated skin contained 5x more moisture in the stratum corneum.

EXFOLIATE OVERNIGHT RENEW CREAM 10% AHA

- Glycolic Acid 5%
- Malic Acid 2%
- Citric acid 2%
- Lactic Acid 1%

Improve the appearance of your skin today with Lancomed Exfoliate Overnight Renew Cream 10% AHA. It is designed to slough off dead cells in the outermost layer of the skin and promote cell turnover. The result: skin looks more even and radiant. The Overnight Renew Cream is an exfoliating product that, unlike its competitors, stays on the skin and continues to work even after cleansing. In addition, it has a rich formula that nourishes, moisturises and repairs the skin from the inside out.

- Removes dead skin cells and improves skin texture.
- Helps to keep pores clean and unclogged.
- Gives the skin a refreshed and revitalised complexion that lasts longer.
- Leaves skin smoother and more radiant.
- This cream is non-irritating and non-comedogenic.
- Contains no allergic fragrances.

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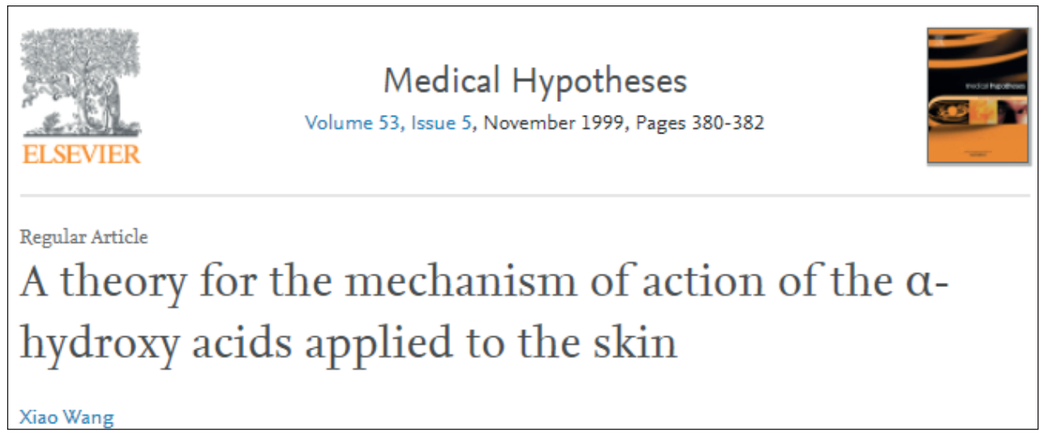
STUDY REFERENCES


ELSEVIER

Medical Hypotheses
Volume 53, Issue 5, November 1999, Pages 380-382

Regular Article

A theory for the mechanism of action of the α-hydroxy acids applied to the skin

Xiao Wang

The α-hydroxy acids reduce the calcium ion concentration in the epidermis and remove calcium ions from the cell adhesions by chelation. The cell adhesions are thereby disrupted, resulting in desquamation. The decrease of calcium ion level so brought about in the epidermis also tends to promote cell growth and retard cell differentiation, giving rise to a younger-looking skin.

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Clin Cosmet Investig Dermatol. 2010; 3: 135–142.
Published online 2010 Nov 24. doi: 10.2147/CCID.S9042
PMCID: PMC3047947
PMID: 21437068

Applications of hydroxy acids: classification, mechanisms, and photoactivity

Andrija Kornhauser,[1] Sergio G Coelho,[2] and Vincent J Hearing[2]

- In low concentrations (4%–10%) of AHA, they are ubiquitous components of nonprescription creams and lotions that are promoted as being effective for ameliorating skin aging.
- AHAs can affect and modify the processes of cell proliferation, cytokine excretion, and induction of apoptosis and can act as antioxidant/chelators, influence the skin barrier function, and act as moisturizers. Some investigators, therefore, still recommend that caution should be taken when using these products, in particular with their chronic use.

Experimental Dermatology ADF
Volume 12, Issue s2
October 2003
Pages 57-63

Biological effects of glycolic acid on dermal matrix metabolism mediated by dermal fibroblasts and epidermal keratinocytes

Yuri Okano, Yumiko Abe, Hitoshi Masaki, Uma Santhanam, Masamitsu Ichihashi, Yoko Funasaka

First published: 03 November 2003 | https://doi.org/10.1034/j.1600-0625.12.s2.9.x | Citations: 64

Related Information

Glycolic Acid not only directly accelerates collagen synthesis by fibroblasts, but it also modulates matrix degradation and collagen synthesis through keratinocyte-released cytokines. It contributes to the recovery of photodamaged skin through various actions, depending on the skin cell type.

BJD British Journal of Dermatology
IMPROVING PATIENT OUTCOMES IN SKIN DISEASE WORLDWIDE
Volume 145, Issue 1
July 2001
Pages 3-9

Topically applied lactic acid increases spontaneous secretion of vascular endothelial growth factor by human reconstructed epidermis

M. Rendl, C. Mayer, W. Weninger, E. Tschachler

The data demonstrate that the topical application of AHAs modulates the secretion of cytokines by KCs. Regulation of KC-derived growth factors and cytokines by AHAs might represent a mechanism contributing to their therapeutic effects in disorders such as photoageing.

EXFOLIATE PODIATRY 10% AHA + 2.0% BHA FOOT CREAM

- Glycolic Acid 5%
- Malic Acid 2%
- Citric acid 2%
- Lactic Acid 1%
- Salicylic Acid 2%
- Urea 5%

Thanks to the Lancomed Exfoliate Podiatry 10% AHA + 2.0 BHA foot cream, soft and smooth feet are now easier to achieve than ever. It exfoliates the dead skin cells on the feet to reveal the new, lighter layers underneath. This podiatry foot cream is designed to stimulate the fibroblasts in the dermis to produce more collagen. This improves the skin's elasticity, hydration and smooth appearance and supports the formation of healthy new cells. In addition, this cream acts as a refatting agent to restore lipids and quickly generate moisture.

- Intensely exfoliates rough skin and prevents dry rough skin.
- Penetrates dry damaged skin on the feet and heels.
- Soothes and calms itching and irritation
- Helps the skin to generate new cells.
- This cream is non-irritating and non-comedogenic.
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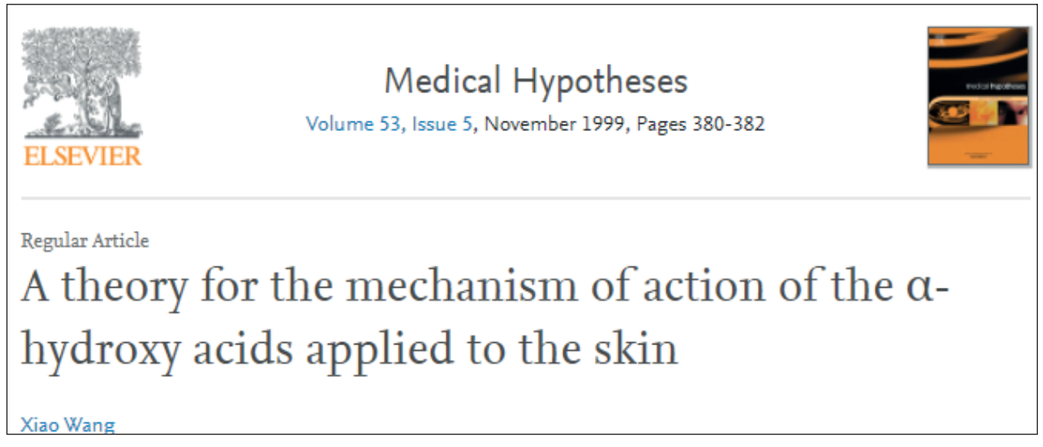
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BHA: Beta Hydroxy Acids

BHA INGREDIENTS MAY BE LISTED AS

- Salicylic acid (or related substances, such as salicylate, sodium salicylate, and willow extract)*
- Beta hydroxybutanoic acid
- Tropic acid
- Trethocanic acid

SALICYLIC ACID (SA)

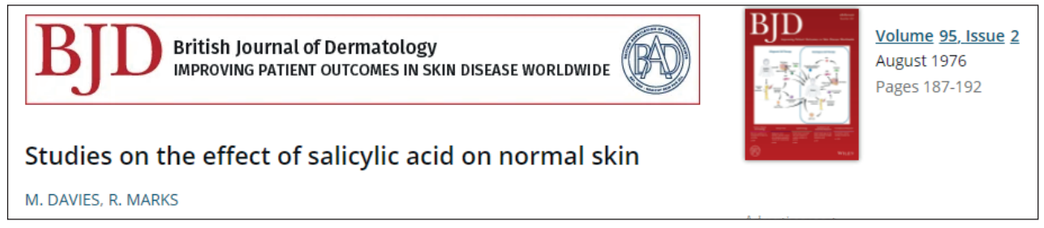
Kligman described SA as a β-hydroxy acid, but Yu and Van Scott have classified it as a phenolic aromatic acid.

SA is a lipid-soluble agent, in contrast with the alpha hydroxy acids (such as glycolic acid) and therefore it miscible with epidermal lipids and sebaceous gland lipids in hair follicles.

BENEFITS OF SALICYLIC ACID

- Salicylic acid is widely used in cosmetic formulations (concentration 2%–4%) and also therapeutically as a keratolytic (peeling) agent to treat skin conditions, such as calluses, keratoses, acne, and photoaging.
- SA decreases secretion of sebum in patients with acne.
- SA decreases adhesion of corneocytes, and causes loosening of these cells and their subsequent detachment.

STUDY REFERENCES


BJD British Journal of Dermatology

IMPROVING PATIENT OUTCOMES IN SKIN DISEASE WORLDWIDE

Volume 95, Issue 2

August 1976

Pages 187-192

Studies on the effect of salicylic acid on normal skin

M. DAVIES, R. MARKS

This study suggested that salicylic acid causes desquamation by dissolution of intercellular cement material.

BJD British Journal of Dermatology
IMPROVING PATIENT OUTCOMES IN SKIN DISEASE WORLDWIDE

Volume 103, Issue 2
August 1980
Pages 191-196

Detection of the action of salicylic acid on the normal stratum corneum

D. L. ROBERTS, R. MARSHALL, R. MARKS

This study has been proven that salicylic acid enhances the shedding of corneocytes and suggest that this compound in some way decreases corneocyte to corneocyte cohesion.

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Clin Cosmet Investig Dermatol. 2015; 8: 455–461.
Published online 2015 Aug 26. doi: 10.2147/CCID.S84765
PMCID: PMC4554394
PMID: 26347269

Salicylic acid as a peeling agent: a comprehensive review

Tasleem Arif

This paper reviews shown that Salicylic acid is a safe and efficacious peeling agent for a number of dermatological and cosmetic problems, including acne vulgaris, melasma, photodamage, freckles, and lentigines.

Urea

Urea is a unique physiological substance. It has frequently been used in dermatological therapy for more than 20 years. It is a natural moisturizing factor contained within normal human skin and released in eccrine sweat fluid, which facilitates the hydration of corneocytes and maturation of the stratum corneum.

BENEFIT FOR SKIN

- Dose dependent of urea application improve cutaneous barrier function and expression of antimicrobial defense in normal human skin.
- Emollients containing urea have been shown to significantly increase the hydration of the skin measured by skin capacitance, and therefore directly increase skin elasticity and smoothness.
- Maintenance of healthy skin and management of skin disorders.
- The study has been shown that using 5% urea moisturizer and the 10% urea lotion improved atopic dermatitis and were very well tolerated.
- Other study has been shown that 5% Urea emulsion improve all treated areas of Ichthyosis.

STUDIES REFERENCE

Review | Open Access | Published: 01 October 2021

Urea in Dermatology: A Review of its Emollient, Moisturizing, Keratolytic, Skin Barrier Enhancing and Antimicrobial Properties

Jaime Piquero-Casals, Daniel Morgado-Carrasco, Corinne Granger, Carles Trullàs, América Jesús-Silva & Jean Krutmann

Multiple clinical trials on the use of urea-containing formulations have shown significant clinical improvement in many of the dermatosis presenting with scaly and dry skin such as atopic dermatitis, ichthyosis, xerosis, seborrheic dermatitis and psoriasis, among others.

Original Paper

Skin Pharmacology and Physiology

Skin Pharmacol Physiol 2016;29:135–147
DOI: 10.1159/000445955

Received: December 29, 2015
Accepted: April 4, 2016
Published online: June 2, 2016

The Effect of an Emollient Containing Urea, Ceramide NP, and Lactate on Skin Barrier Structure and Function in Older People with Dry Skin

Simon G. Danby[a] Kirsty Brown[a] Tim Higgs-Bayliss[a] John Chittock[a]
Lujain Albenali[a, b] Michael J. Cork[a–c]

[a]Academic Unit of Dermatology Research, Department of Infection, Immunity and Cardiovascular Disease, Faculty of Medicine, Dentistry and Health, University of Sheffield Medical School, [b]Paediatric Dermatology Clinic, Sheffield Children's Hospital, and [c]Department of Dermatology, Royal Hallamshire Hospital, Sheffield, UK

In a prospective study of 42 individuals > 60 years old, application of a 5% urea-containing cream showed increased skin hydration compared to a control emollient.

EXPOSURE SPF 30+ BRIGHTENING FACIAL CREAM

- Active Ingredient
- Combination of chemical sunscreens
- Kojic Acid
- Vitamin C
- Vitamin E
- Scutellaria Extract
- Mulberry Bark Extract
- Bearberry
- Licorice

The Exposure Brightening UV Shield SPF 30+ is a brightening sunscreen with a high protection factor of 30+. It immediately provides optimal broad-spectrum UVA and UVB protection. It visibly brightens and unifies your complexion and reduces the appearance of new pigmentation spots as well as the production of melanin. It is enriched with Vitamin E to protect the skin from environmental pollution. Several active ingredients like Kojic Acid, Vitamin C, Scutellaria Extract, Mulberry Bark Extract and Bearberry Biogreen block melanin and lighten the skin. Licorice extract contains an active called Glabridin, which inhibits tyrosinase, the enzyme that causes pigmentation in response to sun exposure.

- Contains no allergic fragrances.
- Brighter and radiant complexion.
- Increases the luminosity of the skin.
- Quercetin creates a protective film on the surface of the skin against UVA and UVB.
- Activates natural immune and cell protection.

UV Radiation and the Skin

UV radiation (UV) present in sunlight is classified as a "complete carcinogen" because it is both a mutagen and a non-specific damaging agent and has properties of both a tumor initiator and a tumor promoter. Throughout the lifetime, human accumulate damage generated by UV radiation. UV causes inflammation, immune changes, physical changes, impaired wound healing and DNA damage that promotes cellular senescence and carcinogenesis. However, UV also benefits human health by mediating natural synthesis of vitamin D and endorphins in the skin, therefore UV has complex and mixed effects on human health.

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UVB BLOCKERS INCLUDING

- Aminobenzoates
- Cinnamates
- Salicylates
- Octocrylene
- Ensulizole
- Camphor derivatives

UVA BLOCKERS INCLUDING

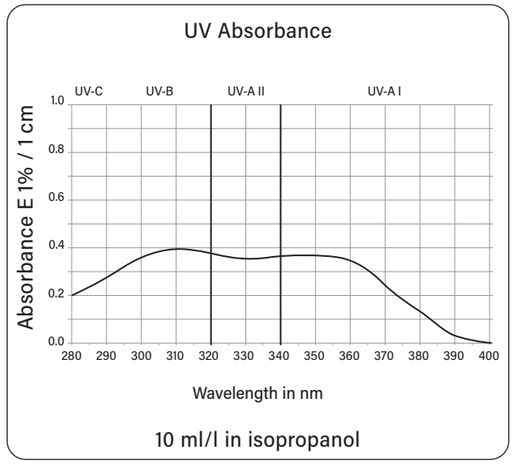
- Benzophenones
- Anthranilates
- Avobenzones
- Ecamsule

UVA & UVB FILTERS

SUNSCREEN AGENT

- Homosalate
- Octocrylene
- Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine
- Butyl Methoxydibenzoylmethane
- Ethylhexyl Salicylate

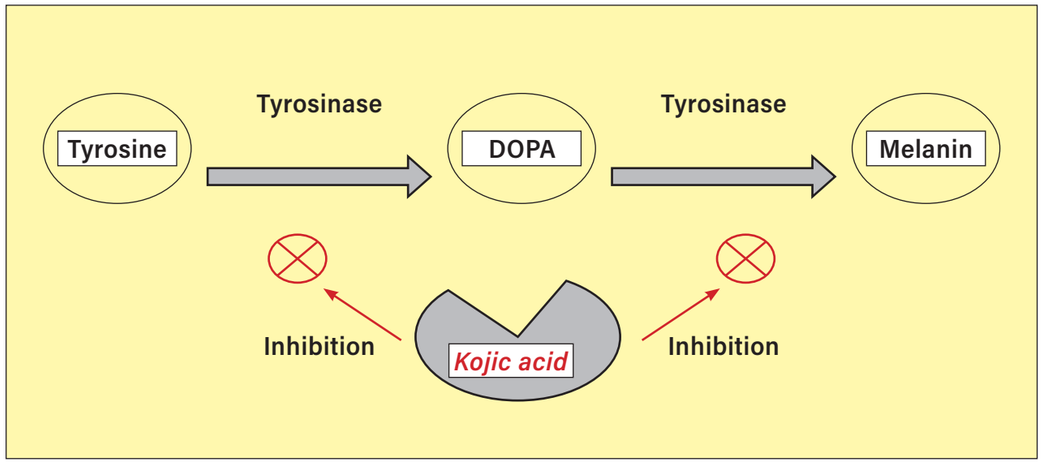
The combination of UVA & UVB Filters
VERY EFFECTIVE BROAD SPECTRUM ABSORBER



KOJIC ACID

Kojic Acid is a metabolic product of the fungal species *Acetobacter, Aspergillus,* and *Penicillium*.

- Kojic acid and its derivatives are used as anti-oxidant, anti-proliferative, anti-inflammatory, radio protective and skin-lightening agent.
- It has the ability to act as a UV protector, suppressor of hyperpigmentation in human and restrainer of melanin formation, due to its tyrosinase inhibitory activity.
- Kojic acid showed the potential inhibition of cellular NF-κB activity in human keratinocytes. NF-κB activation is probably involved in kojic acid induced anti-melanogenic effect.
- Several studies are performed to evaluate the mechanisms of depigmentation and safety of Kojic Acid. They suggested that the best range of concentrations for KA topical preparation is 1% or less because in these ranges, it melts show effective and safe properties.
- Clinical studies have shown effectiveness of 1% KA cream therapy for 6 months in photo-hypersensitive melasma patients.
- Melasma patients who had used 1% KA cream were followed for 2 years and no significant side effect or adverse reaction was observed.



Kojic acid applications in cosmetic and pharmaceutical preparations. Majid Saeedi, Masoumeh Eslamifar, Khadijeh Khezri. Biomedicine & Pharmacotherapy Volume 110, February 2019, Pages 582-593.

VITAMIN C

Vitamin C is associated with several beneficial properties, including the promotion of collagen synthesis, photoprotection from ultraviolet A and B radiation, lightening of hyperpigmentation, and improvement of a variety of inflammatory dermatoses.

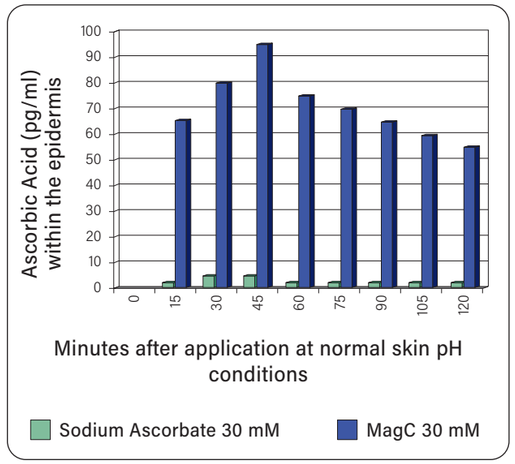
To provide the maximum benefit from Vitamin C, it is recommended that a stable form of Vitamin C is used in personal care preparations.

Magnesium Ascorbyl Phosphate is an esterified derivative of ascorbic acid, it is one of the most stable derivatives of ascorbic acid known. It is also very stable in cosmetic formulations. Magnesium Ascorbyl Phosphate penetrates into skin and there it is metabolized to ascorbic acid. Due to this process its efficacy is better than the one of pure ascorbic acid.

REFERENCE STUDIES

MagC™ rapidly permeates the epidermis and is converted to ascorbic acid with long term duration. Sodium ascorbate however, does not permeate the epidermis under physiologic pH (i.e., neutral~7) conditions. Acidic conditions (i.e., below 3.5) are required for ascorbic acid penetration.

Epidermal Transportation of Magnesium Ascorbyl Phosphate (MagC™) and conversion of MagC™ to Ascorbic Acid *in vitro*



REFERENCE STUDIES

Ann Dermatol. 2016 Feb; 28(1): 129–132. PMCID: PMC4737824
Published online 2016 Jan 28. doi: 10.5021/ad.2016.28.1.129 PMID: 26848238

Effects of Magnesium Ascorbyl Phosphate on the Expression of Inflammatory Biomarkers after Treatment of Cultured Sebocytes with *Propionibacterium acnes* or Ultraviolet B Radiation

Weon Ju Lee,✉ Sang Lim Kim, Kyou Chae Lee, Mi Yeung Sohn, Yong Hyun Jang, Seok-Jong Lee, and Do Won Kim

The results showed that MAP decreased the sebum peroxidation in cultured sebocytes treated with P. acnes and UVB radiation. It has mild anti-inflammatory and antioxidative effects in cultured sebocytes.

VITAMIN E

Vitamin E is an important fat-soluble antioxidant and has been in use for more than 50 years in dermatology.

- It protects the skin from various deleterious effects due to solar radiation by acting as a free-radical scavenger.
- Vitamin E is the treatment of burns, surgical scars, and wounds.
- Vitamin E prevents lipid peroxidation of serum from bacterial-induced leakage through follicles and sebaceous glands, thus preventing inflammation due to peroxide irritation.

SCUTELLARIA EXTRACT

***Scutellaria baicalensis* Georgi** root has been used as a traditional Chinese medicine to alleviate inflammation, allergy, and fever as well as a treatm.ent for several cancers.

Main bioactive components: Baicalin, baicalein, wogonin, and wogonoside, flavonoid also identified. All these compounds have significant pharmacological effects.

REFERENCE STUDIES

PLoS One. 2017; 12(2): e0171513. PMCID: PMC5300169
Published online 2017 Feb 9. doi: 10.1371/journal.pone.0171513 PMID: 28182699

Bifunctional effects of O-methylated flavones from *Scutellaria baicalensis* Georgi on melanocytes: Inhibition of melanin production and intracellular melanosome transport

Michiko Kudo,# Kumiko Kobayashi-Nakamura,# and Kentaro Tsuji-Naito*

Andrzej T Slominski, Editor

- *S. baicalensis* extract and its active components, wogonin and wogonoside, possessed a strong inhibitory effect on melanogenesis without cytotoxicity.
- *O*-methylated flavones, such as wogonin, reversibly suppress melanosome transport via MLPH downregulation. Our findings reveal the potential applicability of S. *baicalensis* extracts and its flavones for skin lightening and the treatment of hyperpigmentation.

Article

Inhibitory Effect and Mechanism of Scutellarein on Melanogenesis

Liyun Dai [1], Lihao Gu [1] and Kazuhisa Maeda [1,2,*]

Scutellarein and baicalein are bioactive flavones purified from the medicinal plant Scutellaria baicalensis Georgi (SBG).

The results revealed that scutellarein has an inhibitory effect on melanin production at the concentration of any cytotoxicity; inhibition of ˙OH generation also was observed.

The mechanism of action of scutellarein is inhibit tyrosinase expression, which ultimately affected the synthesis of melanin in cells.

MULBERRY BARK EXTRACT

Morus alba L. or white mulberry has long-standing ethno medicinal significance. Various parts of the plant have been used in traditional Asian medicine.

PHYTOCHEMICAL COMPONENTS INCLUDE:

- Alkaloids
- Flavonoids
- Flavones
- Flavanones
- Stilbenes
- Benzophenones
- Coumarin derivatives
- Terpenoids

Morus is one of the few genera to contain prenylated flavonoids. Prenyl flavonoids are credited with enhanced biological effects attributed to the prenyl side-chains.

The bioactive principles from Morus alba root bark are reported to have antibacterial, antiviral, antioxidant, hypoglycemic, neuroprotective, nephroprotective, antiulcer, analgesic and anti-inflammatory properties.

REFERENCE STUDIES

Molecules. 2017 Apr; 22(4): 514.
Published online 2017 Mar 23. doi: 10.3390/molecules22040514
PMCID: PMC6154579
PMID: 28333105

Anti-Melanogenic Properties of Greek Plants. A Novel Depigmenting Agent from *Morus alba* Wood

Eliza Chaita,[1] George Lambrinidis,[2] Christina Cheimonidi,[3] Adamantia Agalou,[4] Dimitris Beis,[4] Ioannis Trougakos,[3] Emmanuel Mikros,[2] Alexios-Leandros Skaltsounis,[1] and Nektarios Aligiannis[1,*]

Isabel C. F. R. Ferreira, Academic Editor

This study confirm the use of Morus alba as a valid source of anti-melanogenic agents. The methanol extract of Morus alba wood demonstrated the highest tyrosinase inhibition among the 900 extracts tested, as well as a significant reduction in intracellular tyrosinase and melanin content in B16F10 melanoma cells.

Molecules. 2016 Sep; 21(9): 1130.
Published online 2016 Sep 2. doi: 10.3390/molecules21091130
PMCID: PMC6274457
PMID: 27598113

Characterization of a New Flavone and Tyrosinase Inhibition Constituents from the Twigs of *Morus alba* L.

Long Zhang,[1] Guanjun Tao,[1] Jie Chen,[1,2] and Zong-Ping Zheng[1,*]

Isabel C. F. R. Ferreira, Academic Editor

"The phytochemicals in the twigs of M. alba were systematically studied. A total of 17 compounds, including one new compound, were isolated and their structures were determined by ESI-MS and NMR data. Among them, steppogenin, 2,4,2',4'-tetrahydroxychalcone, morachalcone A, oxyresveratrol, and moracin M were found to exhibit significant tyrosinase inhibitory activity and were the main components responsible for the strong tyrosinase inhibitory activity, suggesting that M. alba twig or some of its constituents might become the promising sources in nutraceuticals and cosmeceuticals to inhibit tyrosinase activity in food products or be used in cosmetics as skin-whitening agents."

Whitening and Antierythemic effect of a cream containing *Morus alba* extract

Naveed Akhtar[1], Jehad Hisham[1], Haji M. Shoaib Khan[1], Barkat Ali Khan[1*], TariqMahmood[1] and Tariq Saeed [2]

1. Department of Pharmacy, Faculty of Pharmacy and Alternative Medicine, The Islamia University of Bahawalpur, Pakistan.
2. College of Pharmacy, University of the Punjab, Lahore, Pakistan.

Article history: Received: 25December, 2010, revised: 23 February, 2011, accepted: 11 September, 2011, Available online: 5 April 2012

Mulberry Morus Alba has high phenolic compounds which have high levels of total Anthocyanin. These phenolics have tyrosinase inhibition activity, one of the modes of antiaging activity. Akhtar et al. reported decrease in erythema and melanin contents in the treated skin using same formulation.

BEARBERRY EXTRACT

Bearberry (Arctostaphylos uva-ursi) has been proposed as a natural antioxidant additive due to the high contents of phenolic compounds in leaves. It is a medicinal plant traditionally employed for the treatment of urinary tract infections due to high contents of arbutin (hydroquinone β-D-glucoside), which is now mainly used as a natural skin-whitening agent in cosmetics. Bearberry

THE MAIN CONSTITUENTS

- Glycosides arbutin (5%–15%).
- Methylarbutin (up to 4%).
- Small quantities of the free aglycones.
- Other constituents include ursolic acid, tannic acid, gallic acid, p-coumaric acid, syringic acid, galloylarbutin, gallo-tannins, and flavonoids, notably glycosides of quercetin, kaempferol, and myricetin.

Arbutin, the b-D-glucopyranoside derivative of hydroquinone, is a naturally occurring plant derived compound found in the dried leaves of a number of bearberry (Arctostaphylos uva-ursi).

- Arbutin, inhibits tyrosinase activity competitively but at non-cytotoxic concentrations in a dose dependent manner in cultured melanocytes.
- It inhibits melanosome maturation and is less cytotoxic to melanocytes than hydroquinone.

REFERENCE STUDIES

› Yakugaku Zasshi. 1992 Apr;112(4):276-82. doi: 10.1248/yakushi1947.112.4_276.

[Pharmacological studies on leaf of Arctostaphylos uva-ursi (L.) Spreng. IV. Effect of 50% methanolic extract from Arctostaphylos uva-ursi (L.) Spreng. (bearberry leaf) on melanin synthesis]

[Article in Japanese]
H Matsuda [1], S Nakamura, H Shiomoto, T Tanaka, M Kubo

Effects of 50% methanolic extract (U-ext) from the leaf of Arctostaphylos uva-ursi (L.) Spreng. (bearberry leaf) on melanin synthesis were investigated in vitro. The U-ext and arbutin isolated from the bearberry leaf had an inhibitory effect on tyrosinase activity. Furthermore, the U-ext inhibited the production of melanin from dopa by tyrosinase and from dopachrome by autoxidation. These results suggest that the bearberry leaf was found to be an effective inhibitor of the production of melanin.

Research Article

A single extraction step in the quantitative analysis of arbutin in bearberry (*Arctostaphylos uva-ursi*) leaves by high-performance liquid chromatography

Irene Parejo, Francesc Viladomat, Jaume Bastida, Carles Codina

First published: 17 August 2001 | https://doi.org/10.1002/pca.602 | Citations: 44

The arbutin content of bearberry leaves was found to vary from 6.30 to 9.16% expressed on a dry weight basis. Autumn is shown to be a better period than spring for the collection of plant material in order to obtain the highest yield of arbutin.

LICORICE EXTRACT

Glycyrrhiza Glabra Root Extract is cultivated extensively in India and has been used in traditional Chinese medicine.

MODE OF ACTIONS

- It acts as dispersing the melanin, inhibit of melanin biosynthesis and decreasing free radical production effect to inhibit cyclooxygenase activity.
- It contain Glabridin, which is polyphenolic flavonoid. It prevents Ultraviolet B induced pigmentation and inhibit superoxide anion and cyclooxygenase activity to exerts anti-inflammatory.
- It contain Liquiritin, which induces skin lightening by dispersing melanin.
- It has been tested in the treatment of melasma with good results and very mild irritation.

REFERENCE STUDIES

The Inhibitory Effect of Glabridin from Licorice Extracts on Melanogenesis and Inflammation

TOMOHIRO YOKOTA, HIROYUKI NISHIO, YASUO KUBOTA, MASAKO MIZOGUCHI

First published: 28 July 2006 | https://doi.org/10.1111/j.1600-0749.1998.tb00494.x | Citations: 229

Glabridin is the main ingredient in hydrophobia fraction of licorice extract affecting on skins. The result shown that topical applications of 0.5% glabridin inhibits UVB-induced pigmentation and erythema. Anti-inflammatory effects of glabridin in vitro were also shown by its inhibition of superoxide anion productions and cyclooxygenase activities.

2011 International Conference on Bioscience, Biochemistry and Bioinformatics
IPCBEE vol.5 (2011) © (2011) IACSIT Press, Singapore

GLYCYRRHIZA GLABRA EXTRACT CREAM: EFFECTS ON SKIN PIGMENT "MELANIN"

It is concluded that the decreased skin melanin content after application of formulation may be attributed to the tyrosinase inhibitory activity of Glycyrrhiza glabra extract, also the antioxidants present in extract may contribute to decrease in skin melanin content.

EXPOSURE SPF 50+ HIGH PROTECTION DAY CREAM

- Zinc Oxide
- Panthenol
- Vitamin E

Enriched with 100% titanium dioxide and zinc oxide, Lancomed Exposure forms a barrier on the skin surface to reflect sun rays. It contains panthenol, a skin-soothing provitamin, to help regenerate the skin barrier. With its antioxidant formula, this SPF Day Cream provides optimal broad-spectrum UVA and UVB protection. Therefore, you can rely on it regarding the prevention of photoaging, cell damage, and other UV related skin diseases.

- Contains no allergic fragrances.
- Activates natural immune and cell protection.
- Prevents sunburn and ageing of the skin.
- Uses Vitamin E to protect the skin from environmental pollution.
- Creates a protective film on the skin surface against UVA and UVB.

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Sunscreens

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Inorganic sunscreens are particles that scatter and reflect UV rays back to the environment. They act as a physical barrier to indent ultraviolet and UV light.

The most commonly used particulate sunscreens are titanium dioxide and zinc oxide. They are considered broad spectrum as they cover the entire ultraviolet spectrum. The inorganic sunscreens are also referred to as sunblocks, a term coined from their mechanism of photoprotection.

ZINC OXIDE

Zinc Oxide is a safe and effective ingredient in photoprotective products. It is photostable, nonphotoreactive. It has little potential for irritation or sensitization. Smaller, micronized zinc oxide is considered as a broad-spectrum UV protectant.

Microfine zinc oxide protects against a wide range of UVA, including UVA 1 (340 to 400 nm). It is very photostable and does not react with other UV filters.

PANTHENOL

When applied topically, D-Panthenol is readily absorbed and rapidly converted enzymatically to pantothenic acid, a constituent of coenzyme A.

Various studies confirmed dexpanthenol's moisturizing and skin barrier enhancing potential. It prevents skin irritation, stimulates skin regeneration.

It has been shown that topical dexpanthenol acts like a moisturizer with barrier-improving properties; in addition, it exerts wound healing effects.

VITAMIN E

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EXPOSURE SPF 50+ HIGH PROTECTION BODY SPRAY

- Combination of chemical sunscreens
- Beta-Glucan
- Panthenol
- Vitamin E

The Exposure SPF 50+ High Protection Body Spray protects the skin from various deleterious effects caused by solar radiation by acting as a free-radical scavenger. It thereby strengthens your skin's natural defence against sunlight. The innovative formula inhibits melanin release by blocking melanocytes, prevents cell damage caused by UVB radiation and slows down premature photoaging. It is enriched with Vitamin E, which has antitumorigenic and photoprotective properties to reinforce the barrier function of the skin and provide a soothing protective film over the skin. The spray contains the natural active ingredient "Witch Hazel Water" which increases skin cell growth and helps to reduce irritation. The product is absorbed by the skin within seconds and leaves no residue. It also provides the skin with the necessary moisture and makes the skin visibly smoother and more radiant.

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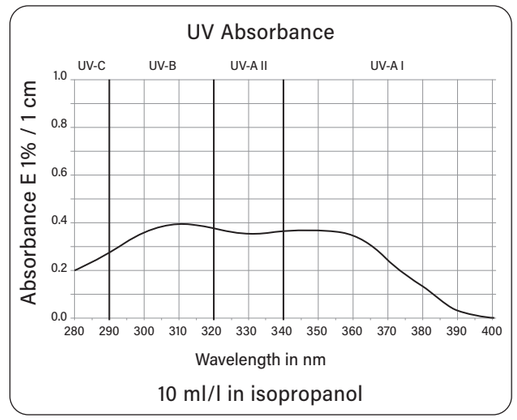
- Benzophenones
- Anthranilates
- Avobenzones
- Ecamsule

UVA & UVB FILTERS

SUNSCREEN AGENT

- Homosalate
- Octocrylene
- Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine
- Butyl Methoxydibenzoylmethane
- Ethylhexyl Salicylate

The combination of UVA & UVB Filters
VERY EFFECTIVE BROAD SPECTRUM ABSORBER



BETA-GLUCAN

Beta-Glucan is a Proteoglycan that is derived from Mushrooms. It has been prepared for the purpose of skin conditioning agents as well as humectant, and anti-irritant agent.

Beta-Glucan which use in EXPOSURE SPF 50+ HIGH PROTECTION BODY SPRAY has been confirmed that contains 92.25% Glucose.

Main Biological effects of Beta-Glucan
Skin moisturizing effects

	Dry Contents (%)	Skin moisturizing Index		
		Before	120 min After	Δ Index
Negative Control	Distillated Water	34.76±6.5	30.93±3.2	-3.83±6.4
Positive Control	Hyaluronic acid (1%)	32.73±5.3	35.88±3.6	3.15±2.4
Test material	RADICAN-S20 (1%)	39.64±8.1	47.71±4.5	8.07±3.1

Coreneometer result

	Dry Contents (%)	TEWL (transepidermal water loss) ($g/h/cm^2$)		
		Before	120 min After	Δ Index
Negative Control	Distillated Water	7.30±2.1	7.38±7.7	0.08±1.4
Positive Control	Hyaluronic acid (1%)	7.70±2.9	5.20±1.6	-2.56±0.4
Test material	RADICAN-S20 (1%)	7.50±5.2	4.10±1.2	-3.40±2.1

Tewameter result

Beta-Glucan has better moisturizing effect than Hyaluronic acid at the same dry content.

Panthenol

When applied topically, D-Panthenol is readily absorbed and rapidly converted enzymatically to pantothenic acid, a constituent of coenzyme A.

Various studies confirmed dexpanthenol's moisturizing and skin barrier enhancing potential. It prevents skin irritation, stimulates skin regeneration.

It has been shown that topical dexpanthenol acts like a moisturizer with barrier-improving properties; in addition, it exerts wound healing effects.

VITAMIN E

Vitamin E: it is an important fat-soluble antioxidant and has been in use for more than 50 years in dermatology.

It protects the skin from various deleterious effects due to solar radiation by acting as a free-radical scavenger.

vitamin E is the treatment of burns, surgical scars, and wounds.

Vitamin E prevents lipid peroxidation of serum from bacterial-induced leakage through follicles and sebaceous glands, thus preventing inflammation due to peroxide irritation.

EXPOSURE SPF 100+ HIGH SOLAR PROTECTION CREAM

- Combination of chemical sunscreens
- Ethylhexyl Salicylate
- Octocrylene
- Homosalate
- Butyl Methoxydibenzoylmethane
- Phenylbenzimidazole Sulfonic Acid

UV Radiation and the Skin

UV radiation (UV) present in sunlight is classified as a "complete carcinogen" because it is both a mutagen and a non-specific damaging agent and has properties of both a tumor initiator and a tumor promoter. Throughout the lifetime, human accumulate damage generated by UV radiation. UV causes inflammation, immune changes, physical changes, impaired wound healing and DNA damage that promotes cellular senescence and carcinogenesis. However, UV also benefits human health by mediating natural synthesis of vitamin D and endorphins in the skin, therefore UV has complex and mixed effects on human health.

TYPE OF UV RADIATION

UV radiation is one part of the electromagnetic spectrum measuring in wavelength from 100 to 400 nanometers (nm). There are three subtypes of UV radiation:

- UVA having the longest wavelengths (315–400 nm): penetrate deep into the skin, through the epidermal junction where the melanocytes reside in the basal layer and are primarily responsible for premature skin aging.
- UVB being mid-range (290–320 nm): creates a tan by increasing melanin production that confers a minimal amount of photoprotection, and also indicates damage to the skin. Overexposure to UVB radiation causes erythema, swelling, and pain, the characteristic signs of sunburn, which generally take several hours to develop.
- UVC being the shortest wavelengths (100–280 nm).

Ambient sunlight is composed primarily of UVA (90%–95%) and UVB (5%–10%) energy, with most solar UVC absorbed by the ozone layer.

UV AND PIGMENTATION

The regulatory mechanisms that lead to pigmentation are complex and at present not completely understood. However, extensive data suggest that UV-induced DNA damage and/or its repair produce initiating signals that induce an increase in melanogenesis after UV irradiation.

NATURAL SKIN PIGMENTS FOR PHOTOPROTECTION: MELANIN AND MELANOGENESIS

Skin tone is related to the presence of several biochromes that contribute to the defense against solar radiation, the most important colored biomolecules determining skin color is melanin.

Melanin is produced in specialized cells called melanocytes that are mostly distributed in the epidermal–dermal junction, and then distributed to surrounding keratinocytes, which are the most abundant cells in the epidermis. The physiological response of skin against solar radiation depends on the production, distribution, type, and quantity of melanin synthesized in melanocytes and transferred to keratinocytes as well as skin thickness.

Melanin content in the basal layers of the epidermis is substantially higher in Black skin compared to Asian or White skin, although the number of melanocytes is virtually identical in skins of different ethnicity.

Human skin contains two types of melanin: eumelanin and pheomelanin. Their ratio determines the race and the Fitzpatrick skin phototype.

Eumelanin is dark, from black to brown, whereas pheomelanin is a red or yellow pigment. Pheomelanin is predominant in light phenotypes, blond or red hair. Eumelanin is much more photoprotective than pheomelanin. In fact, after UV exposure, pheomelanin can easily become a photosensitized agent by stimulating lipid peroxidation and other reactions leading to a high amount of ROS and subsequent undesirable reactions, it is prone to photodegradation, sun-induced erythema and edema in fair-skinned individuals.

In all skin types, DNA damage occurs to a greater extent in the upper layers of the epidermis, while the lower layers of the skin are protected as the melanin content of the skin increases.

Sunscreens

Sun exposure without skin protection can be harmful anytime and anywhere, particularly during the summertime. Sunscreens are used worldwide as an integral part of the photoprotection strategy.

Chemical sunscreens are known as organic sunscreens. Their mechanism of action is based on their chemical structure involving an aromatic compound conjugated with a carbonyl group. This structure allows high-energy UV rays to be absorbed, causing the molecule to achieve an excited state. As the molecule returns to the ground state, it will release the lower energy of longer wavelengths. Broad-spectrum sunscreens absorb UV radiation from both the UVA and UVB portions.

UVB BLOCKERS INCLUDING

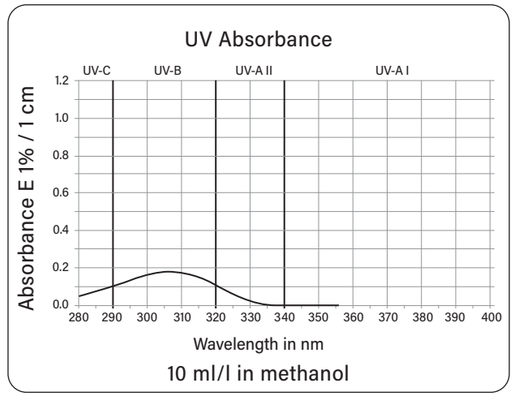
- Aminobenzoates
- Cinnamates
- Salicylates
- Octocrylene
- Ensulizole
- Camphor derivatives

UVA BLOCKERS INCLUDING

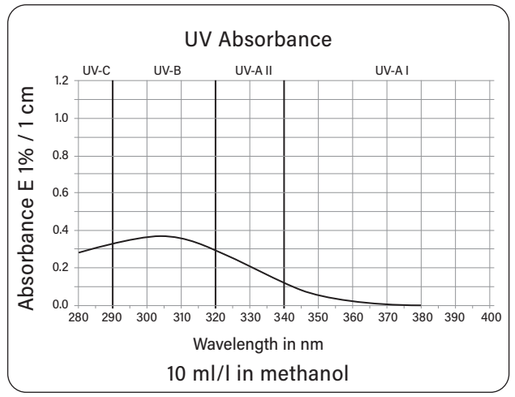
- Benzophenones
- Anthranilates
- Avobenzones
- Ecamsule

Sunscreen SPF 100 Cream

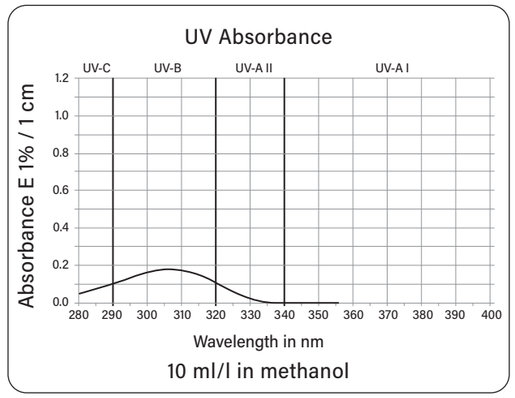
Ethylhexyl Salicylate



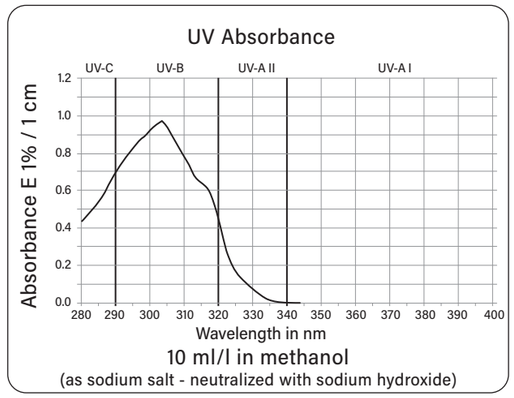
Octocrylene



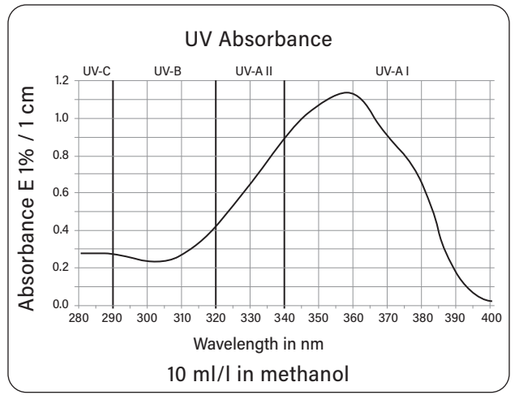
Homosalate



Phenylbenzimidazole Sulfonic Acid



Butyl Methoxydibenzoylmethane



The combination of UVA & UVB Filters
VERY EFFECTIVE BROAD-SPECTRUM ABSORBER

VITAMIN E

Vitamin E: it is an important fat-soluble antioxidant and has been in use for more than 50 years in dermatology.

- It protects the skin from various deleterious effects due to solar radiation by acting as a free-radical scavenger.
- Vitamin E is the treatment of burns, surgical scars, and wounds.
- Vitamin E prevents lipid peroxidation of serum from bacterial-induced leakage through follicles and sebaceous glands, thus preventing inflammation due to peroxide irritation.

LYSOME HYPER PIGMENT DISCOLORATION CORRECTOR SERUM

- Hydroxyphenoxy Propionic Acid
- Undecylenoyl phenylalanine
- Hedychium Coronarium Root Extract
- Alpha-Arbutin

This Hyper Pigment Discoloration Serum is designed to suppress the enzymes that stimulate melanin. It reduces skin pigment production and increases skin luminosity. It contains a unique formula that slows the process by which UV light causes pigmentation, preventing pigmentation problems. Lysome Serum is safe and effective for dark spots, age spots and hyperpigmentation. It also helps to prevent cell damage caused by UVB radiation and reduces the release of inflammatory cytokines.

- Protects against infrared radiation and its effects.
- Visibly reduces black spots to illuminate the skin complexion.
- Reduces autophagy faced to UVA and blue light.
- This serum is non-irritating and non-comedogenic.
- Contains no allergic fragrances.

RADIANSKIN™

Hydroxyphenoxy Propionic Acid is a pure molecule whose safety has been widely demonstrated within the recommended use conditions and which erases dark spots from the face and the hands.

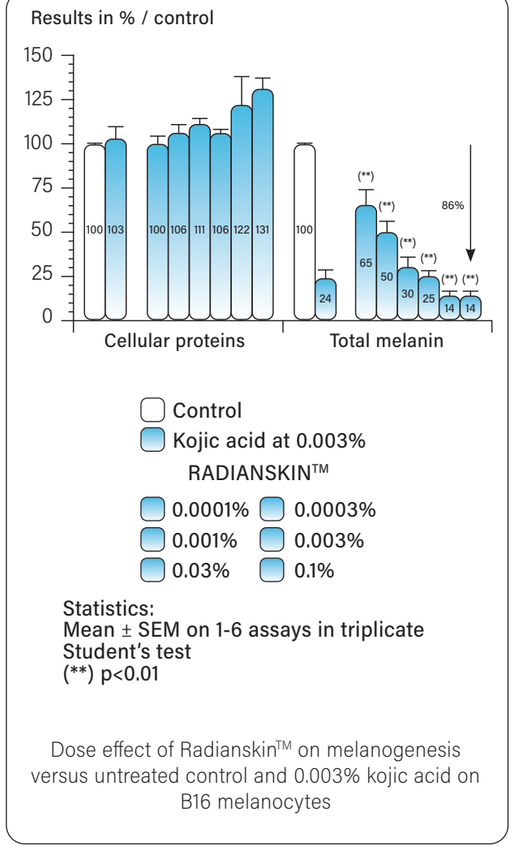
MECHANISM OF ACTION

- Blocking the release of melanin by the melanocytes, an alternative to the inhibition of tyrosinase, pathway already broadly investigated.
- Prevents the cell damage caused by UVB radiation and reduces the release of inflammatory cytokines. Therefore it helps slow down the premature photoaging of the skin.

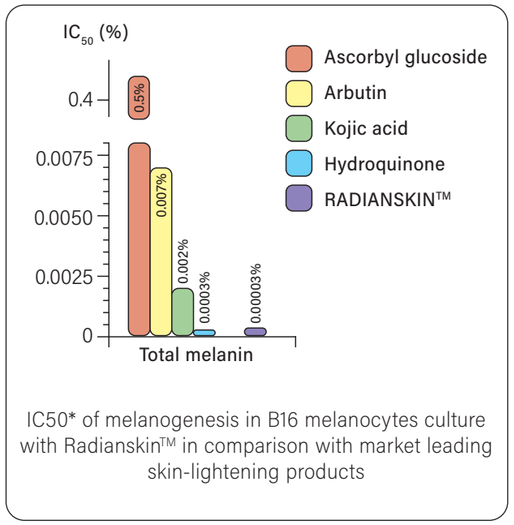
IN VITRO STUDIES

It safely reduces melanogenesis with greater in vitro efficacy than leading products

Evaluate the ability of Hydroxyphenoxy Propionic Acid to reduce melanogenesis on B16 melanocytes in cell culture, in comparison with market leading skin brightening products.



Dose effect of Radianskin™ on melanogenesis versus untreated control and 0.003% kojic acid on B16 melanocytes



IC50* of melanogenesis in B16 melanocytes culture with Radianskin™ in comparison with market leading skin-lightening products

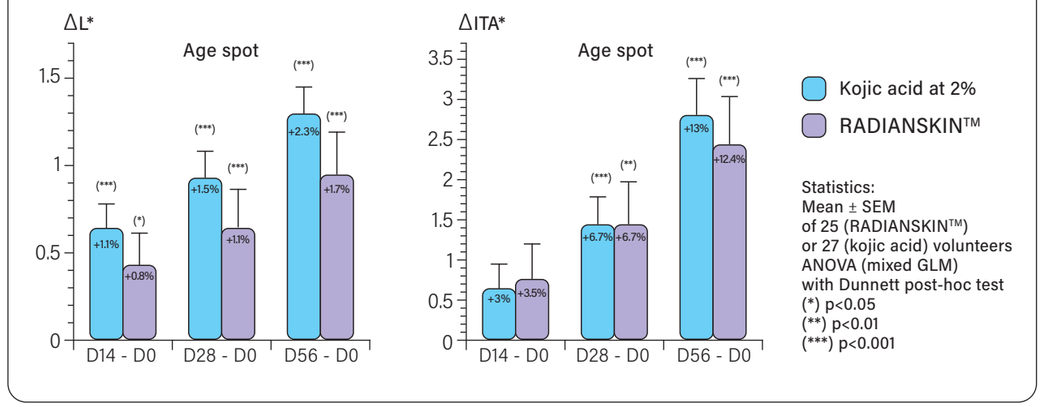
Results: From very low concentrations, Hydroxyphenoxy Propionic Acid reduces melanogenesis by up to 86% with a dose-dependent effect and no cytotoxicity.

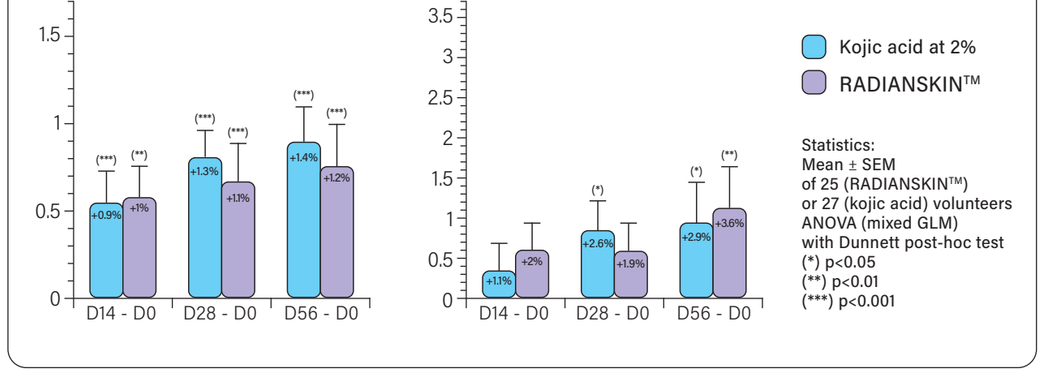
Results: Hydroxyphenoxy Propionic Acid shows a greater depigmenting effect than ascorbyl glucoside, kojic acid and arbutin, and equivalent efficacy to hydroquinone without cytotoxicity.

IN VIVO STUDIES ON FACE

Within 14 days, Hydroxyphenoxy Propionic Acid reduces age spots and unifies the complexion with similar efficacy to 2% kojic acid.

Evaluate the ability of Hydroxyphenoxy Propionic Acid to reduce age spots and unify the complexion





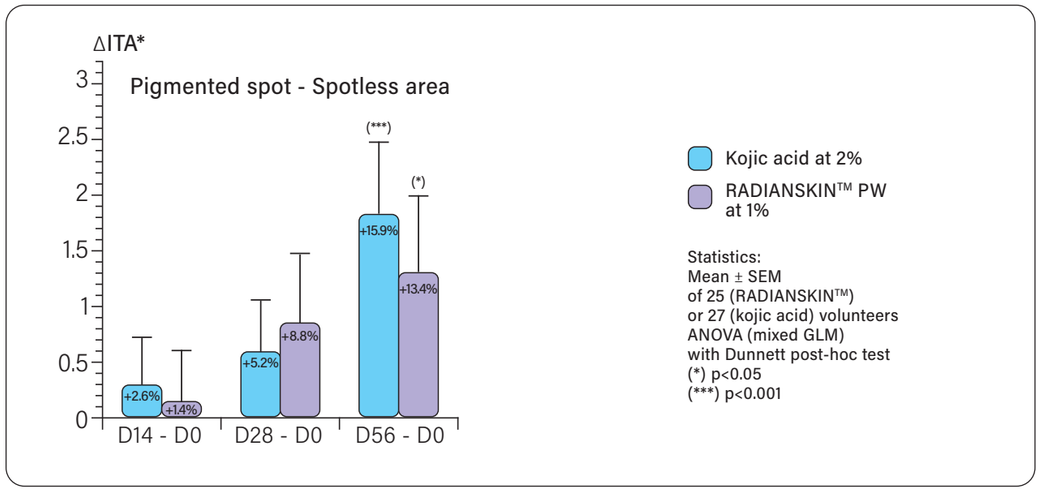
Results: The lightening effect of Hydroxyphenoxy Propionic Acid is shown from 14 days in a significant and proportional increase in the parameters (L* and ITA°) vs before treatment. This efficacy is similar to that of the leading product (2% kojic acid).

Test conducted on a panel of 25 Asian women presenting age spots after 8 weeks of twice-daily use of 1% Hydroxyphenoxy Propionic Acid and 2% kojic acid (benchmark) on each half of the face.

IN VIVO STUDIES ON FACE

Within 14 days, Hydroxyphenoxy Propionic Acid reduces age spots and unifies the complexion with similar efficacy to 2% kojic acid.

Evaluate the ability of Hydroxyphenoxy Propionic Acid to reduce age spots and unify the complexion



ΔITA° with percentage of improvement between areas with and without age spots versus (D0).

The efficacy of Hydroxyphenoxy Propionic Acid on complexion evenness is shown after 56 days with up to 13.4% increase in the difference in the ITA° parameter between areas with and without age spots

From 14 days, Hydroxyphenoxy Propionic Acid reduces age spots and the contrast between age spots and spotless areas, giving visibly even and brighter skin.

UNDECYLENOYL PHENYLALANINE

SEPIHWHITE

MSH MECHANISM OF ACTION α-MSH ANTAGONIST

1. **Strong affinity with the α-MSH-receptor MC1R: 96%**
   - MC1R: melanocytes transmembrane receptor, activated by α-MSH.
   - It stimulates the eumelanin (brown-black pigment) synthesis cascade.
   - α-MSH: hormone causing melanin synthesis in response to UV rays.
2. **Inhibits adenylate cyclase: 100%**
   - Adenylate cyclase: transmembrane protein activated by MC1R, it produces cAMP from ATP.
3. **Decreases intracellular cAMP in melanocytes: -34%**
   - cAMP: second messenger, enables transduction of a signal from the exterior to the interior of the cell.
4. **Inhibits protein kinase A: 100%**
   - Protein kinase A: activated by 4 cAMP molecules (cofactor). This activates tyrosinase by phosphorylation.
5. **Inhibits tyrosinase: -83%**
   - Tyrosinase: enzyme that catalyzes melanin production by tyrosine oxydation.

UNDECYLENIC ACID Plant derived

PHENYLALANINE Key essential amino acid

IN VIVO TEST

SUPERFAST EFFICACY ON PHOTOTYPES IV &V FROM 7 DAYS

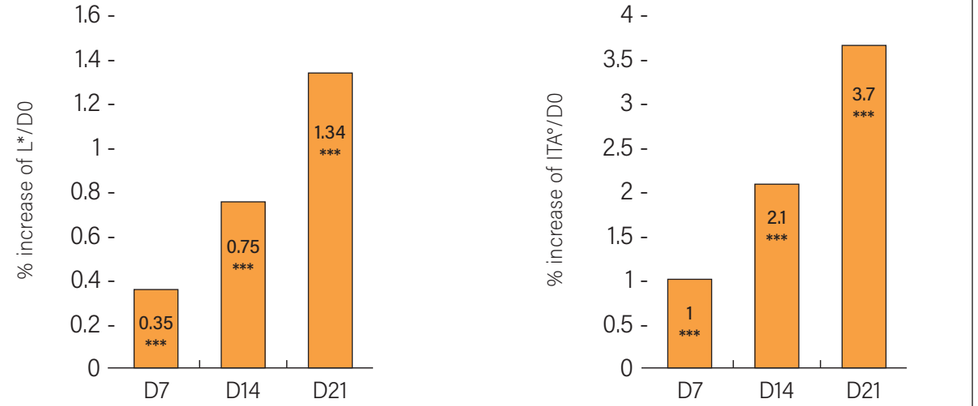
Protocol:

- Volunteers: 22 Indian & African women with **phototypes IV & V**
- Formula at 2% of Undecylenoyl phenylalanine applied on the forearms, 2 times a day for 21 days

Evaluation:

- Spectrocolorimeter
- Self evaluation
- Pictures

Clinical efficacy of 2% Undecylenoyl phenylalanine African & Indian skins



Volunteers with positive effects

L*: skin luminosity

ITA°: individual typology angle / lightening effect

a*: erythema parameter

***p<0.001

IN VIVO TEST

SUPERFAST EFFICACY ON PHOTOTYPES IV &V ON DARK SPOTS

Protocol:

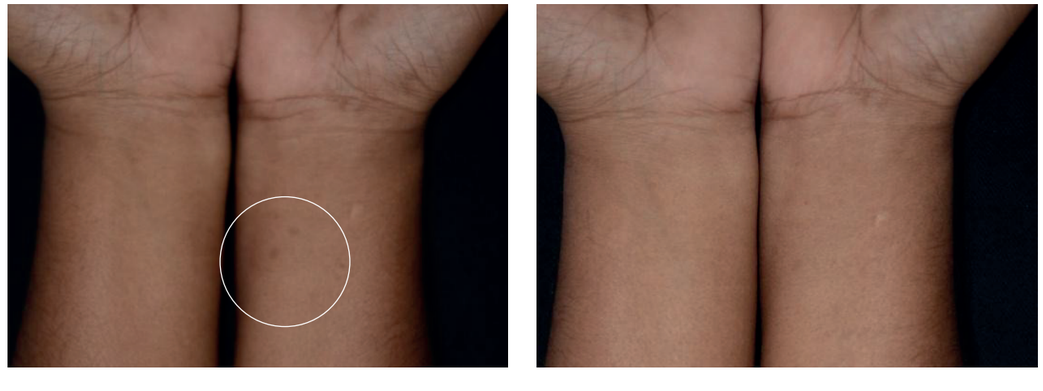
- Volunteers: 22 Indian & African women with phototypes IV & V.
- Formula at 2% of Undecylenoyl phenylalanine applied on the forearms, 2 times a day for 21 days.

Evaluation:

- Spectrocolorimeter.
- Self evaluation.
- Pictures.

Undecylenoyl phenylalanine visibly reduces dark spots & illuminate the complexion on dark skins.

Visible reduction of number of dark spots (for 83% of the concerned volunteers with spots)



IN VIVO TEST

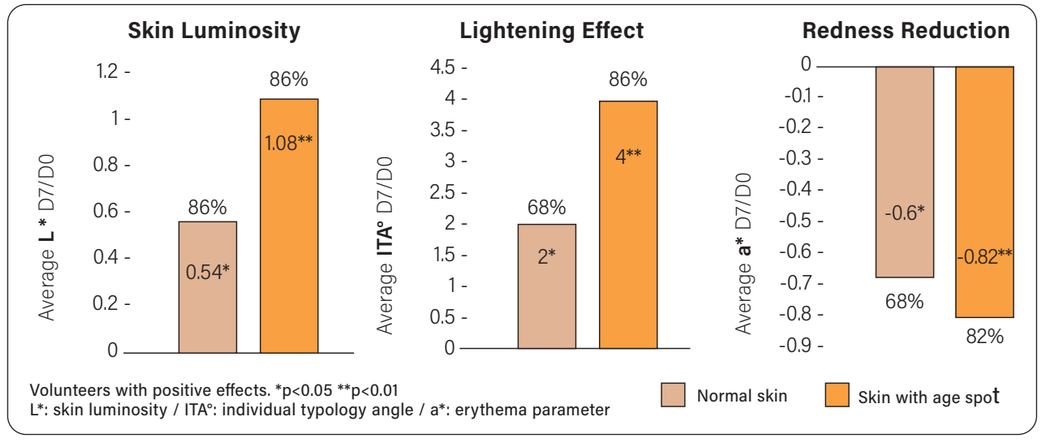
SUPERFAST EFFICACY ON PHOTOTYPES III & IV FROM 7 DAYS

Protocol:

- Volunteers: 23 Thai women / presenting age spots / aged 36-59 years / phototypes III & IV.
- Formula at 2% of Undecylenoyl phenylalanine applied on the entire face, twice a day for 7 days.

Evaluation on the entire face and areas with spots by chromameter.

In only 7 days, Undecylenoyl phenylalanine reveals skin radiance without irritation.



UNDECYLENOYL PHENYLALANINE

IN VIVO TEST

LONG TERM EFFICACY ON PHOTOTYPES II & III AFTER SUN TAN: PREVENTION OF SPOTS

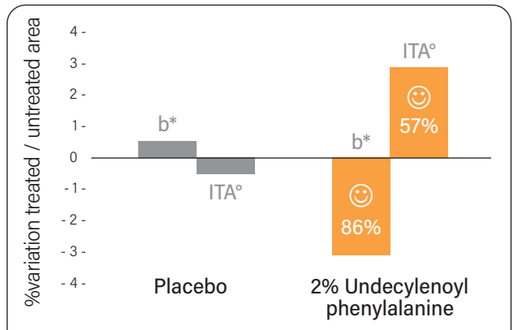
Protocol:

- Volunteers: 14 Caucasian women / Phototype II or III.
- Irradiation (UV 0.8DEM) of application areas on the back at D0, D2 and D4.
- Formula at 2% Undecylenoyl phenylalanine applied on the back, 2 times per day starting D7, for 49 days.

Evaluation

- Measurement of the lightening activity By a chromameter.

Lightening effect & melanization parameter after 49 days



volunteers with positive effects.
ITA°: individual typology angle
b*: melanization parameter (skin "less yellow")

Skin is lighter (Increase ITA°) & less "yellow" (decrease b*: melanization parameter).

Undecylenoyl phenylalanine increase skin luminosity & prevent the appearance of spots on tanned skins.

HEDYCHIUM CORONARIUM ROOT EXTRACT SAKADIKIUM™

Hedychium coronarium root extract is extracted from the rhizomes of wild butterfly ginger. The rhizomes are the reserve of vital metabolites for the plant. They are mainly composed of sugars, a real energetic source.

THE PHYTOCHEMISTRY OF THE EXTRACT

- Monosaccharides & Disaccharides: present: glucose, fructose, disaccharide saccharose, mannose and galactose traces.
- Polysaccharides < 5% of total sugars: Benefits for humectant, skin barrier, tissus regeneration.

Hedychium coronarium root extract (as RM) contains 35% to 65% of total sugars on equivalent dry extract.

IN VIVO TEST

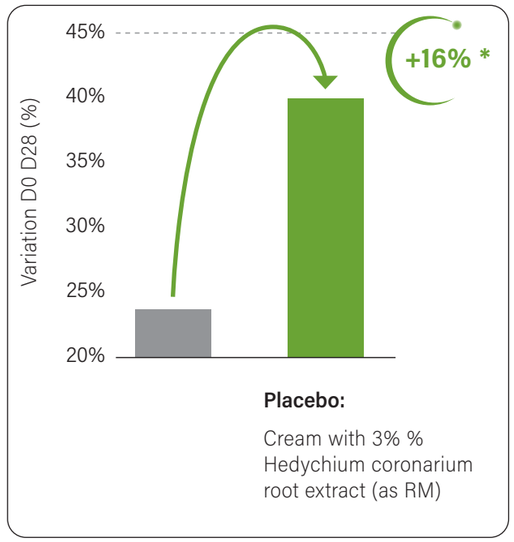
VISIBLE BRIGHTNESS PERCEPTION
PERCEPTION OF TRAINED EVALUATORS OF BRIGHTENING EFFECT

Protocol:

- 2 groups of 20 Women from 45 to 55 years old, stressed & active urban smokers (10 cigarettes per day).
- Cream containing 3% Hedychium coronarium root extract (as RM) vs placebo.
- Application twice a day on the face.
- 28 days of application.
- Scoring (0 to 9) at D0 & D28 by trained evaluation technicians.

The brightening effect is 16% higher with 3% Hedychium coronarium root extract (as RM) vs placebo.**

Perception of trained evaluators
Brightening effect with a cream containing 3% Hedychium coronarium root extract (as RM) vs placebo (scoring scale 0 to 9) at D0 & D28



* statistically significant (test t: 0,05)
** As RM = as raw material

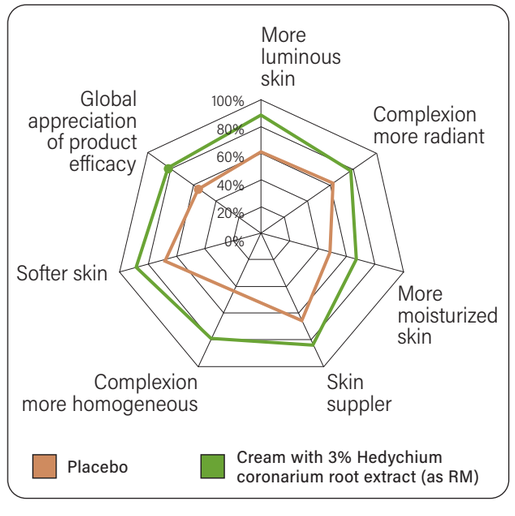
VISIBLE BRIGHTNESS PERCEPTION
SELF EVALUATION

Protocol:

- 2 groups of 20 Women from 45 to 55 years old, stressed & active urban smokers (10 cigarettes per day).
- Cream containing 3% Hedychium coronarium root extract (as RM) vs placebo.
- Application twice a day on the face.
- 28 days of application.
- Self evaluation by the panel volunteers.

As Delta cream with 3% Hedychium coronarium root extract (as RM) versus placebo is >15% for each of those criteria, we are very confident in assuming benefits from Hedychium coronarium root extract (as RM).

Panel volunteers self-evaluation % of people perceiving an improvement with a cream containing 3% Hedychium coronarium root extract (as RM) or with placebo



REGULATION OF AUTOPHAGY
INNOVATIVE PATHWAY TO CLEAN THE CELLS

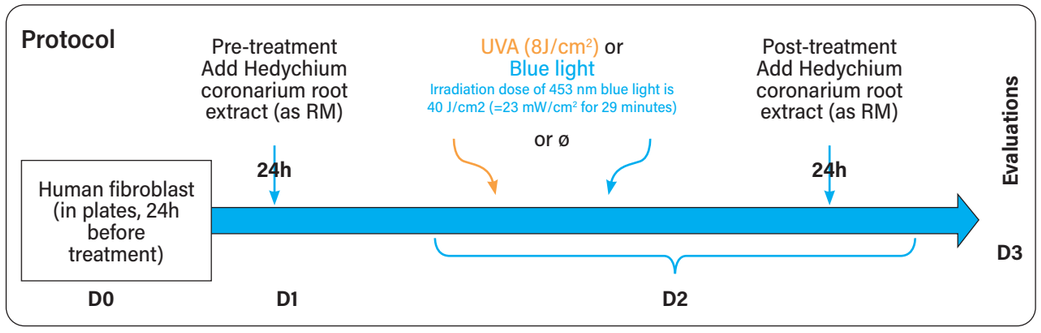
Autophagy controls important physiological functions where cellular components need to be degraded and recycled. This cleansing mechanism involves mainly the lysosomes, a digestive system of cells that "eats" damaged compounds in the cells (proteins, carbohydrates and lipids).

* *Lysosomes are cellular organites whose function is to clean part of its undesirable content via autophagy. The action of lysosomes is facilitated by about forty enzymes.*

The 2016 Nobel Prize in Physiology or Medicine to Yoshinori Ohsumi for his discoveries of mechanisms for autophagy.

REGULATION OF AUTOPHAGY
REGULATION OF AUTOPHAGY FACED TO BLUE LIGHT & UV

IN VIVO TEST



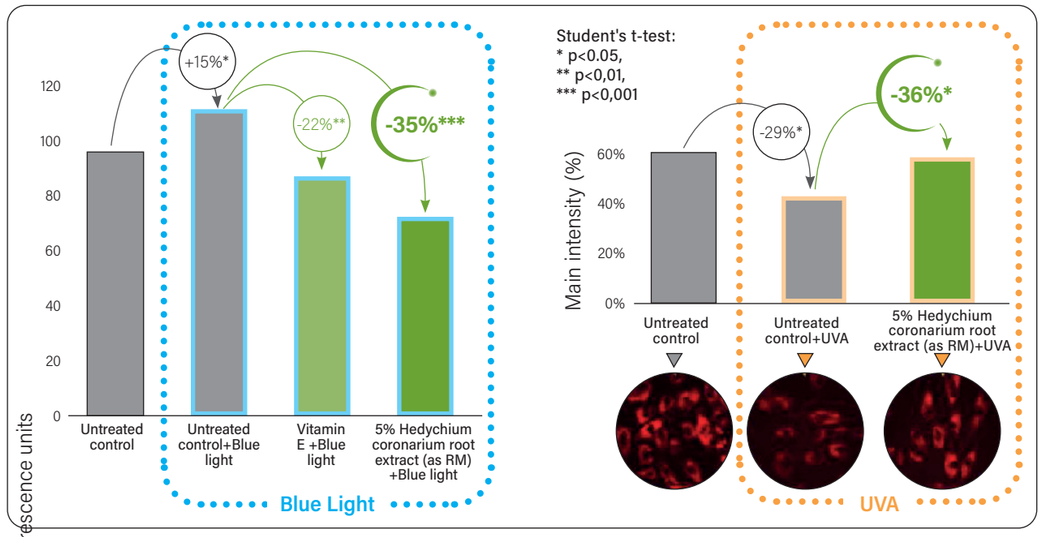
- **Lysosomal autophagic activity** after blue light irradiation is measured with a specific probe (MDC, monodansylcadaverin with Tecan Safire II machine) vs irradiated suitable control & vs irradiated Vitamin E - 200µM.
- **Lysosomal network protection** against UVA irradiation is measured with a fluorescent probe selecting organelles acids like lysosome (LysoTracker®) vs irradiated suitable control. The probe is more selective for acidic organelles than the classically used neutral red or acridine orange dyes.

REGULATION OF AUTOPHAGY
REGULATION OF AUTOPHAGY FACED TO BLUE LIGHT & UV

RESULT

Lysomal autophagic activity measurement (with 0,5%Hedychium coronarium root extract (as RM) + Blue light

Lysomal network protection (with 0,5%Hedychium coronarium root extract (as RM) + Blue light



- Hedychium coronarium root extract (as RM) regulates autophagic activity on fibroblasts exposed to blue light for a detoxification benefit. Hedychium coronarium root extract (as RM) protects the cells. Then the autophagic activity does not need to be over-expressed.
- Hedychium coronarium root extract (as RM) protects the lysosomal network on fibroblasts exposed to UVA thanks to a barrier effect (Zhao Y et al., 2013, J.Invest. Dermatol., 133(6): 1629-37). This spectrum of light is known to induce autophagy in skin cells.

Alpha-Arbutin

Arbutin is a compound of hydroquinone and D-glucose, and it has been over 30 years since there have been serious studies on the skin lightening action of this substance.

- Arbutin has the effect of reducing melanin content at a concentration that has little effect on the viability of cultured human melanocytes.
- Arbutin was shown to inhibit melanin production in B16 cells stimulated by α-MSH and abrogate the hyperpigmentation effects of α-MSH in brownish guinea pig and human skin explants in organ culture experiments.
- Kiato et al. reported that α-arbutin inhibited monophenolase activity of mushroom TYR with potency slightly lower than arbutin or hydroquinone.
- Funayama et al. reported that α-arbutin inhibited diphenolase activity of TYR derived from murine melanoma 10 times more potently than β-arbutin.
- The treatment of the human skin model with α-arbutin (250 µg per tissue) reduced melanin content to a 40% level of the control, without causing cell death. These results indicate that alpha-arbutin is an effective and safe ingredient for skin-lightening.
- The study group (n = 54) applied the cream containing the plant extract (final concentration of arbutin 2.51%) twice a day on the discolored side for 8 weeks. The results showed that the cream with the plant extract decreased melanin level in the skin pigmentation spot, compared to the control group (n = 48) applied with a placebo cream without the active ingredient. During 8 weeks of application, the melanin level of the test group decreased from 182.60 ± 39.41 to 168.76 ± 36.30 ($p < 0.000001$), and there was no significant change from 158.9 ± 34.41 to 166.84 ± 39.72 in the control group. Clinical improvement was observed in 75.86% of the female patients with melasma and 56.00% of the female patients with solar lentigines.

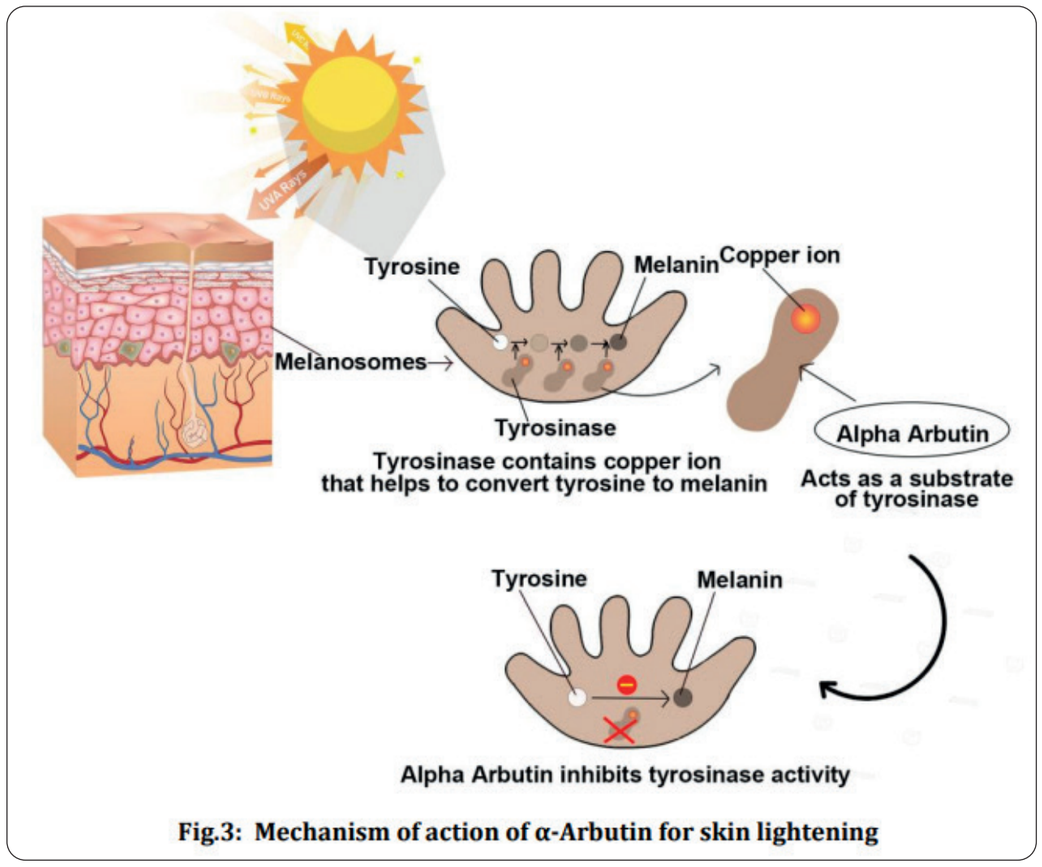


Fig.3: Mechanism of action of α-Arbutin for skin lightening

Alpha Arbutin as a Skin Lightening Agent: A Review. NIKHIL CHANDORKAR, SRUSHTI TAMBE, PURNIMA AMIN, CHANDU S MADANKAR. International Journal of Pharmaceutical Research | Apr - Jun 2021 | Vol 13 | Issue 2

SEBOSTASE HYDRO PURIFIYING FACE GEL

- Vitamin E
- Vitamin B5
- Allantoin
- Sulfate Free

Vitamin E

Vitamin E is a group of lipophilic compounds. It is exclusively synthesized by plants.

- It has been used for over 50 years in dermatology and plays an important role in maintaining skin health, and.
- It has antioxidant activity. For the skin, protecting the epidermis and dermis against oxidative stress induced by environmental factors.
- It is ability to scavenge free radicals and become part of lipid structures, it protects against lipid peroxidation and slows skin ageing due to its the major lipid-soluble antioxidant in humans.
- Some research also indicates that vitamin E displays strong photoprotective, firming, hydrating and anti-ageing properties, as well as improving the elasticity, structure and softness of the epidermis and dermis.
- It is thought that vitamin E, integrated into the intercellular cement and lipid structures, protects the skin against solar UVB radiation thus, against skin redness.
- It plays a role in the healing of wounds of varying aetiology; in the treatment of dermatological conditions such as subcorneal pustular dermatoses, cutaneous amyloidosis, atopic dermatitis, epidermolysis bullosa, psoriasis, acne vulgaris and scleroderma; in skin cancer prevention; and in the treatment of Hailey–Hailey disease.
- Butt et al. evaluated the usefulness of vitamin E in protecting skin against thermal trauma. The results indicated that the clinical transplantation of keratinocytes preconditioned with vitamin E alone or in combination with skin fibroblasts in skin substitutes, could be used to treat thermally damaged skin.

VITAMIN B5

Dexpanthenol is enzymatically oxidized to pantothenic acid, which is distributed into the tissues, mainly as coenzyme A which serves as a cofactor for enzyme-catalyzed reactions.

- Particularly in Europe, it has been used in the treatment of wounds and in skin care for decades.
- Topical dexpanthenol acts as a moisturizer, improving stratum corneum hydration, reducing transepidermal water loss and maintaining skin softness and elasticity.
- It activates fibroblast proliferation, which is of relevance in wound healing, has been observed both in vitro and in vivo.
- It has been shown to have an anti-inflammatory effect on experimental ultraviolet-induced erythema.
- Local use of dexpanthenol was highly effective in the treatment or prevention of skin irritancy.

ALLANTOIN

Allantoin has been used in cosmetic and pharmaceutical preparations for over 70 years with different therapeutic purposes and especially as a wound healing booster. It is found in plants like Comfrey.

- Allantoin (comfrey root) from a synthetic derivative known as aluminum dihydroxy allantoinate. It has been marketed as moisturizer to prevent dryness and irritation as well as keratolytic properties to soften the skin.
- It has calming effect and wound healing properties; it is often used for skin rashes and irritation.
- It decreases Transepidermal Water loss (TEWL) and retain water in skin. It acts as skin moisturizer.

SEBOSTASE ATOPIC NEURO CREAM

- Madecassoside: 0.20% (Main active ingredient)
- CeramideBIO + α-Bisabolol: 0.50% (as raw material)
- Palmitoyl-tripeptide-8: 0.30% (as raw material)
- Saccharide Isomerate: 1.00% (as raw material)

SEBOSTASE ATOPIC NEURO CREAM suitable for dry or sensitive skin prone to irritation, flaking and desquamation. Formulated with a biomimetic complex, it combines nature with scientific and technical restructuring agents. For this reason, this neuro cream provides a continuous basic requirement for proper hydration and optimal skin comfort. It works by preventing or reversing neurogenic signs to provide efficient soothing benefits. It also provides the skin with essential restorative elements for its comfort.

- Intensely nourishes and repairs the skin.
- Provides a unique skin barrier recovery complex by tapping moisture.
- Helps control the symptoms of psoriasis and prevent reoccurrence.
- This cream is non-irritating and non-comedogenic.
- Contains no allergic fragrances.

Dermatitis/Eczema

Eczema is the name for a group of conditions that cause the skin to become itchy, inflamed and red in lighter skin tones or brown, purple, gray or ashen in darker skin tones. Eczema is very common. In fact, more than 31 million Americans have some form of eczema.

TYPES OF ECZEMA

According to National Eczema Association, there are seven different types of Eczema:

- Atopic dermatitis.
- Contact dermatitis.
- Neurodermatitis.
- Dyshidrotic eczema.
- Nummular eczema.
- Seborrheic dermatitis.
- Stasis dermatitis.

Atopic Dermatitis (AD)

ATOPIC DERMATITIS (AD)

It is a specific form of eczema, and it is the most common chronic inflammatory skin disease.

Atopic dermatitis has a complex etiology including environmental factors and genetic which lead to abnormalities in the epidermis and the immune system.

CAUSE OF AD

- Atopic dermatitis is part of the atopic triad (atopic dermatitis, allergic rhinoconjunctivitis, and asthma). Patients with the atopic triad have a defective barrier of the skin, upper respiratory, and lower respiratory tract which leads to their symptomatology.
- If one parent is atopic, there is more than a 50% chance that their offspring will develop atopic symptoms. If both parents are affected, up to 80% of offspring will be affected.
- Genetic alterations include loss of function mutations of filaggrin (Filament Aggregating Protein), an epidermal protein that is broken down into natural moisturization factor. Filaggrin mutations are present in up to 30% of atopic dermatitis patients and may also predispose patients to ichthyosis vulgaris, allergic rhinitis, and keratosis pilaris.

EPIDEMIOLOGY

Atopic dermatitis is seen in approximately 10% to 30% of children and 2% to 10% of adults in developed countries.

It is divided into three subsets based on the age of onset:

- **Early-onset atopic dermatitis** (birth to 2 years old): most common type of atopic dermatitis, with approximately 60% of cases starting by age 1. Sixty percent of cases resolve by 12 years old.
- **Late-onset atopic dermatitis:** symptoms begin after the onset of puberty.
- **Senile onset atopic dermatitis:** an unusual subset with onset in patients older than 60 years old.

PATHOPHYSIOLOGY

Atopic dermatitis patients have a defective skin barrier that is easily affected to xerosis and environmental irritants and allergens that lead to inflammation, and the classic clinical findings of atopic dermatitis.

The defective skin barrier allows irritants and allergens to penetrate the skin and cause inflammation. Scratching of the skin also stimulates keratinocytes to release inflammatory cytokines.

TREATMENT / MANAGEMENT

There are four main components:

- Trigger avoidance.
- Daily skin care.
- Anti-inflammatory therapy.
- Other complementary modalities.

Neurodermatitis

NEURODERMATITIS

It is a skin condition usually confined to one or two patches of skin. It affecting up to 12% of the total population, and women are more affected than men. It rarely goes away without treatment, and continued scratching can irritate nerve endings in skin, intensifying both itching and scratching. Over time, chronic scratching causes itchy patches of skin to become dry, leathery and thickened, called lichenification. Neurodermatitis is also known as lichen simplex chronicus.

CAUSE OF NEURODERMATITIS

The exact cause of neurodermatitis is not entirely understood, It may be that this disease develops when nerves in your skin overreact with trigger such as environmental factors, systemic disorders, and psychological factors.

TREATMENT / MANAGEMENT

National Eczema Association reported that treatment for neurodermatitis is aimed at healing skin and ending the itch-scratch cycle.

- Use Corticosteroids to help calm inflammatory and itch as well as soften thickened skin.
- In case of skin very thick, dermatologist may inject a steroid into the patch.
- Use non-steroid such as calcineurin inhibitors and ointment to control itch.
- Use occlusive treatments to cover the affected area can help control itching and make it harder to scratch.
- Use some oral medication.
- Use moisturizer daily, cool compresses and wearing loose-fitting, non-irritating clothing while keep fingernails short limits damage cause by scratching.

Madecassoside

It is a pure active ingredient (95%) from Centella asiatica leaves.

MODE OF ACTION

- Soothing Action:
  - Reducing the overproduction of inflammation mediators (IL-1α. PGE2).
  - Reducing the PNNs adhesion to keratinocyte, responsible of self-induces inflammation.
  - Cell protection against psoriatic environment (SKALP).
- Respect & protection of cells:
  - Preservation of proliferative potential of keratinocyte (HLE).
  - Antioxidant activity.
- Skin barrier & Moisturization:
  - Increase Filaggrin, source of NMF and structural protein of cornified envelope (reduces by inflammatory cytokines).
  - Increase Aquaporin-3, involved in water circulation within the epidermis.
- Dermal matrix restructuration & protection
  - Increase collagen type I & III.
  - Decrease MMp-1, (TNFα).

IN VIVO TESTS FOR MODERATE PSORIASIS-PRONE SKIN

Protocol tests

- Double-blind study vs placebo.

  (Ref: 16 - Dermscan 14D0393).
- **2 Tested products:**

  P1: Placebo / P2: Placebo **+ 0.2% MADECASSOSIDE**, applied twice daily on defined zone of the body (with/without lesions), during 56 days.
- **Panel:** 23 volunteers & 2 groups (1 of 10 using Madecassoside & 1 group of 12 using placebo), boys & girls (aged from 5 months to 7 years old), with light atopic dermatitis (EASI[1] score from 1 to 4).
- **Analyse:**

  Evaluation of the redness/desquamation/ roughness by a dermatologist - scale from 1 (none) to 5 (severe) [1]EASI: Eczema Area Severity Index.

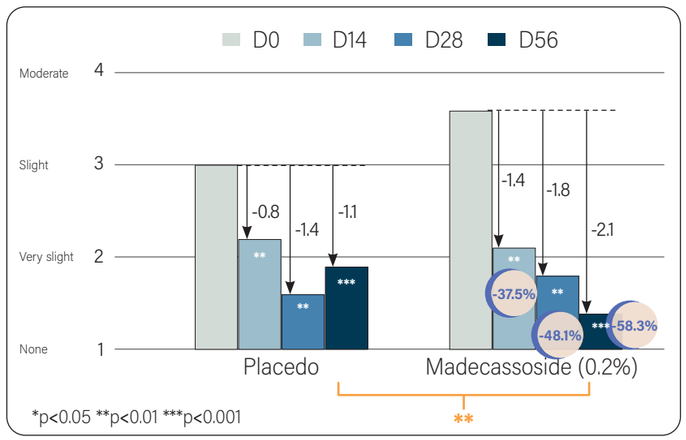
Evaluation Tests:

- The redness (erythema score).
- The desquamation.
- The roughness.

Realized by a dermatologist.

Scale from 1 (none) to 5 (severe).

Erythema score reduction

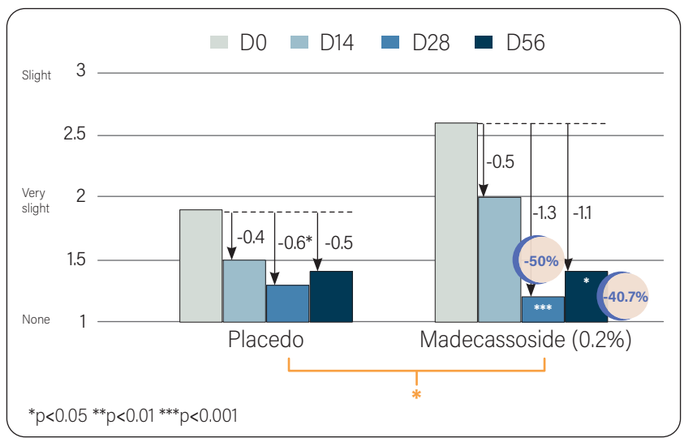


After 56 days, MADECASSOSIDE at 0.2% significantly reduces redness:

- -58.3%*** vs. D0.
- 1.6* times vs. placebo.

MADECASSOSIDE reduces redness.

Desquamation reduction score

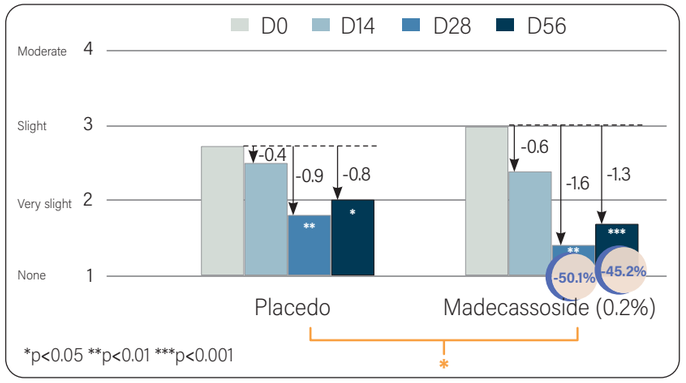


After 28 days, MADECASSOSIDE at 0,2% significantly reduces desquamation:

- -50%*** vs. D0.
- 2.6* times vs. placebo.

MADECASSOSIDE makes the atopic dermatitis prone skin smoother!

Roughness score reduction



After 28 days, MADECASSOSIDE at 0,2% significantly reduces roughness:

- -50.1%** vs. D0.
- 1.5* times vs. placebo.

MADECASSOSIDE reduces roughness skin.

IN VIVO TESTS FOR MODERATE PSORIASIS-PRONE SKIN

Protocol tests:

- **2 Tested products:**

  Formula with 0.2% MADECASSOSIDE vs. Placebo

  Application for 56 days, twice a day.

- Panel: 2 groups of volunteers <u>with moderate psoriasis:</u>

  local PASI* = 5-9 scored by a dermatologist

→ 13 volunteers with 0.2% MADECASSOSIDE

→ 10 volunteers with Placebo

- **Analyse:**

  Evaluation realized by a dermatologist - Scale from 1 (none) to 5 (severe)

- **Histological study:**

  Skin surface samples / D0, D28, D56 / Tape strippings (Diagnoskin®) on areas with PASI

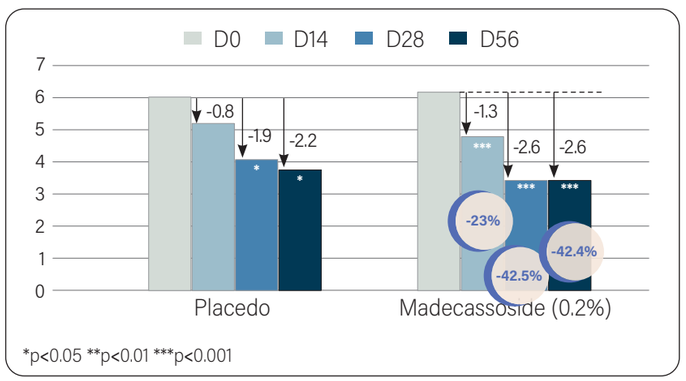
  PASI: Psoriasis Area Severity Index

  *p<0.05

Evaluation Tests:

- LOCAL PASI Score
- Anti-redness
- Reduction of desquamation
- Reduction of itching sensation
- Self-Evaluation
- Histological Study
  - Hydration state of Stratum Corneum (Diagnoskin®)
  - Evaluation of corneocyte maturation

Local PASI score reduction

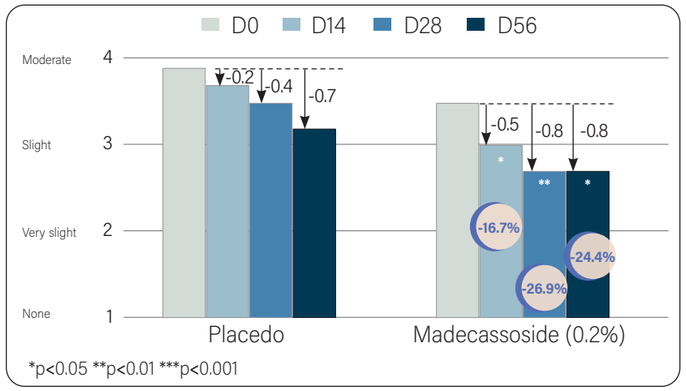


Local PASI: How is it calculated?

- Sum of erythema + Induration + Scaling score.
- Score from 0 to 12.

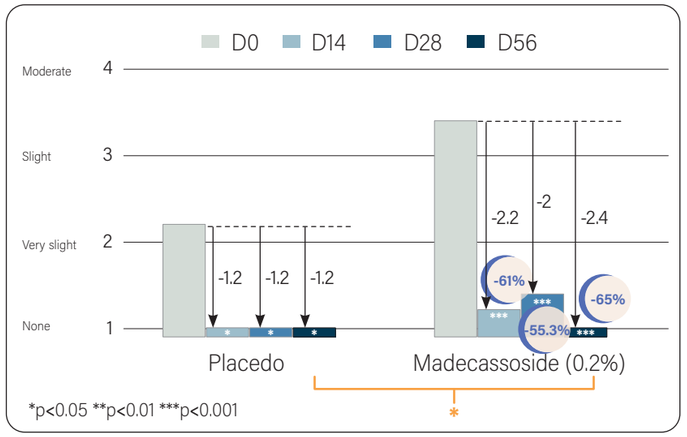
0.2% MADECASSOSIDE, helps to reduce the local PASI score from D14 and up to D56 by -42.4%***.

Erythema score value reduction



After 28 days, MADECASSOSIDE at 0,2% significantly reduces erythema score by -26.9%** vs. D0.

Itching score reduction

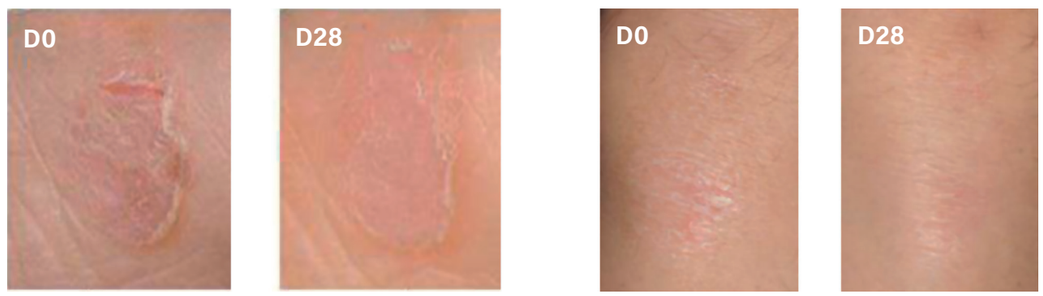


After 56 days, MADECASSOSIDE at 0,2% significantly reduces itching sensation:

- -65%*** vs. D0.
- 1.7* times vs. placebo.

IN VIVO TESTS FOR MODERATE PSORIASIS-PRONE SKIN (FOOT AREA)

MACRO PHOTOGRAPHS OF DESQUAMATION ARE REDUCTION



Average case *Maximum case*

0.2% MADECASSOSIDE, significantly reduces the lesion size of volunteers: up to -12.7% (average)*

IN VIVO CONCLUSION

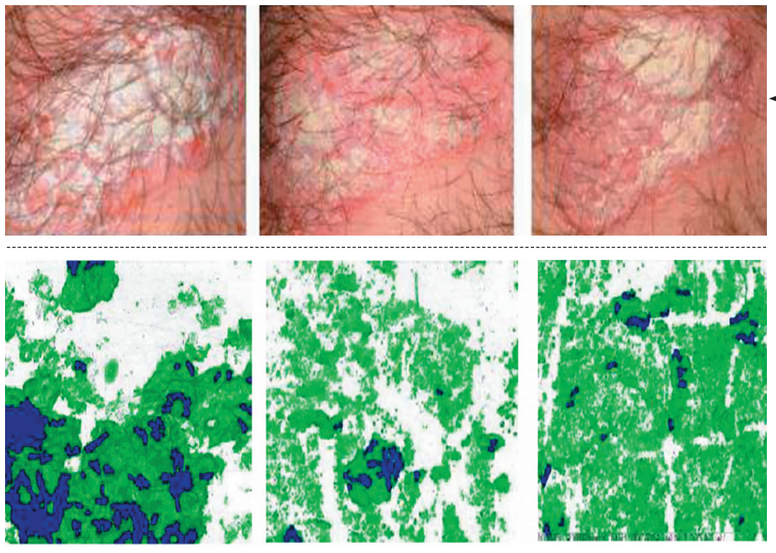
This study showed the ability of MADECASSOSIDE containing formula to improve the skin condition of volunteers presenting with moderate psoriasis-prone skin:

0.2% of MADECASSOSIDE:

- Reduces local PASI score up to 42.5%*** vs D0
- Reduces redness up to -26.9%-** vs D0
- Reduces itching sensation up to -56%*** vs D0
- Reduces lesion size up to -12.7% vs D0
- Increased consumer satisfaction vs. Placebo

HISTOLOGICAL STUDY ON MODERATE PSORIASIS-PRONE SKIN

STAINING FROM SKIN SAMPLES SURFACE



PASI score: D0: 8, D28: 6, D56: 5.

← D56-D0: ↓ Induration & scaling score

D56: apparition of lipids (yellow).

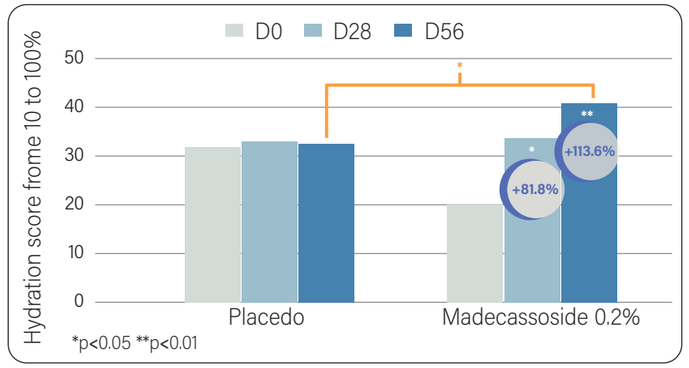
Squames

Homogeneous surface

With 0.2% MADECASSOSIDE:

- Reduction of squames/thickness (blue areas)
- Homogeneous surface/Skin texture refining (complexity & intensity of green areas)
- Positive effect on desquamation

Evaluation of the hydration state of the stratum corneum



After 56 days, MADECASSOSIDE at 0,2% significantly moisturizes skin:

- +81.8* in D28 vs. D0
- +113.6** in D56 vs. D0
- significantly vs. placebo

MADECASSOSIDE increases the hydration of the Stratum Corneum up to +113.6%**

CeramideBIO + α-Bisabolol SYMREPAIR 100

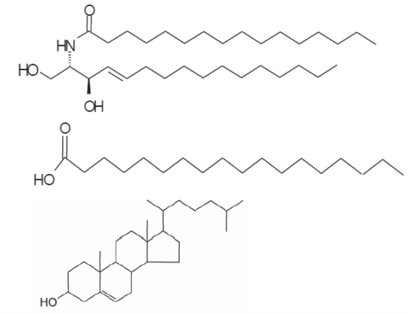
BIOMIMETIC LIPID COMPLEX

LIPID BILAYER = THE "MORTAR" OF YOUR EPIDERMIS

3 key skin components

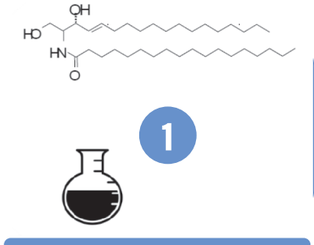
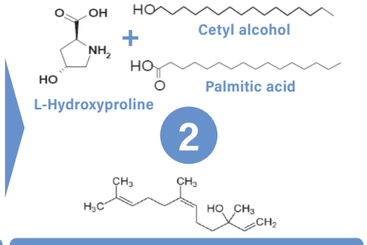
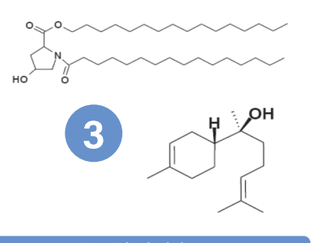
	Cer	:	FFA	:	Chol
Molar ratio	1	:	1	:	1
Weight ratio	2	:	1	:	1

Ceramides + **Free fatty acids** + **Cholesterol**



Inspiration for the Biomimetic complex in CeramideBio+Bisabolol

NATURE-INSPIRED COMPLEX

The skin lipid bilayer contains ceramides, free fatty acid & cholesterol.	Researcher has synthesized a pseudo-ceramide close to the natural ceramide present in the skin.	CeramideBio is combined with stearic acid & phytosterols to mimic the skin components.
		
Natural bisabolol is a well-known component of Chamomile.	Researcher obtains nature-identical Bisabolol by cyclisation from Nerolidol.	Our Bisabolol Its purity is similar to natural Bisabolol with 95% α-Bisabolol without Farnesol.
SOURCE	OPTIMIZATION	RESULT

SYNERGISTIC COMPLEX TO STRENGTHEN SKIN'S BARRIER

CeramideBIO
+ Stearic acid
+Phytosterols

1

3 key components
of skin lipid bilayer

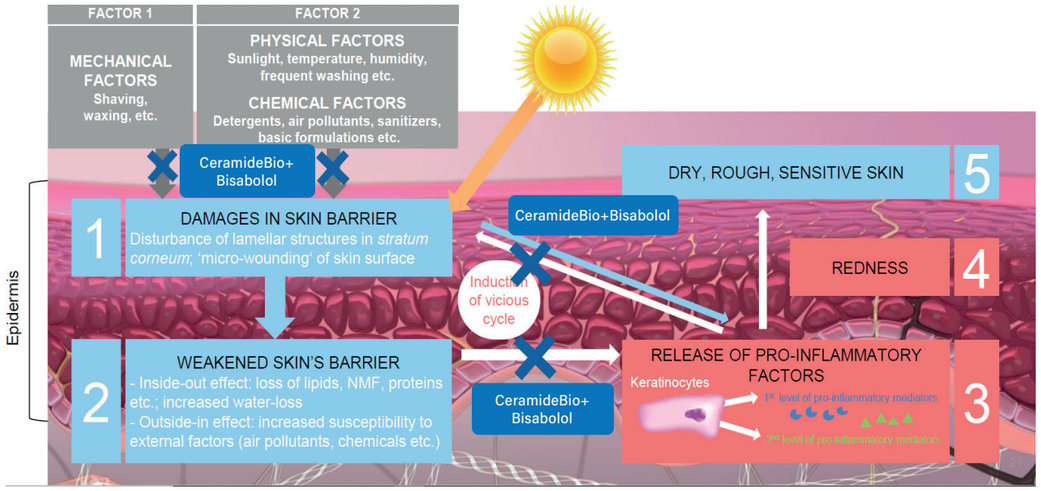
+

(α-Bisabolol)

2

Instant
soothing

SYNERGISTIC COMPLEX
combining
FUNDAMENTAL SKIN RESTORING COMPOUNDS
with
BISABOLOL



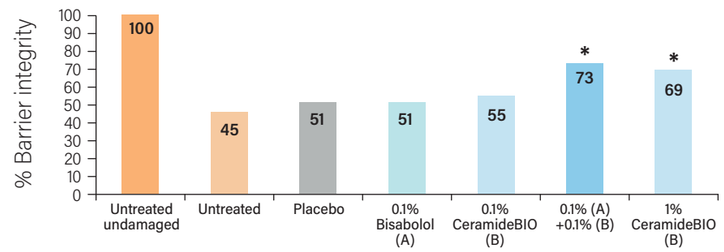
SYNERGISTIC COMPLEX TO STRENGTHEN SKIN'S BARRIER

SKIN RECOVERY COMPLEX			
1	*BARRIER FORTIFICATION*	Restores & strengthens skin's barrier integrity	***TEWL***
2	*ANTI-DEHYDRATION*	Improves significantly the water holding	***Capacitance***
3	*DRYNESS REDUCTION*	Reduces visibly the skin dryness aspect	***Visual Scoring***
4	*SKIN RELIEF*	Soothes significantly skin erythema	***Redness***

SYNERGISTIC BARRIER REPAIR

BARRIER INTEGRITY EVALUATION - *clinical study (based on **TEWL**)*

On day 5 after SDS damage



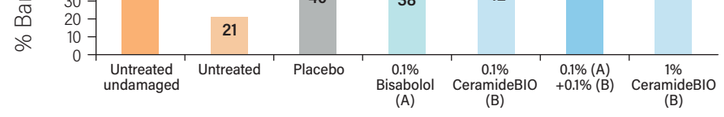
Synergistic effect in barrier reparation
with
0.1% CeramideBio
+0.1% Bisabolol

Protocol:
- 20 subjects (male & female) with winter-dry skin
- Skin barrier disruption by treatment with 2% SDS for 24h (occlusive) - test area: volar forearm
- Application of test products twice daily - measurement of TEWL on day 5

*Significance versus Placebo: *p<0.05*

BARRIER INTEGRITY EVALUATION - *clinical study (based on **redness**)*

On day 3 after SDS damage



Synergistic effect in barrier reparation
with
0.1% CeramideBio
+0.1% Bisabolol

Protocol:
- 20 subjects (male & female) with winter-dry skin
- Skin barrier disruption by treatment with 2% SDS for 24h (occlusive) - test area: volar forearm
- Application of test products twice daily - measurement of TEWL on day 3

*Significance versus Untreated: *p<0.05*

Palmitoyl tripeptide-8

Palmitoyl tripeptide-8 is a synthetic peptide ester based on a α-melanocyte stimulating hormone (α-MSH).

- The ingredient supplier performed several efficacy tests. In in vitro models, palmitoyl tripeptide-8 showed the ability to significantly inhibit IL-8 production up to 32% in UVB irradiated keratinocytes, which was comparable to α-MSH, and also in IL-1 stimulated fibroblasts, reaching 64% inhibition which is greater that the achieved by α-MSH.
- skin explants exposed to substance P, palmitoyl tripeptide-8 significantly reduced the number of dilated capillaries and the size of dilated vessels up to 30% and 51%, respectively. Edema was also reduced by 60% due to palmitoyl tripeptide-8.
- In vivo the efficacy of a formulation containing palmitoyl tripeptide-8 for the treatment of persistent redness in patients with rosacea who had been successfully treated with topical or oral therapy.

Saccharide Isomerate

Saccharide Isomerate (RM) has composition similar to that of the carbohydrate complex (NMF) found in human skin. It derived from dextrose monohydrate from maize kernels.

MECHANISM OF ACTION

- Unique binding mechanism to the skin that is not washed off.
- The removal of Saccharide Isomerate (RM) occurs only by the natural process of desquamation.
- Proven binding to amino acid lysine (free ε-amino groups) at the corneocytes.

SEBOSTASE EXTREME DRY SKIN CREAM

- Undaria Pinnatifida Extract
- Helichrysum Stoechas Callus Culture Lysate
- Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus
- Phospholipids + Sphingolipids (Ceramides)
- Urea
- Squalane

If you are struggling with extremely dry or chapped skin, the Lancomed Sebostase Extreme Dry Skin Cream should be your new go-to product. It was developed to promote the balance of the skin microbiota and thus strengthen the skin's natural defences. The Extreme Dry Skin Cream works by building the lipid barrier of the stratum corneum to balance the skin's water content. The best part is that it does all of this while protecting the skin's natural barrier. Moreover, the Extreme Dry Skin Cream is rich in natural sugars to improve the skin's appearance, moisturise and soften it.

- Brings balance and relief to dry skin
- Promotes hydration, softness and suppleness of the skin
- Is non-comedogenic, anti-pruritic and anti-relapse
- Contains no allergic fragrances

Sebostasis

Sebostasis means a reduction in the activity of sebaceous glands. The result is dry skin (xerosis cutis) and brittle hair.

In sebostasis, skin and hair are dry due to low sebum production. The sweat secretion is frequently relatively slight (hypohidrosis). If the skin has been degreased too extensively through frequent bathing or showering and the use of soaps or foam baths, treatment consist of ointments, emollient, lotion or cream.

Persons with this skin type tend to readily to develop asteatotic states with itching using standard cleansing measures. The regreasing results in circumscribed pityriasiform desquamation. There is also a tendency to asteatotic conditions on the side of upper arms, the side of trunk, and the lower legs.

Sebostasis is a sign of complex constitutional type (atopy), with tendency to allergy (Hay fever, bronchial asthma and

atopic dermatitis). Itchthyosis vulgaris is also related to sebostasis. Because of the dryness of sebostatic skin, the invasion by pathogenic microorganisms is usually more difficult. Persons with sebostasis suffer less often from seborrheic diseases such as acne vulgaris, seborrheic dermatitis, and rosacea.

The etiology of sebostasis is not know. It has, however, been confirmed that this type of constitution can be inherited.

TREATMENT/MANAGEMENT

Regreasing measures with ointment or emulsions of the water in oil type are indicated, as well as restriction of washing with soap.

In particular, one should avoid frequent showering and bathing with the use of foaming detergents. Skin are ointments and moisturizers are appropriate, as are medicated bath oils, which serve to keep the skin. lubricated.

Patients with sebostatic skin often do not tolerate well powder, dye painting, alcoholic solution.

Undaria Pinnatifida Extract WAKAPAMP

Undaria Pinnatifida Extract is an Algae that we use from the fertile bases., it also known as Mekabu.

HYDROLIPIDIC FILM: HLF

It is an emulsion of water and lipids that cover our skin epidermis. It acts to lock in moisture and defense against non-resident bacterial. This is the best ally of skin moisture and skin microbiota. Main consist of HLF are: Perspiration, water, sebum and lipids

CONSEQUENCES OF THE ALTERATION OF HLF

Its alteration or absence is characteristic of delipidated epidermis and triggers more than a conventional dehydration, but rather a severe dryness of the skin and a strong sensation of discomfort.

KEY INDICATORS OF AN IMPAIRED HLF:

- Skin may be lipid dry or Essential Fatty Acids deficient, this is when your skin is literally stripped due to limited sebaceous gland excretions.
- Skin has a reactive appearance.
- It can appear hot/burning, possibly itchy
- Skin shows signs of roughness, it is dull
- Indicates loss of structural integrity

WHAT CAN IMPAIR THE HLF

- **Genetic:** You could be predisposed to this; this is the case of naturally very dry skins.
- **Ageing:** sebum production is decreasing with aging
- **Incorrect Products:** Using products not suited to your skin type.
- **Soap Cleansing:** The excessive removal of the hydrolipidic film strips the epidermis of its protection.

If the HLF fails to do its job then a domino effect occurs which will lead to more serious skin conditions and complaints.

Undaria Pinnatifida Extract **reconstitutes** the HLF of the skin by promoting the synthesis of its main components:

- Surface Lipids:
  - Epidermal lipids
  - Balanced sebum
- Surface Water
  - By promoting proteoglycans synthesis , it helps to bind moisture to the skin.

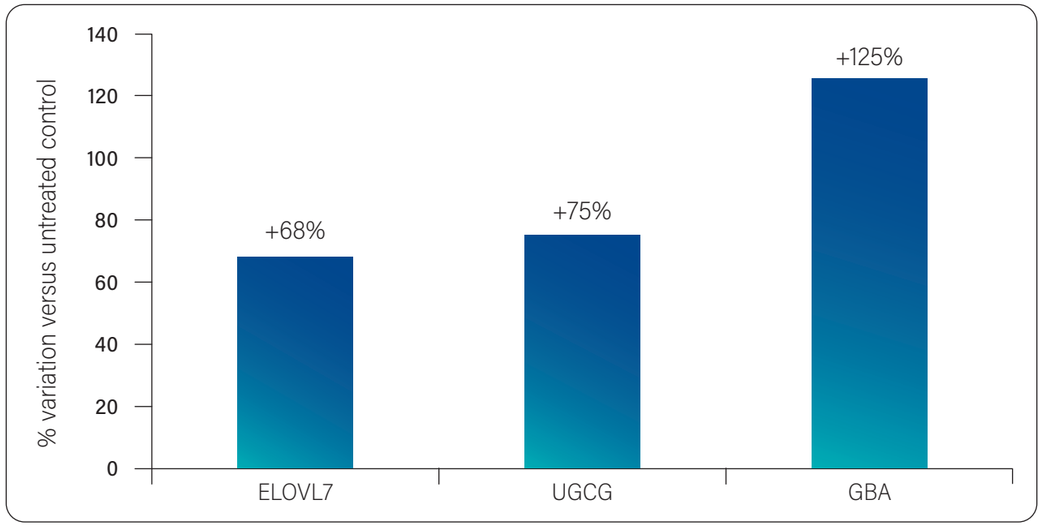
Components of skin surface lipids

	Epidermal lipids %	Sebum %
Glycerides	30-35	30-50
Free Fatty Acids	8-16	15-30
Wax Esters	-	26-30
Squalene	-	12-20
Cholesterol Esters	15-20	3-6
Cholesterol	20-25	1.5-2.5

Sebaceous gland lipids. Picardo and al; Dermato-Endocrinology I:2, 68-71; March/April 2009

RESTORING HLF - PRODUCTION OF EPIDERMAL FATTY ACIDS

UNDARIA PINNATIFIDA EXTRACT (RM) STIMULATES THE EXPRESSION OF GENES INVOLVED IN THE SYNTHESIS OF EPIDERMAL LIPIDS



(RM) = Raw material

0.1% Ex-vivo test

Protocol:

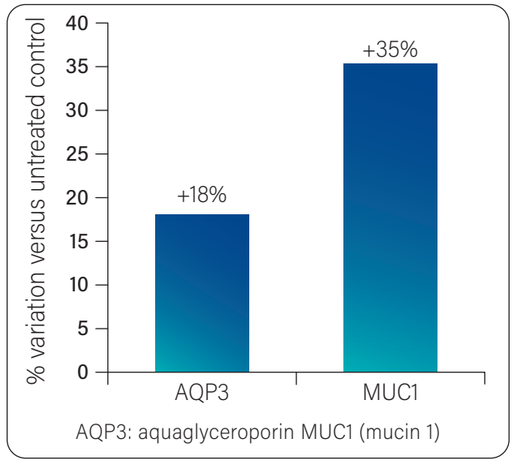
Topical application of 0.1% Undaria Pinnatifida Extract (RM) on reconstructed human skin for 24H. Full genome analysis of genes expression.

Result:

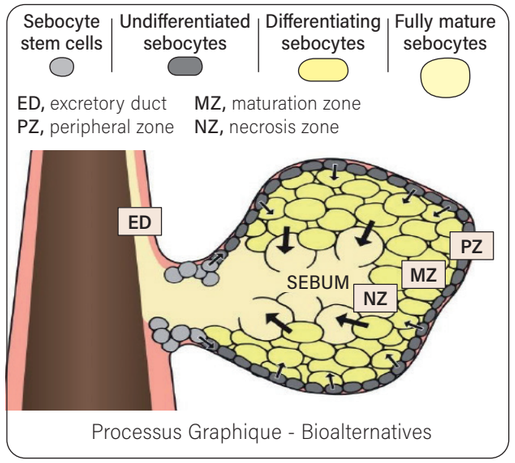
- ELOVL7 (fatty acid elongase), promote the synthesis and elongation of fatty acids.
- UGCG (UDP-glucose ceramid glucosyltransferase), involved in the production of glucosylceramide.
- GBA (glucosylceramidase beta), converts glycosylceramides in ceramids, essential lipids for the barrier function of the skin.

RESTORING HLF - PRODUCTION OF SEBUM

UNDARIA PINNATIFIDA EXTRACT (RM) PROMOTES THE DIFFERENTIATION OF SEBOCYTES



AQP3: aquaglyceroporin MUC1 (mucin 1)



Processus Graphique - Bioalternatives

0.02% In-vitro test.

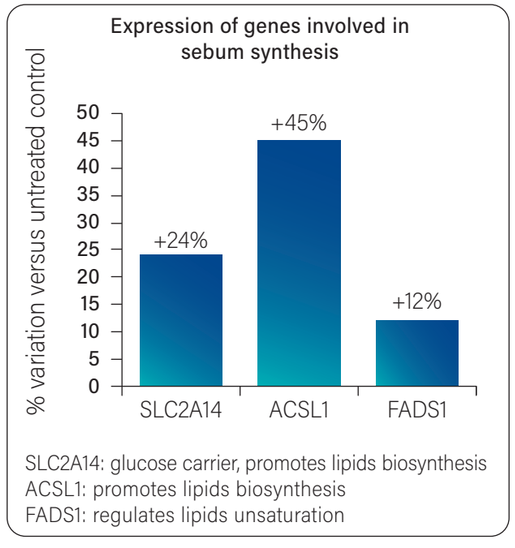
Sebum discharge occurs in the final stages of differentiation of sebocytes.

Improving the quantity of sebum available for the emulsion of the HLF goes through the improvement of sebocytes differentiation.

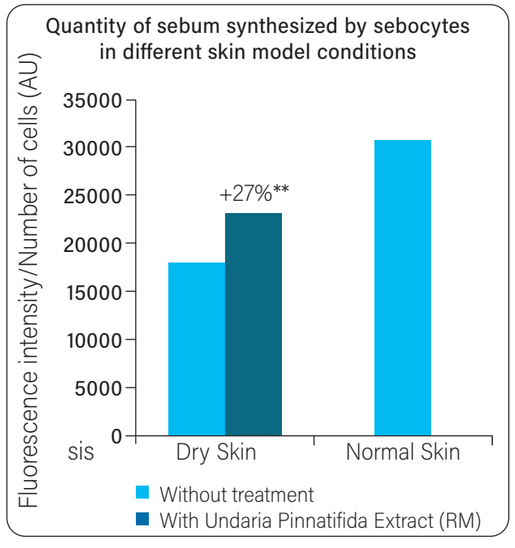
MUC1 is a differentiation factor.

AQP3 promotes water and glycerol storage, thus enhancing the size of mature sebocytes.

UNDARIA PINNATIFIDA EXTRACT (RM) INCREASES SEBUM PRODUCTION BY SEBOCYTES



SLC2A14: glucose carrier, promotes lipids biosynthesis
ACSL1: promotes lipids biosynthesis
FADS1: regulates lipids unsaturation



FADS1 (fatty acid desaturase 1).

ACSL1 (acyl-CoA synthetase long-chain family member 1).

SLC2A14 (solute carrier family 2 member 14):

**p<0.01 student test.

0.02% in-vitro test.

Protocol:

- Human sebocytes cultivated with 0.02% Wakapamp for 24H.
- Analysis of genes expression (mRNA) by RT-qPCR.
- Human sebocytes cultivated with different concentration of DHT (DiHydro-Testosteron) to imitate dry and normal skin conditions.
- Incubation with 0.02% Wakapamp for 8 days to quantify sebum production.

UNDARIA PINNATIFIDA EXTRACT (RM) IMPROVES THE QUALITY OF SEBUM PRODUCED BY SEBOCYTES

Along with increased sebum secretion rate, quantitative modification of sebum is important for the emulsion of HLF.

The most characteristic products of sebaceous secretion are squalene and wax ester:

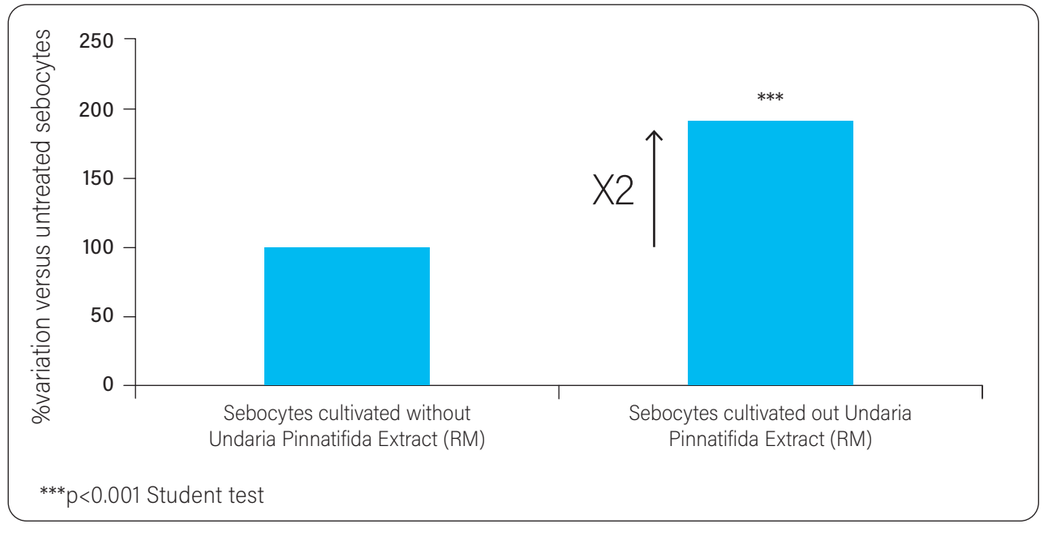
- They are unique to sebum and not found anywhere else in the body.

  They correspond to major components supplying the skin with protection.
- The hydrolipidic emulsion obtained from squalene is less fatty and less thick than those obtained with triglycerides (fatty acids and glycerides).

	Epidermal lipids %	Sebum %
Glycerides	30-35	30-50
Free Fatty Acids	8-16	15-30
Wax Esters	-	26-30
Squalene	-	12-20
Cholesterol Esters	15-20	3-6
Cholesterol	20-25	1.5-2.5

Sebaceous gland lipids. Picardo and al; Dermato-Endocrinology I:2, 68-71; March/April 2009.

UNDARIA PINNATIFIDA EXTRACT (RM) INCREASES THE QUANTITY OF SQUALENE & WAX ESTHER IN SEBUM



***p<0.001 Student test

Undaria Pinnatifida Extract (RM) increases the quantity of sebum produced by sebocytes in a model of dry skins and its quality, with: 2X more squalene & wax ester.

0.01% In-vitro test

Protocol:

Human sebocytes cultivated with specific concentration of DHT (DiHydro-Testosteron) to imitate dry skin conditions. Incubation with 0.01% Undaria Pinnatifida Extract (RM) for 6 days, Quantification of lipids synthesis.

EFFECT OF UNDARIA PINNATIFIDA EXTRACT (RM) ON SKIN WATER CONTENT

The water used to emulsionate the HLF:

- Is trapped into the cornified layer.
- Finds its origins in the deeper layers of the skin.

Undaria Pinnatifida Extract (RM) :

- Improves the water storage capacities of the dermis to increase the global water reservoir of the skin.
- reinforces stratum corneum cohesion to trap water diffusing from the deeper layers.

RESTORING WATER CAPTURE. UNDARIA PINNATIFIDA EXTRACT (RM) STIMULATES THE EXPRESSION OF GENES INVOLVED IN PROTEOGLYCANS SYNTHESIS

0.1% Ex-vivo test

Protocol:

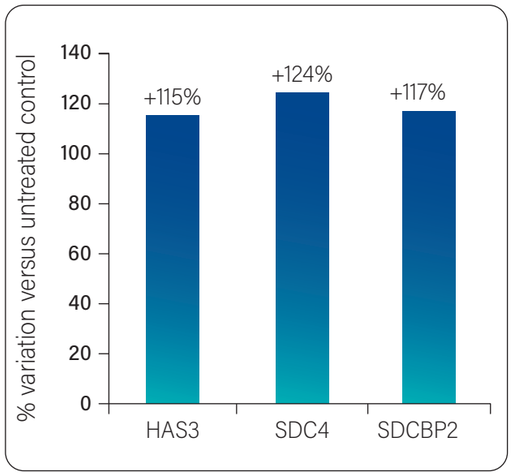
Topical application of 0.1% Wakapamp on reconstructed human skin for 24H. Full genome analysis of genes expression.

Hyaluronic acid and heparan sulfate proteoglycans are GAGs components. Stimulating their synthesis participate to increase water reservoir capacities of the skin.

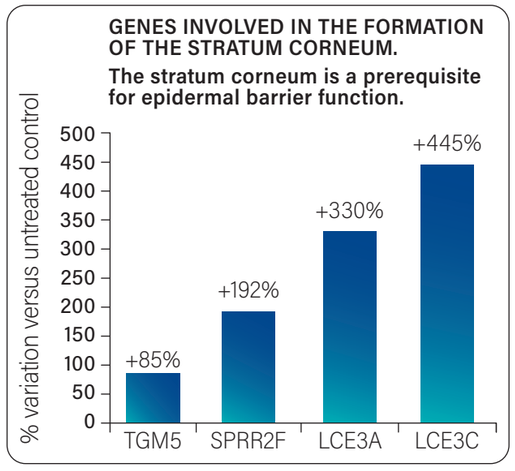
HAS3: Hyaluronic Acid Synthase 3.

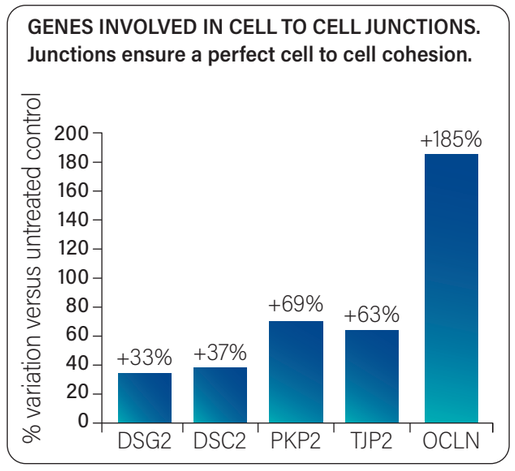
SDC4: syndecan 4, a transmembranous proteoglycan heparan-sulphate.

SDCBP2: syndecan binding protein 2.



BARRIER DAMAGES REPARATION. UNDARIA PINNATIFIDA EXTRACT (RM) STIMULATES THE EXPRESSION OF GENES INVOLVED IN THE INTEGRITY OF SKIN BARRIER





0.1% Ex-vivo test

Protocol:

Topical application of 0.1% Wakapamp on reconstructed human skin for 24H. Full genome analysis of genes expression.

SPRR2F coding Small Proline-Rich protein 2F, incorporated in cornified envelop.

LCE3A, LCE3C coding Late Cornified Envelope protein incorporated into the plasma membrane of keratinocytes by transglutaminase.

TGM5 coding transglutaminase 5 that fixes the involucrin to the plasma membrane.

DSG2: desmoglein.

DSC2: desmocollin.

PKP2: desmosomal plaque protein which binds the cytokeratin intermediate filaments.

TJP2: Tight Junction Protein 2.

OCLN: occludin.

UNDARIA PINNATIFIDA EXTRACT (RM) RECONSTITUTES THE HLF OF THE SKIN BY PROMOTING THE SYNTHESIS OF ITS MAIN COMPONENTS:

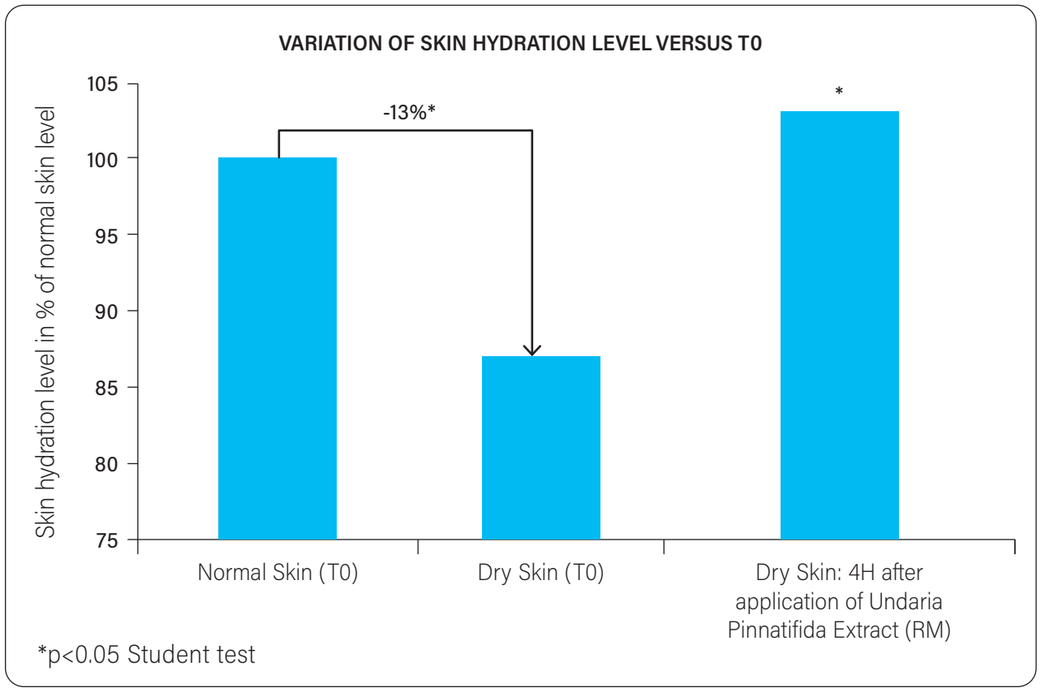
Surface lipids:

- Increases the expression of genes involved in epidermal lipids synthesis.
- Increases the expression of factors involved in sebocytes differentiation and maturation.
- Increases the quantity and quality of sebum produced by sebocytes.

Surface water:

- Increases the expression of genes involved in the constitution of skin water reservoir.
- Increases the expression of genes involved in the formation of skin barrier function.
- Increases the expression of genes involved in epidermis cohesion and sealing.

UNDARIA PINNATIFIDA EXTRACT (RM), OVERALL EFFECT ON SKIN HYDRATION LEVEL



0.1% In-vivo test

Protocol:

44 volunteers aged between 22 and 60 years old.

22 with normal skin

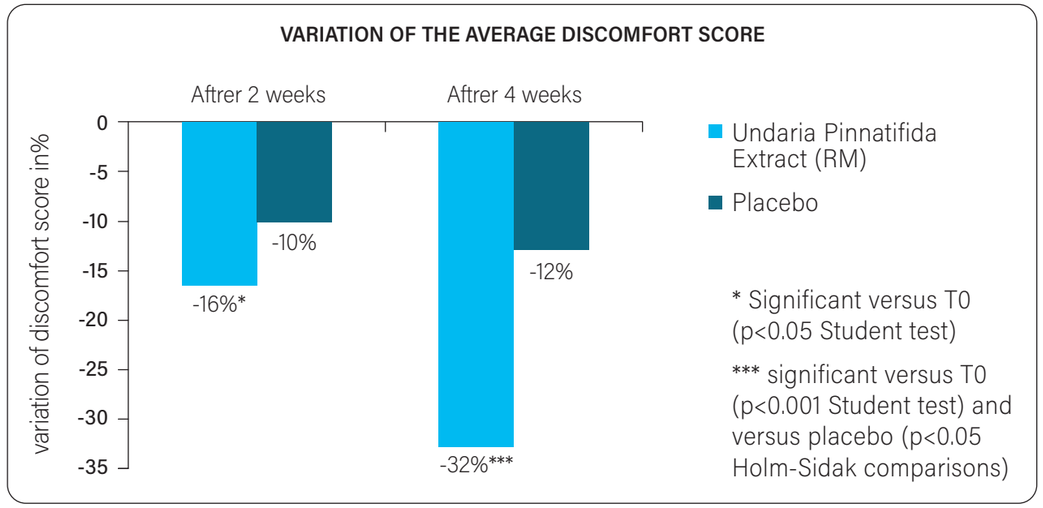
22 with dry skin on forearm.

Application of 0.1% Undaria Pinnatifida Extract (RM) . Measure of skin hydration level by Corneometer.

Result:

Dry skins treated with Undaria Pinnatifida Extract (RM) recover a hydration level similar to thus of normal skin WITHIN ONLY 4H.

BENEFITS OF UNDARIA PINNATIFIDA EXTRACT (RM) ON SKIN DISCOMFORT



Discomfort:

= intensity of brow-lowering

+ intensity of cheek raising or eyelid tightening

+ intensity of nose wrinkling or upper-lip raising

+ intensity of lip raising or lip stretch

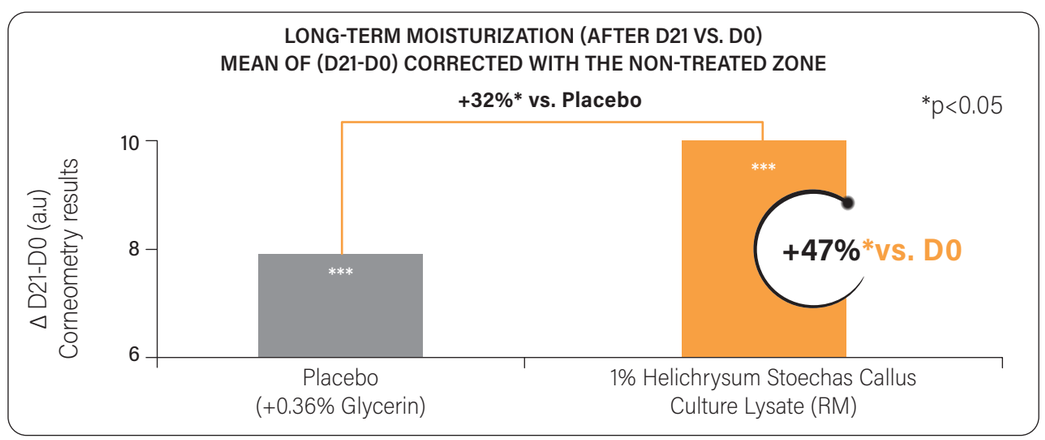
+ intensity of eye closing

Each action was coded on a 5 level intensity scale (1= trace / 5= maximum)

Treatment with Undaria Pinnatifida Extract (RM) provides dry skins with a significant reduction in discomfort within only 2 weeks.

HYDRACHRYSUM™ Helichrysum Stoechas Callus Culture Lysate

HELICHRYSUM STOECHAS CALLUS CULTURE LYSATE (RM) MADE UP FROM PLANT CELLS LYSATE (PLANT CELLS + MEDIUM) FROM HELICHRYSUM STOECHAS THROUGH HIGH TECHNOLOGY



IN VIVO PROVEN EFFICACY ON MOISTURIZATION

Protocol:

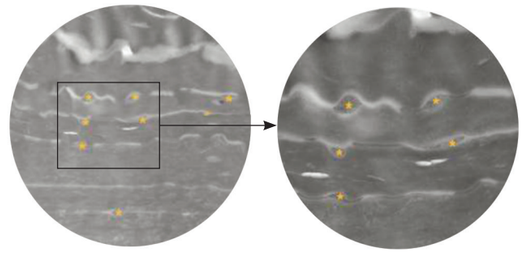
- 22 volunteers with very dry skin (<30 a.u).
- Evaluation of skin hydration after D21 vs. D0.
- 2 daily applications on the legs for 21 days during the winter season (January) of emulsion with 1% Helichrysum Stoechas Callus Culture Lysate (RM) or Placebo (eq glycerin % content in Helichrysum Stoechas Callus Culture Lysate (RM) at 1%) or Non-treated zone.
- Corneometry - Corneometer® CM 825.

In 21 days, Helichrysum Stoechas Callus Culture Lysate (RM) at 1% ensures an intense & long-term hydration vs. placebo!

Skin hydration is increased by +32%* vs. placebo & +47%* vs. D0.

EX VIVO: LACUNAE, VISUAL MARKER OF MOISTURIZATION

With Helichrysum Stoechas Callus Culture Lysate (RM)



The number of **lacunae** after 5 days:

+150%* vs. non-treated explants.

+82%* vs. Glycerin.

Protocol:

- Quantification of Lacunae on 3 groups of 3 explants with skin barrier disruption induced by 40 tape-stripping mimicking very dry skin (TEWL>40g/m²h) & INFLAMM'DRYNESS™.
- Formula with 1% Helichrysum Stoechas Callus Culture Lysate (RM) vs. 0.36% Glycerin or Non-Treated Explants.
- Application 1H after the tape-stripping and once a day for 5 days.
- Visual quantification on 3 pictures per formula.

A LONG-TERM MOISTURIZATION

- Helichrysum Stoechas Callus Culture Lysate (RM) Ensures an intense & long-term hydration.
- +32%* vs. Placebo
- +47%* vs. D0

WHAT ARE LACUNAE?

- Inter-cellular water inclusions embedded within the lipids bilayers of the stratum corneum [1].
- Resulting from corneodesmosomes degradation during the progression from the mid-SC to outer-SC. Their hydrophilic molecules bind with water and create the lacunae [2,3].
- Containing hydrophilic molecules (proteins, enzymes, hyaluronan...) [2,4].
- Forming a lacunar system (continuous or discontinuous) that expand laterally in the SC [2].
- Up to 40% of the SC volume [5].

The discovery of lacunae brings a new vision and unveils a structure much more dynamic, flexible & adaptable.

Lacunae in the stratum corneum play the role of extracellular water reserve that can accelerate skin moisturization and leads to:

- Increased skin suppleness & elasticity.
- Better desquamation
- Enhanced inter-cellular exchanges.

[1] Prausnitz et al. (2012), Skin Barrier and Transdermal Drug Delivery / [2] T-K Lin et al.(2012), Shedding of Human Corneocytes / [3] Menon GK, Elias PM (1997), Morphologic basis for a pore-pathway in mammalian stratum corneum. / [4] Haftek JPM/SFC (2017), Electron microscopy in studies of the epidermal barrier function /[5] Elias PM.(2017) The how, why and clinical importance of stratum corneum acidification.

BREAKS THE INFLAMM'DRYNESS™ VICIOUS CIRCLE:

RESOLUTION OF INFLAMMATION PROCESS

- **Transcriptomic analysis on RHE**
  - downregulation of TNFRSF21 (-64%)

    -> NF-κB: key issue to control inflammation
  - downregulation of COX-2 (-52%) & CCL20 (-54%) which are key players of inflammation pathway
- **Inflammatory effect on co-culture between dendritic cells & keratinocytes (2D)**
  - pro-inflammatory mediators:

    ↘ 5-HETE (-29%*) / ↘ LTB4 (-24%)
  - pro-resolving mediators:

    ↗ 12-HETE (+41%) / ↗ 15-HETE (+48LS)/ ↗ 17-HDOHE (+26%**)
- **Inflammatory effect on tape-stripped explants (3D)**
  - pro-inflammatory mediators: ↘ PGE2 (-22%)
  - pro-resolving mediators: ↗ 15-HETE (-40%)

STRONG BARRIER FUNCTION & HOMEOSTASIS RESTORATION

- **Reinforcement of the stratum corneum**
  - +77%*** of the thickness
  - +77% of the Stratum compactum
- **Boosting the synthesis of moisturizing elements**
  - +49%*** of Keratohyalin granules (+29% NMF by LC/MS)
- **Transcriptomic analysis on RHE**
  - Over-expression of genes desmoglein 2 (+51%) & desmocollin 2 (+46%) **-> better epidermal integrity**
- **Reduction of intercellular spaces between basal keratinocytes**
  - -61%*** cohesion improvement
- **Tape-stripping-induced TEWL reduction by**
  - 78%** vs. non-treated stripped explants

Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus ECOSKIN™

Alpha-Glucan Oligosaccharide (GOS): obtained by enzymatic synthesis, from vegetable substrate.

Polymnia Sonchifolia Root Juice: 100% vegetable juice, rich in β-fructooligosaccharides (FOS), obtained by cold pressing of yacon tubers (Polymnia sonchifolia).

Lactobacillus probiotic bacteria, (L. casei, L. acidophilus): inactivated (inhibition of their growth).

MODE OF ACTION

- Unique structure of combination of Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus (RM) promotes the balance of the skin microbiota by acting as substrate for commensal bacteria and strengthening the natural defense of the skin.
- It rich of natural sugar (GOS and FOS) that improves skin aspect and comfort.

IN VITRO TEST

FEEDING OF THE SKIN MICROBIOTA

Incubation (48h) of commensal and pathogenic strains, in a reference culture medium containing a carbonated substrate.

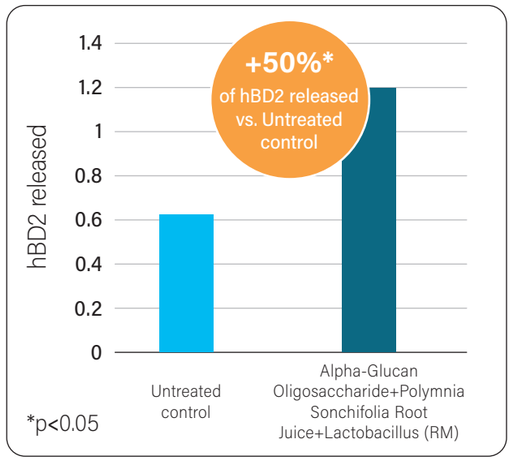
(Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus (RM) vs glucose), at a concentration of 0.5% and 3%. Determination of the quantity of residual substrate.

Result:

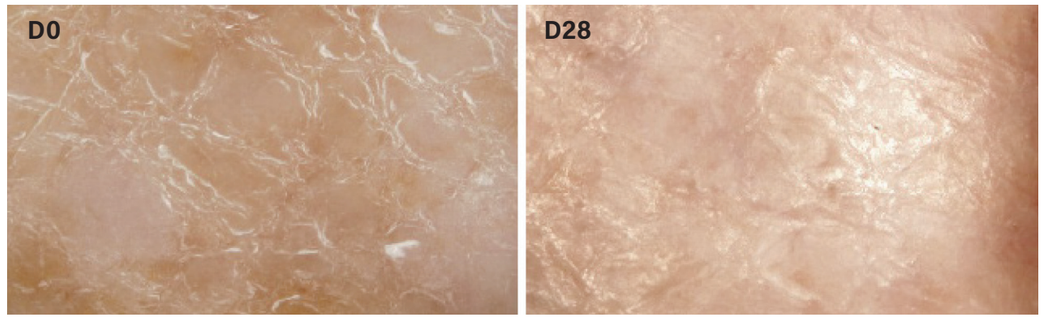
Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus (RM) vs glucose is a source of carbon for the majority of skin commensal microorganisms tested but is not much metabolized by pathogenic microorganisms in our ecosystem. Thus, Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus (RM) vs glucose is the guardian of skin microbiota balance.

STRENGTHENING OF SKIN NATURAL DEFENSES

In vitro study on reconstructed epidermis model. Quantification of hBD2 released by RT-PCR, after 72h of contact with Alpha-Glucan Oligosaccharide+Polymnia Sonchifolia Root Juice+Lactobacillus (RM) at 0.3% vs untreated Control.



IN VIVO TEST



3% Alpha-Glucan Oligosaccharide+ Polymnia Sonchifolia Root Juice+Lactobacillus(RM)

On 15 volunteers with very dry skin. Twice-daily application, during 28 days, of a cream containing 3% Alpha-Glucan Oligosaccharide+ Polymnia Sonchifolia Root Juice+Lactobacillus(RM) vs Placebo. Achievement of pictures and auto-evaluation.

- +41% of smoothing effect vs. Placebo
- -35% of discomfort feeling vs. Placebo
- +32% of nourishing effect vs. Placebo

Alpha-Glucan Oligosaccharide+ Polymnia Sonchifolia Root Juice+Lactobacillus(RM) nourishes the skin and reduces feelings of discomfort such as tugging, tingling and itching characteristic of sensitive and dry skin.

Phospholipids + Sphingolipids (Ceramides)

Ceramides are the major lipid constituent of lamellar sheets present in the intercellular spaces of the stratum corneum(approximately 50 percent) with cholesterol and free fatty acids. These lamellar sheets are thought to provide the barrier property of the epidermis. Ceramides are a structurally heterogeneous and complex group of sphingolipids containing derivatives of *sphingosine* bases in amide linkage with a variety of fatty acids.

BENEFITS OF CERAMIDES

- It play an essential role in structuring and maintaining the water permeability barrier function of the skin.
- In conjunction with the other stratum corneum lipids, they form ordered structures.
- Most skin disorders that have a diminished barrier function present a decrease in total ceramide content with some differences in the ceramide pattern.
- The function of ceramides can be augmented with anti-inflammatory and antibacterial derivatives, it could be due to inhibited proliferative activity of T-cells via mitogen-activated protein kinase and nuclear factor kappa B signaling pathways.

BENEFITS OF CERAMIDES (CONTINUE)

- It has been proven that use of the ceramide cream resulted in a 100-percent improvement in Investigator Global Assessment (IGA) scores and a 67-percent improvement in overall subject skin self-assessment scores after four weeks of use in individuals with atopic dermatitis or other sensitive skin conditions.
- Other study has shown that after 28 days of twice-daily application of ceramide-containing moisturizer, it has more significant improvement on skin hydration, barrier function, and skin pH.
- It has been also proven that single topical application of either the Ceramide cream resulted in a significant increase in skin hydration over time ($P<0.001$), It was also found to significantly decrease TEWL ($P<0.001$) over 24 hours, and was shown to be non-sensitizing to the skin of both adults and children and non-irritating to the skin, eyes and related eye area.

Urea

Urea is a unique physiological substance. It has frequently been used in dermatological therapy for more than 20 years. It is a natural moisturizing factor contained within normal human skin and released in eccrine sweat fluid, which facilitates the hydration of corneocytes and maturation of the stratum corneum.

BENEFIT FOR SKIN

- Dose dependent of urea application improve cutaneous barrier function and expression of antimicrobial defense in normal human skin.
- Emollients containing urea have been shown to significantly increase the hydration of the skin measured by skin capacitance, and therefore directly increase skin elasticity and smoothness.
- Maintenance of healthy skin and management of skin disorders.
- The study has been shown that using 5% urea moisturizer and the 10% urea lotion improved atopic dermatitis and were very well tolerated.
- Other study has been shown that 5% Urea emulsion improve all treated areas of Ichthyosis.

Squalane

Squalene is a triterpene that is an intermediate in the cholesterol biosynthesis pathway. It is one of the most common lipids produced by human skin cells and is a component of human sebum. Squalene is produced naturally by the body, the production of this chemical slows drastically after age thirty, thus contributing to dry skin. It shows some advantages for the skin as an emollient and antioxidant, and for hydration and its antitumor activities.

Squalane is a saturated form of squalene in which the double bonds have been eliminated by hydrogenation, it is less susceptible to oxidation than squalene. it is thus more commonly used as a moisturizer.

BENEFITS OF SQUALANE

- Squalene functions as an efficient quencher of singlet oxygen and prevents the corresponding lipid peroxidation at the human skin surface. It protects human skin surfaces from lipid peroxidation due to exposure to UV light and other sources of oxidative damage.
- It is quickly and efficiently absorbed deep into the skin, restoring healthy suppleness and flexibility without leaving an oily residue.
- It has occlusion properties that leads to increased skin hydration due to reduced water loss.

SEBOSTASE EXTREME ITCHY SKIN CREAM

- Hydroxyphenyl Propamidobenzoic Acid (2% as RM)
- Madecassoside 0.2%
- Tazmania Fruit (1% as RM)
- Magnesium Carboxymethyl Beta-Glucan (0.04% as RM)

Lancomed Sebostase Extreme Itchy Skin Cream gives you instant relief from itchy skin conditions. It is formulated to increase surface cohesion and hydration and strengthen the skin's barrier function. This prevents microbes from binding to skin lesions that cause irritation. Sebostase Itchy Extreme Skin Cream is highly effective as it also rebalances the skin's immune system. It helps to soothe flaky, dry and cracked skin and restore it to its natural, healthy state. In addition, it contains a natural formula that makes it equally suitable for babies, children and adults.

- Alleviates skin discomfort in less than 1 week.
- Perfect for reactive sensitive skin.
- Can be applied on the face and entire body.
- This cream is non-irritating and non-comedogenic.
- Contains no allergic fragrances.

Sebostasis

Sebostasis means a reduction in the activity of sebaceous glands. The result is dry skin (xerosis cutis) and brittle hair.

In sebostasis, skin and hair are dry due to low sebum production. The sweat secretion is frequently relatively slight (hypohidrosis). If the skin has been degreased too extensively through frequent bathing or showering and the use of soaps or foam baths, treatment consist of ointments, emollient, lotion or cream.

Persons with this skin type tend to readily to develop asteatotic states with itching using standard cleansing measures. The regreasing results in circumscribed pityriasiform desquamation. There is also a tendency to asteatotic conditions on the side of upper arms, the side of trunk, and the lower legs.

Sebostasis is a sign of complex constitutional type (atopy), with tendency to allergy (Hay fever, bronchial asthma and atopic dermatitis). Itchthyosis vulgaris is also related to sebostasis. Because of the dryness of sebostatic skin, the invasion by pathogenic microorganisms is usually more difficult. Persons with sebostasis suffer less often from seborrheic diseases such as acne vulgaris, seborrheic dermatitis, and rosacea.

The etiology of sebostasis is not know. It has, however, been confirmed that this type of constitution can be inherited.

Itchy Skin

Itch is the main chief complaint in patients visiting dermatologic clinics and has the ability to deeply impair life quality. Itchy skin is an uncomfortable, irritating sensation that makes you want to scratch. Also known as pruritus, itchy skin is often caused by dry skin. It's common in older adults, as skin tends to become drier with age.

CAUSES OF ITCHY SKIN (MAYO CLINIC)

Causes of itchy skin include:

Skin conditions: Examples include dry skin (xerosis), eczema (dermatitis), psoriasis, scabies, parasites, burns, scars, insect bites and hives.

Internal diseases: Itching on the whole body might be a symptom of an underlying illness, such as liver disease, kidney disease, anemia, diabetes, thyroid problems, multiple myeloma or lymphoma.

Nerve disorders: Examples include multiple sclerosis, pinched nerves and shingles (herpes zoster).

Psychiatric conditions: Examples include anxiety, obsessive-compulsive disorder and depression.

Irritation and allergic reactions: Wool, chemicals, soaps and other substances can irritate the skin and cause rashes and itching. Sometimes the substance: such as poison ivy or cosmetics, causes an allergic reaction. Also, reactions to certain drugs, such as narcotic pain medications (opioids) can cause itchy skin.

TREATMENT/MANAGEMENT

Whenever possible, treatment should be directed at the primary cause of itch.

Nonpharmacologic interventions: frequent moisturization is helpful to restore the skin barrier, especially as xerosis can both cause and exacerbate pruritus. Avoid overbathing and overdrying their skin with soaps and cleansers, use lighter clothing and run lukewarm water when bathing. Moisturization with a refrigerated emollient often helps considerably.

Local pharmacologic therapies: topical and intralesional corticosteroids can improve both inflammation and associated itch in inflammatory dermatoses. Both topical steroids and calcineurin inhibitors can help itch in conditions such as atopic dermatitis, psoriasis, and lichen planus.

Systemic therapies: Oral H1 antihistamines such as hydroxyzine and diphenhydramine are often the first line of treatment for generalized itch. However, the evidence for their use is limited mainly to histamine-mediated conditions. Oral immunosuppressants such as cyclosporine, azathioprine, and mycophenolate mofetil have efficacy in itch from inflammatory conditions such as atopic dermatitis.

Hydroxyphenyl Propamidobenzoic Acid (as RM) SYMCALMIN™

INSPIRED BY OAT AVENANTHRAMIDES

- Oat (Avena sativa) has been traditionally used to relief itching for centuries.
- Avenanthramides: polyphenols exclusively found in Oat with anti-itch activity.
- Oat extract standardized in 100 ppm avenanthramides is efficient vs short-term itching sensations (mild to moderate itchy rash.

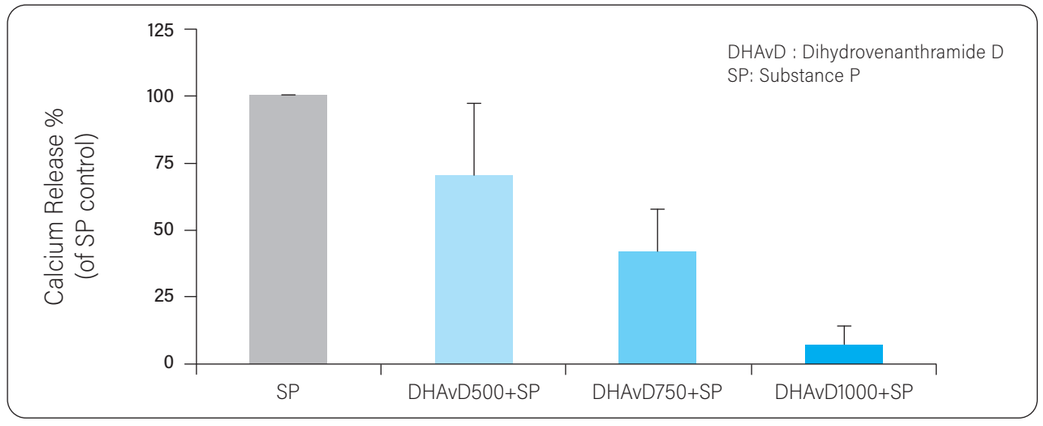
A higher concentration of avenanthramides is needed to be efficient against more long-term chronic itching episodes associated with dry mature skin and dermatoses. However, avenanthramides are present at relatively low content in oat and natural-based product contains lower amounts of avenanthramides.

Dihydroavenanthramide D orHydroxyphenyl Propamidobenzoic Acid has revealed to be the best candidate considering its stability and proven mechanism of action against itching mediators.

IN VITRO STUDY

NK-1 RECEPTOR MODULATION

Dihydroavenanthramide D action vs calcium release in response to substance-P / NK-1 interaction.



Dihydroavenanthramide D dose dependently **reduces** substance P -induced calcium release in **NK-1R overexpressing** cells.

=> Hydroxyphenyl Propamidobenzoic Acid: **NK-1R mediator & Mast cell stabilizer. Avoid Mast cell degranulation.**

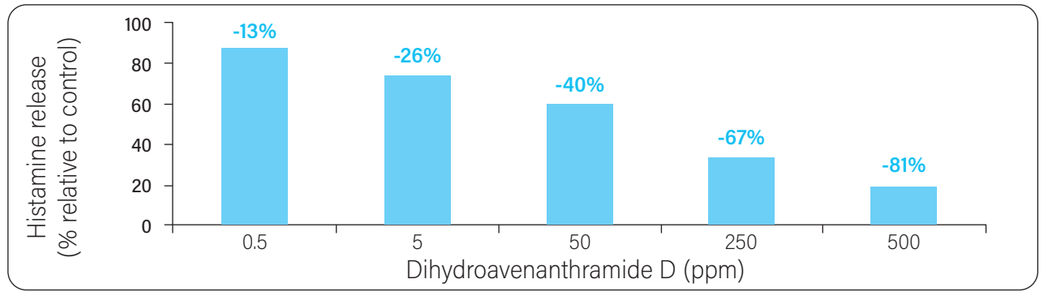
Protocol:

Effect of Dihydroavenanthramide D on calcium release in response to substance-P interaction with NK-1 receptor on NK-1R overexpressing cells. Dihydroavenanthramide D was tested at concentrations of 500ppm (1% Hydroxyphenyl Propamidobenzoic Acid (as RM)), 750 ppm (1,5% Hydroxyphenyl Propamidobenzoic Acid (as RM)) and 1000 ppm (2% Hydroxyphenyl Propamidobenzoic Acid (as RM)) in association with Substance P as NK-1 agonist vs Substance P alone. Calcium release was measured by fluorescence at 340 and 380 nm for 120s.

IN VITRO STUDY

HISTAMINE RELEASE REDUCTION

Dihydroavenanthramide D action in response to substance-P stimulation.



Dihydroavenanthramide D dose-dependently reduces the release of histamine, marker of itchiness from peritoneal mast cells, stimulated by substance P.

Highest inhibitory activity at 500 ppm = 1% Hydroxyphenyl Propamidobenzoic Acid (as RM).

Protocol:

Study to determine the effect of Dihydroavenanthramide D on histamine release from peritoneal mast cells stimulated by susbtance P (10 µmol).

Secreted histamine quantified by measuring the fluorescence intensity using a spectrofluorometer.

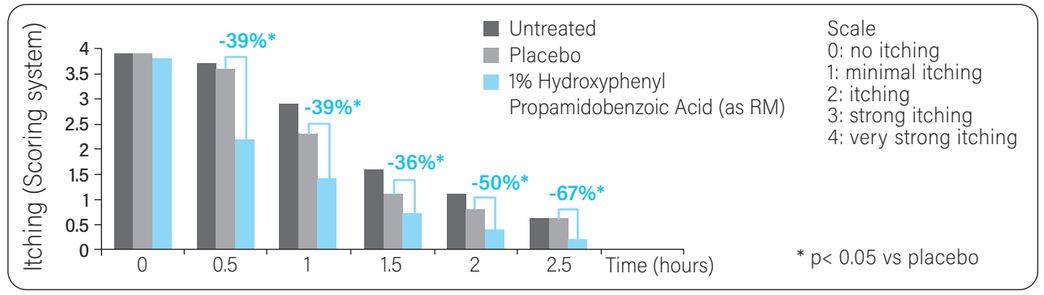
The tested concentrations correspond to respectively 0,001% - 0,01% - 0,1% & 1% Hydroxyphenyl Propamidobenzoic Acid (as RM).

Results are mean % of histamine release calculated with the value of the respective solvent control (ethanol 0.5%).

IN VIVO STUDY

IMMEDIATE ITCH RELIEF

Prick test evaluation of histamine-induced itch sensation on human skin.



Hydroxyphenyl Propamidobenzoic Acid (as RM) clearly reduces the itching sensation in only 30 min by 39% vs placebo!

Protocol:

Itching induced by histamine hydrochloride - 10 subjects (4 females & 6 males) aged 19-49.

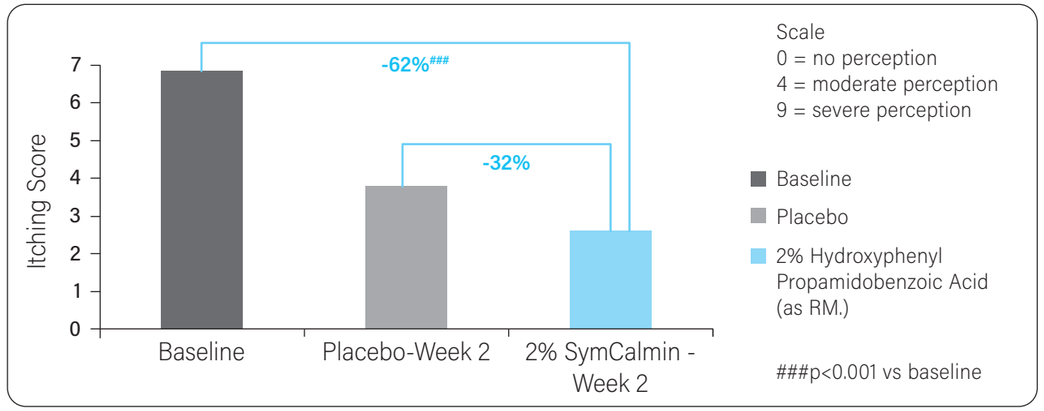
Self-visual assessment using scoring scale.

Once application of 1% Hydroxyphenyl Propamidobenzoic Acid (as RM) (500ppm Dihydroavenanthramide D) or placebo on inner sides of forearms.

IN VIVO STUDY

LONG-TERM ITCH RELIEF

Cross-over study - evaluation by investigator on dry mature skin.



Hydroxyphenyl Propamidobenzoic Acid (as RM) significantly reduces itching sensation by 62% after 2 weeks.

Protocol:

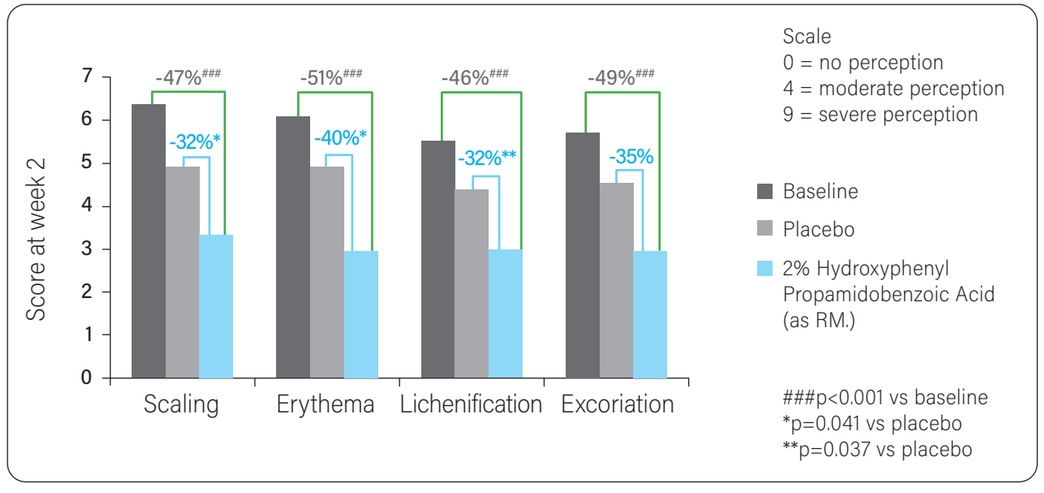
4 week double-blind cross-over study on 40 subjects aged 35-80 with dry & itchy skin (itch rating score 5 on a 10-point scale).

20 Subjects use SymCalmin® at 2% (1000 ppm / 0.1% Dihydroavenanthramide D) or Placebo for the first 2 weeks and cross over at week 2 to use the other product (Hydroxyphenyl Propamidobenzoic Acid (as RM) 2% or the Placebo) for the 2 remaining weeks. Itching evaluated by score scaling from 0 – none to 9 – Severe. Self-assessment evaluation.

IN VIVO STUDY

REDUCTION OF ITCHING-RELATED SYMPTOMS AFTER 2 WEEKS

Cross-over study - evaluation by investigator on dry mature skin.



Excoriation: abrasions of the skin caused by scratching or rubbing.

Lichenification: epidermis thickening due to chronic scratching.

Scaling skin is the loss of the outer layer of the epidermis in large, scale-like flakes.

Hydroxyphenyl Propamidobenzoic Acid (as RM) significantly reduces the clinical symptoms associated with dry itchy skin such as scaling, erythema, excoriation & lichenification after 2 weeks.

Protocol:

4 week double-blind cross-over study on 40 subjects aged 35-80 with dry & itchy skin (itch rating score 5 on a 10-point scale). 20 Subjects use SymCalmin at 2% (1000 ppm / 0.1% Dihydroavenanthramide D) or Placebo for the first 2 weeks and cross over at week 2 to use the other product (SymCalmin 2% or the Placebo) for the 2 remaining weeks. Parameters evaluated by score scaling from 0 – none to 9 – Severe: Investigator assessment.

Madecassoside

MADECASSOSIDE

It is a pure active ingredient (95%) from Centella asiatica leaves.

MODE OF ACTION

- **Soothing Action:**
  - Reducing the overproduction of inflammation mediators (IL-1α. PGE2).
  - Reducing the PNNs adhesion to keratinocyte, responsible of self-induces inflammation.
  - Cell protection against psoriatic environment (SKALP).
- **Respect & protection of cells:**
  - Preservation of proliferative potential of keratinocyte (HLE).
  - Antioxidant activity.
- **Skin barrier & Moisturization:**
  - Increase Filaggrin, source of NMF and structural protein of cornified envelope (reduces by inflammatory cytokines).
  - Increase Aquaporin-3, involved in water circulation within the epidermis.
- **Dermal matrix restructuration & protection:**
  - Increase collagen type I & III.
  - Decrease MMp-1, (TNFα).

IN VIVO TEST FOR MODERATE PSORIASIS-PRONE SKIN

TESTS PROTOCOL & EVALUATION

Evaluation Tests:

- LOCAL PASI Score.
- Anti-redness.
- Reduction of desquamation.
- Reduction of itching sensation.
- Self-Evaluation.
- Histological Study:
  - Hydration state of Stratum Corneum (Diagnoskin®).
  - Evaluation of corneocyte maturation.

PROTOCOL TESTS

- **2 Tested products:**

Formula with 0.2% MADECASSOSIDE vs. Placebo

Application for 56 days, twice a day.

- **Panel:** 2 groups of volunteers with moderate psoriasis:

local PASI* = 5-9 scored by a dermatologist

→ 13 volunteers with 0.2% MADECASSOSIDE

→ 10 volunteers with Placebo.

- **Analyse:**

Evaluation realized by a dermatologist - Scale from 1 (none) to 5 (severe).

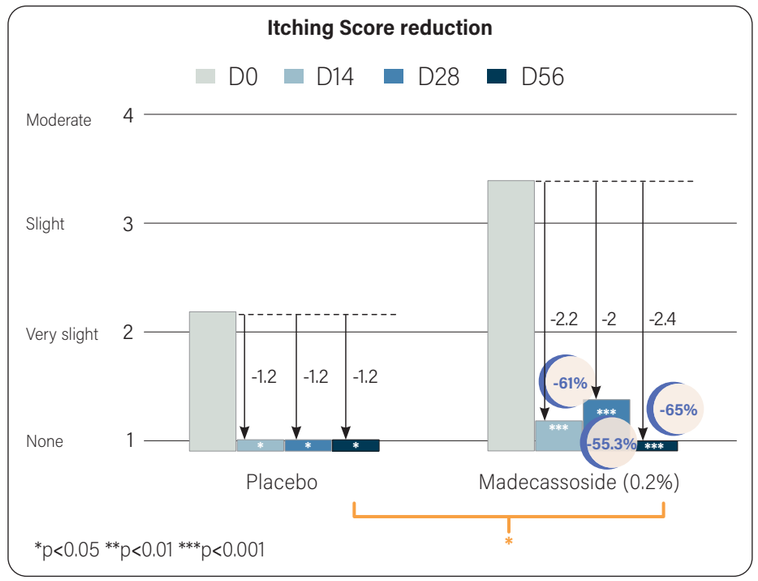
- **Histological study:**

Skin surface samples / D0, D28, D56 / Tape strippings (Diagnoskin®) on areas with PASI.

PASI: Psoriasis Area Severity Index.

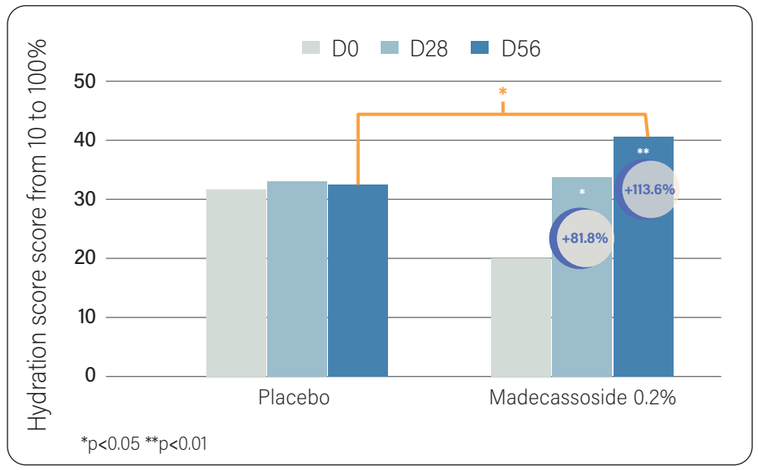
*p<0.05.

IN VIVO TEST FOR MODERATE PSORIASIS-PRONE SKIN



After 56 days, MADECASSOSIDE at 0,2% significantly reduces itching sensation:
-65%*** vs. D0
1.7* times vs. placebo

HISTOLOGICAL STUDY ON MODERATE PSORIASIS-PRONE SKIN



After D56, MADECASSOSIDE at 0,2% significantly moisturizes skin:
+81.8* in D28 vs. D0
+113.6** in D56 vs. D0
significantly vs. placebo

MADECASSOSIDE increases the hydration of the SC up to +113.6%**

Tazmania Fruit (as RM)

TASMANNIA LANCEOLATA FRUIT KNOWN AS MOUNTAIN PEPPER OR ALPINE PEPPER

- Nutritive fruit part of the Aboriginal diet.
- Traditionally used to calm symptoms caused by Arthritis and Infections.

COMPOSITION OF THE BERRY

- **Polygodial:** multifunctional natural active ingredient.
  - Anti-inflammatory property.
  - Broad antimicrobial activity.
  - Calms skin discomforts.
- **Anthocyanins:** protects your skin against free radicals.
  - Cyanidin 3-rutinoside, cyanidin 3-glucoside.
  - Powerful antioxidants.
- **Rutin:** helps to calm reactive skin.
  - Anti-inflammatory property.
  - Anti-allergic effects.
  - Strengthens capillaries.
- **Essential minerals:** nourish your skin!
  - Magnesium: Stimulates cell regeneration & increases energy production.
  - Zinc: Helps decrease rash & alleviate inflammation associated with acne.

TRPV1: Transient Receptor Potential Vanilloid 1

It expressed in keratinocytes & sensory neurons, acts as skin sensor of unpleasant sensations. The channel activation is induced by high temperature and chemical irritant such as capsaicin. In addition, this channel is more prone to activate in present of skin inflammation.

TRPV1 channel activation produces pro-inflammatory cytokines release and burning & itching sensation.

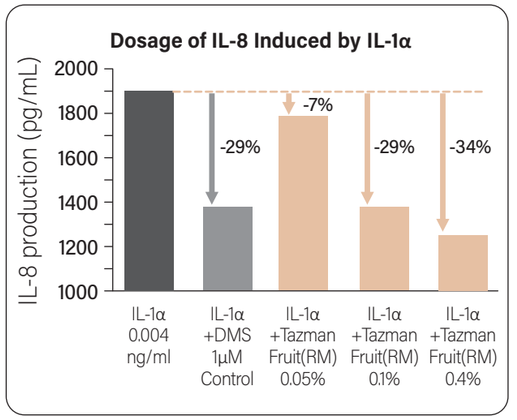
RELATION BETWEEN INFLAMMATION & TRPV1 CHANNEL

Skin inflammation decreases the activation threshold of the TRPV1 channel making it more prone to react to external aggressors. The more the TRPV1 channel is activated, the more inflammatory messengers are released, which in return sensitizes the TRPVI channel.

Mode of action of Tazmania Fruit (as RM)

- Inhibit TRPV1 activation.
- Reduces the release of inflammatory mediators; IL-1α, PGE2.

EFFECT ON INFLAMMATORY CASCADE



Tazmania Fruit (as RM) inhibits the release of IL-8 induced by IL-1α.

It dims the inflammatory cascade for optimal calming effects.

Protocol:

- Quantification of IL-8 production by fibroblasts.
- Inflammation state was induced with IL-1α, a pro-inflammatory mediator.
- Dexamethasone 1µM (DMS), an anti-inflammatory agent was used as a positive control.

Magnesium Carboxymethyl Beta-Glucan (as RM) CM-GLUCAN FORTE

The source for Magnesium Carboxymethyl Beta-Glucan (as RM) is the polysaccharide ß-Glucan from baker's yeast. The ß-Glucan has extraordinary immune enhancing capabilities.

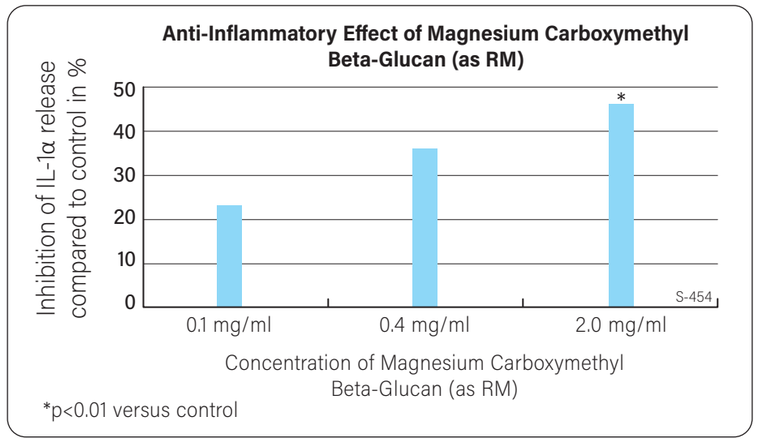
EVALUATION OF THE ANTI-INFLAMMATORY EFFECT OF MAGNESIUM CARBOXYMETHYL BETA-GLUCAN (AS RM)

Study design

- Test on reconstructed human oral epithelium (RHOE).
- The epithelia were preincubated for 6 hours with topically applied Magnesium Carboxymethyl Beta-Glucan (as RM).
- Incubation of RHOE with 0.2% SDS (induction of inflammation) and Magnesium Carboxymethyl Beta-Glucan (as RM).

Test substance: 0.1, 0.4 or 2.0 mg/ml Magnesium Carboxymethyl Beta-Glucan (as RM).

Test parameter: Release of IL-1α.



Magnesium Carboxymethyl Beta-Glucan (as RM) reduces the release of IL-1α by 46%

EFFECT OF MODEL MAGNESIUM CARBOXYMETHYL BETA-GLUCAN (AS RM) ON IL-8 RELEASE IN ATOPIC DERMATITIS MODEL

Study design

Reconstructed human epidermises (RHEs) activated by IL-4/IL-13/IL-22/TNF-α (cytokine mix typical for the chronic phase of atopic skin) + 0.5 mg/ml Magnesium Carboxymethyl Beta-Glucan (as RM).

Test parameter

Expression of Interleukin-8 (IL-8, key parameter in localized inflammation).

IL-8 is strongly expressed by keratinocytes of psoriatic skin and induces keratinocyte proliferation.

Magnesium Carboxymethyl Beta-Glucan (as RM) reduces the release of IL-8 by 53%.

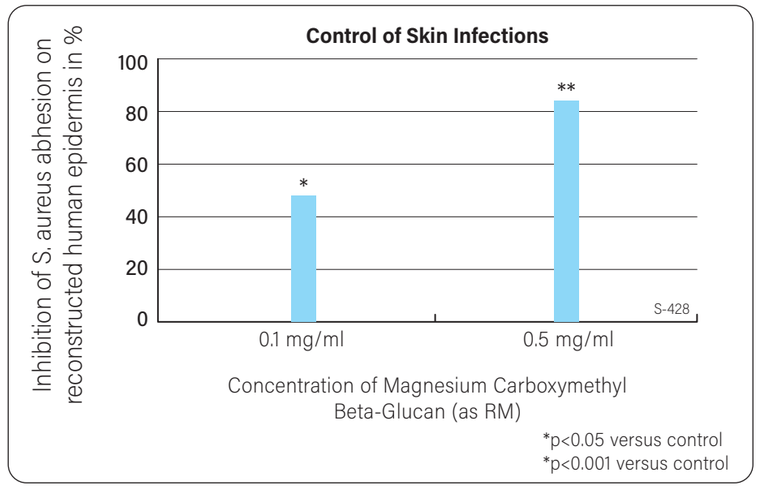
CONTROL OF SKIN INFECTIONS

Staphylococcus aureus can infect tissues when the skin barrier is damaged (as in atopic skin).

Study design

1. Reconstructed human epidermises (RHEs) were pretreated with Magnesium Carboxymethyl Beta-Glucan (as RM) and then «infected» with radiolabeled (3H-adenine) Staphylococcus aureus bacteria.

2. Washing of RHEs. Detection of remaining S. aureus via scintillation counting.



Magnesium Carboxymethyl Beta-Glucan (as RM) reduces Staphylococcus aureus releated infections in atopic skin.

STRENGTHENS THE SKIN BARRIER

Protocol:

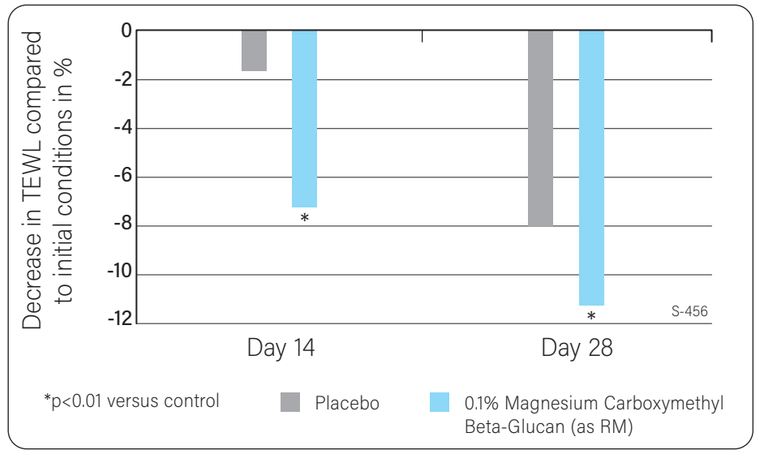
Volunteers: 20 (14 f, 6 m), 27- 61y, previously diagnosed with AD but symptom free during the study period.

Product: Emulsion + 0.1 % Magnesium Carboxymethyl Beta-Glucan (as RM), placebo.

Application:

Twice daily for 28 days, one to each side of the inner side of the forearm.

Parameter: Skin hydration (corneometer), roughness (PRIMOS), transepidermal water loss (tewameter).



Magnesium Carboxymethyl Beta-Glucan (as RM) reduces transepidermal water loss = reinforces the skin barrier function.

HELPS TO ALLEVIATE 6 SYMPTOMS OF ECZEMA

Clinical study conducted with 10 people suffering from eczema.

Test product:

Aqueous solution containing 0.04 % of Magnesium Carboxymethyl Beta-Glucan (as RM).

Application:

Twice daily for 7 days on an eczema patch.

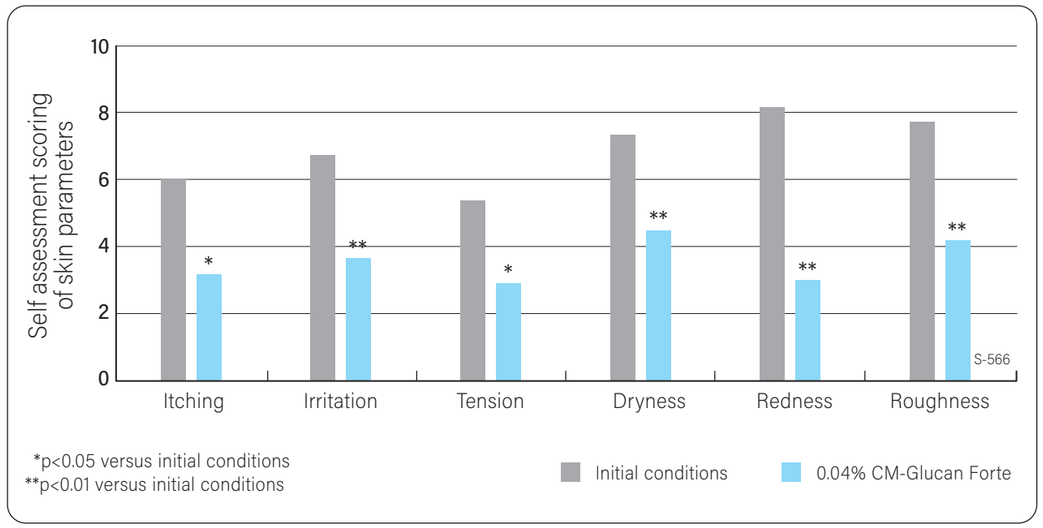
Result:

Magnesium Carboxymethyl Beta-Glucan (as RM) was shown to alleviate 6 distressing symptoms of atopic skin.

+ Immediate comfort to the skin: 80%.

+ Overall skin conditions improved: 70%.

+ Increase in "general well-being": 70 %.



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