



RonaCare[®] Luremin[®]
The nature-identical approach to rejuvenate your skin

Advanced information

Merck | Pigments & Functional Materials



Introduction

RonaCare® Luremin® is a natural-identical active ingredient, produced under sustainable aspects.

It is suitable so improve the living epidermis.

It provides the following properties

- Anti-inflammatory
- Anti-aging
- Retinol-like
- Supports the epidermal humidity



A stable and non irritant active ingredient

RonaCare® Luremin® – efficient and reliable

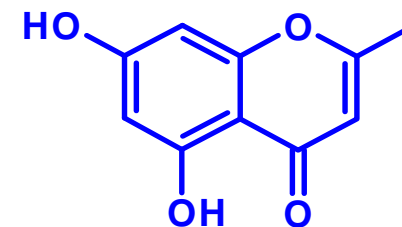
RonaCare® Luremin®

INCI: Dihydroxy methylchromone, Sorbitol

Active: Dihydroxy methylchromone (DHMC)

DHMC: $\geq 5\%$ (HPLC)

White to beige powder



What are you looking for?

Tightening

- *via collagen support*

Refreshing

- *via moisturization support*

Rejuvenating and smoothing

- *via anti-aging efficacy*

With

RonaCare® Luremin®

you are able to improve your skin based on a

nature-identical, non irritant and stable active ingredient.

Useful also in case of sensible skin.

– efficient and reliable –

Nature-identical molecule

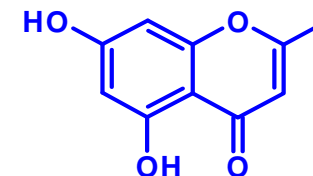
Dihydroxy methylchromone (DHMC)

- is found in a variety of plants and has a share in the activity of e.g. medicinal rhubarb, *Stevia purpurea* (Mexico), *Angelica polymorpha* (China)

Traditional Chinese and Japanese medicine uses certain plants against ailments of skin and infection.

Merck was able to convey the capability of DHMC from the plant to useful cosmetic applications.

The active in **RonaCare® Luremin®** is nature-identical.



Claims fulfilled by RonaCare® Luremin®

- 
- 1) **Collagen and elastin support**
 - 2) **Humidity maintenance**
 - 3) **No skin irritation**
 - 4) **Anti-wrinkle properties**
 - 5) **Stable versus light, oxidation and temperature**
 - 6) **Barrier function support**

Efficacy spectrum of RonaCare® Luremin®

Studies performed (Academia, in-house)	Properties	Methods used
<i>in vitro</i>	<ul style="list-style-type: none"> Gene information 	<ul style="list-style-type: none"> Genetic level - cDNA method
<i>in vitro</i>	<ul style="list-style-type: none"> Collagen protection (0.004%, DHMC) Elastin protection (0.1%, DHMC) Stability information (DHMC) 	<ul style="list-style-type: none"> Reduction of collagenase (MMP-1) release by 40% Inhibition of elastase (MMP-12) activity by 84% Stability tested vs. oxidation via H₂O₂, light and temperature stability
<i>in vitro</i>	<ul style="list-style-type: none"> Humidity maintainance (DHMC) Transglutaminase (TGK) (DHMC) 	<ul style="list-style-type: none"> Supports the hyaluronic acid synthesis 73% stimulation (2*10⁻⁵ Mol) Inhibits hyaluronidase DHMC (4*10⁻² mM) increased the activity of TGK
<i>ex vivo</i>	<ul style="list-style-type: none"> Collagen densification (2% RonaCare® Luremin®) 	<ul style="list-style-type: none"> Significant stimulation of collagen synthesis by 7% (p<0.05)
<i>in vivo</i>	<ul style="list-style-type: none"> Anti-wrinkle properties (2% RonaCare® Luremin®) 	<ul style="list-style-type: none"> Reduces skin roughness and average relief by 12%

Claims fulfilled by RonaCare® Luremin®

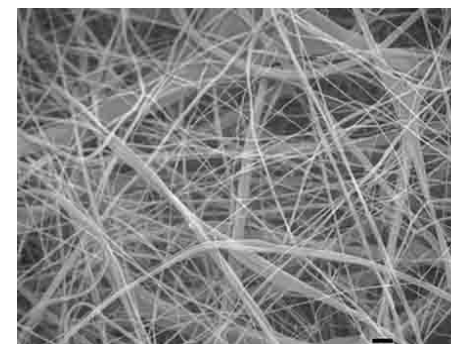
- 
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RonaCare® Luremin®

1) Collagen/Elastin support

Improvement of the skin works via 3 processes stimulating collagen:

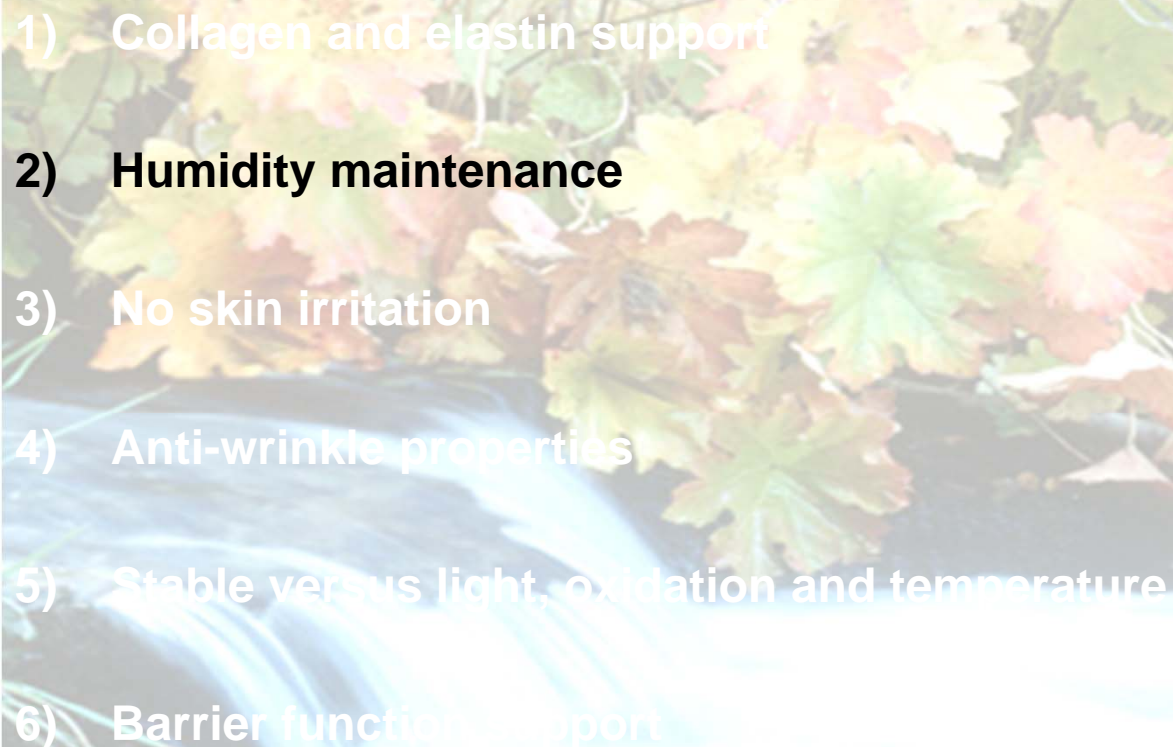
- Genetic level
- Collagen densification – collagen synthesis stimulation by **7%** (ex-vivo, end product)
- Reduction of collagenase (MMP-1) release **by 40%** (in-vitro, DHMC)
- Inhibition of elastase (MMP-12) activity **by 84%** (in-vitro, DHMC)



www.bioscience.org/2004/v9/af/1313/fig6.jpg

RonaCare® Luremin® helps to maintain a tight and firm skin

Claims fulfilled by RonaCare® Luremin®

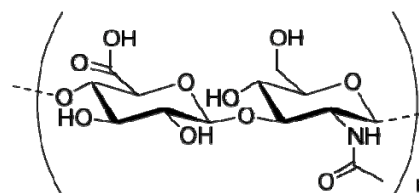
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RonaCare® Luremin®

2) Humidity maintenance – Hyaluron impact

Humidity maintenance in the skin – in epidermis and dermis

- Improvement of the skin volume - skin appears healthy and rejuvenated
- Hyaluronic acid represents body's own molecule and supports connective tissue

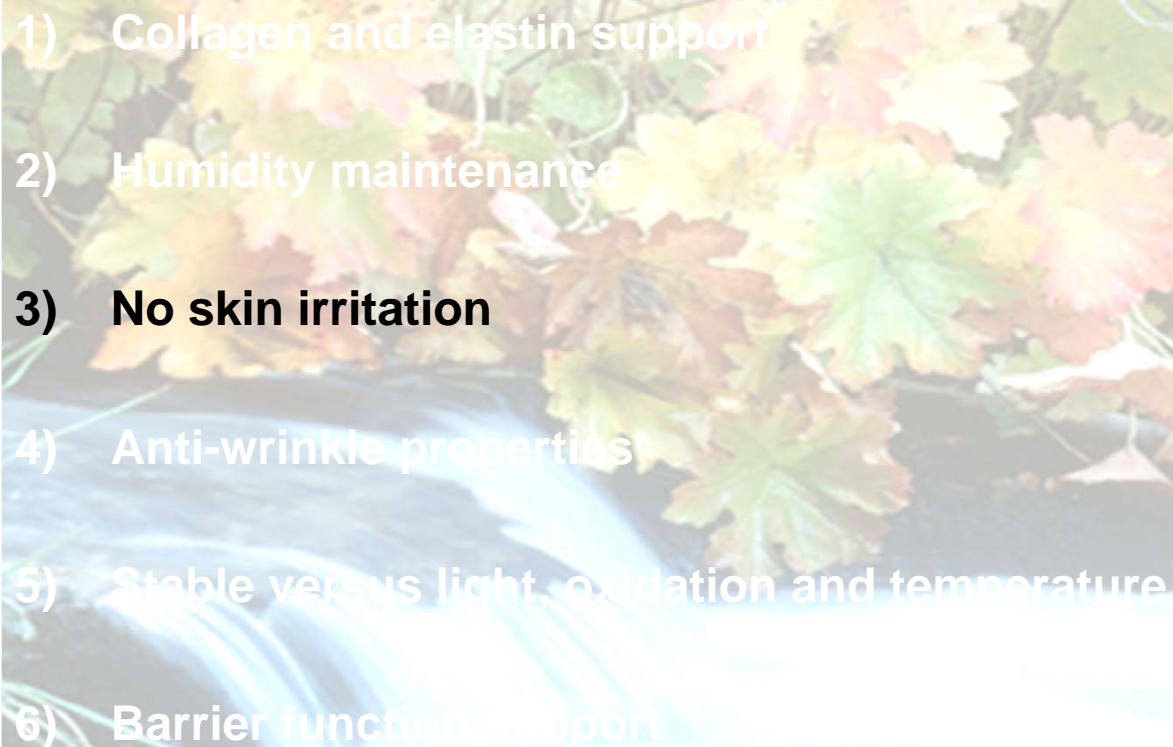


DHMC, the active of RonaCare® Luremin®

- supports the hyaluronic acid synthesis (in-vitro) by **73%**
- inhibits hyaluronidase (in-vitro) and

offers an additional option to improve skin moisture and skin tone

Claims fulfilled by RonaCare® Luremin®

- 
- 1) Collagen and elastin support
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 - 3) **No skin irritation**
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3) Skin tolerance – Skin irritation

The active of RonaCare® Luremin®,
Dihydroxy methylchromone (DHMC) has

- **No** allergenic potential
- **No** potential sensitivity
- **No** phototoxic activity

In addition:

It **decreases** the release of Prostaglandine-2 (PGE2).



[http://www.hilltopstudy.com/images/
Patch/patch%203534021.jpg](http://www.hilltopstudy.com/images/Patch/patch%203534021.jpg)

**The active of RonaCare® Luremin® shows
evident skin soothing features instead of irritation!**

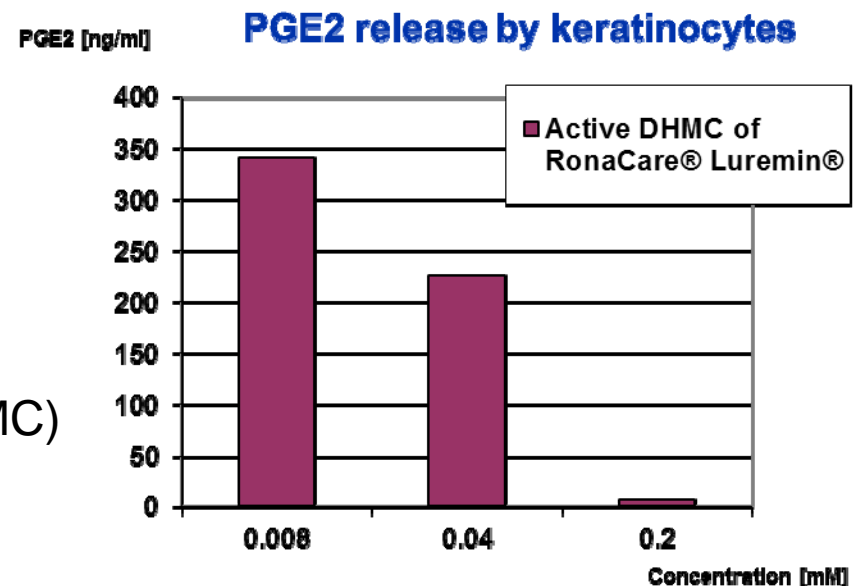
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3) Skin tolerance – *in vitro* evaluation

Treatment of human keratinocytes

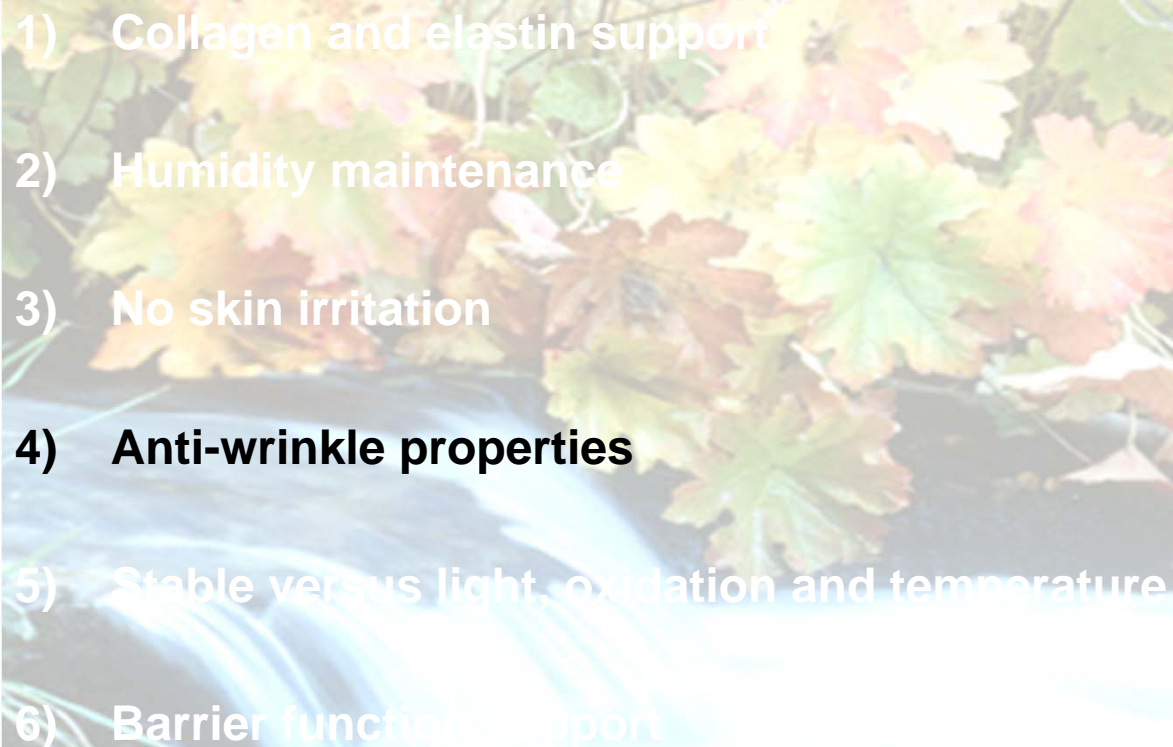
- **Pro-inflammatory** agent:
phorbol myristate acetate (PMA)
Positive reference: Indomethacine

The active in **RonaCare® Luremin®** (DHMC) **decreases** the release of Prostaglandine-2 (PGE2).



The active in RonaCare® Luremin® shows evident skin soothing features instead of irritation!

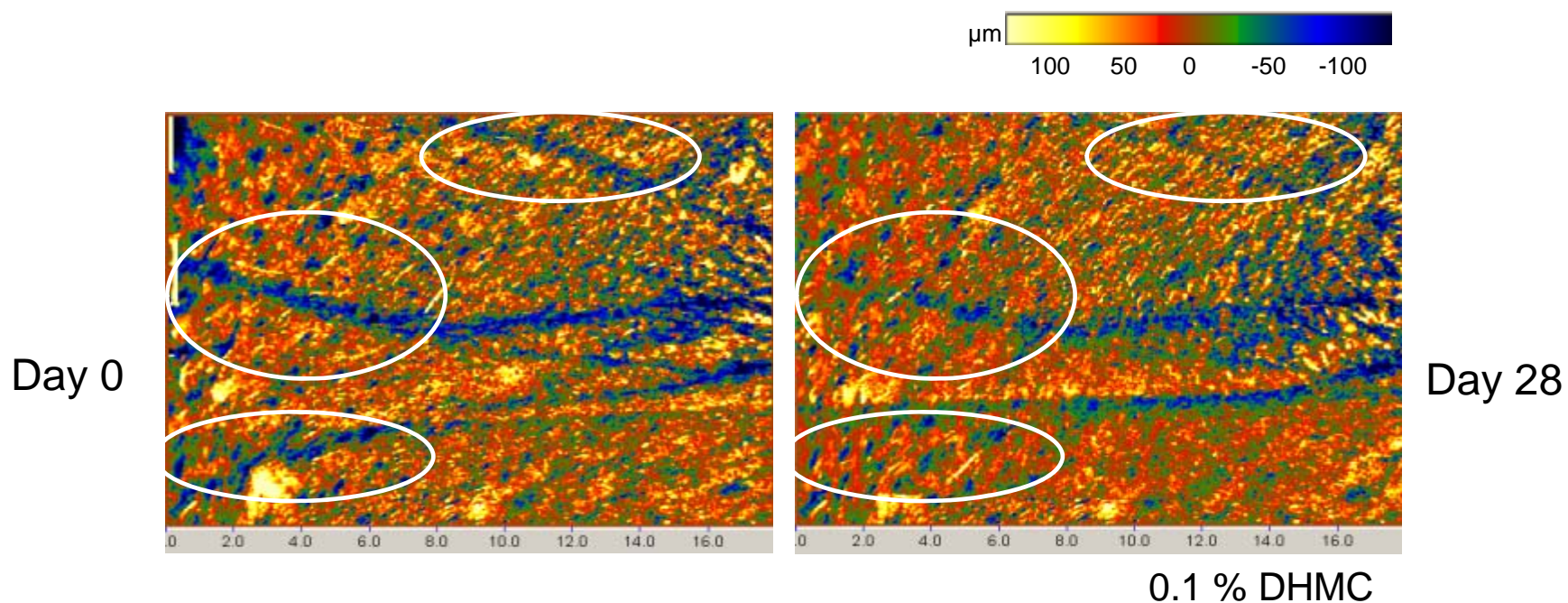
Claims fulfilled by RonaCare® Luremin®

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4) Anti-wrinkle properties – *in vivo* evaluation

Evaluation of the cutaneous relief of Crow’s feet
before and after treatment using Primos 3D (day 0, 28)



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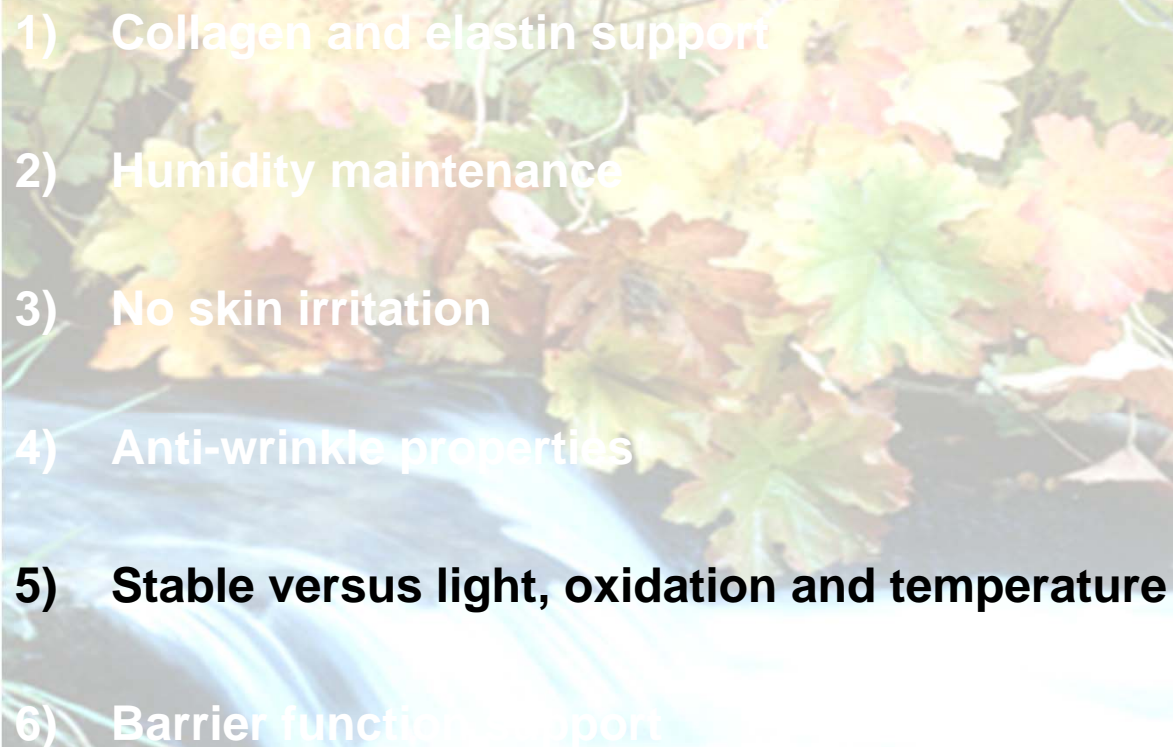
4) Anti-wrinkle properties – *in vivo* evaluation

No anti-wrinkle effect with placebo. Significant anti-wrinkle effect with 0.1% DHMC

- Significant decrease of **12%** in the average roughness (Ra) in **80%** of the volunteers.
- Significant decrease of **11%** in the average relief (Rz) in **85%** of the volunteers.
- Decrease of **8%** in the maximum relief amplitude (Rt) in **80%** of the volunteers.

RonaCare® Luremin® acts as a very good “anti-wrinkle “ and “skin smoothing” product.

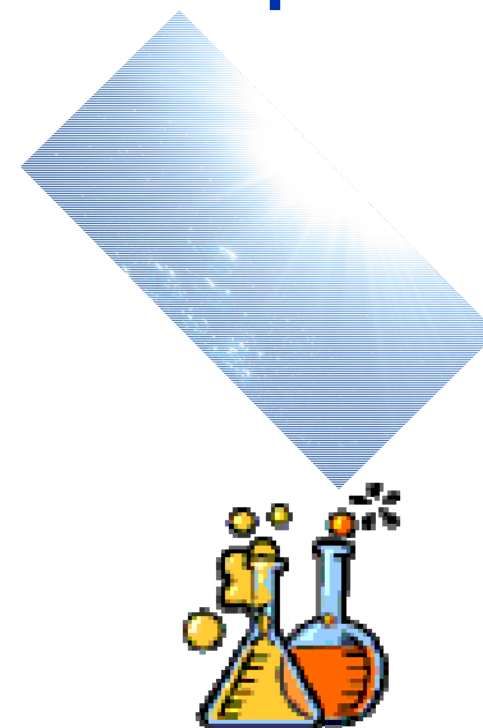
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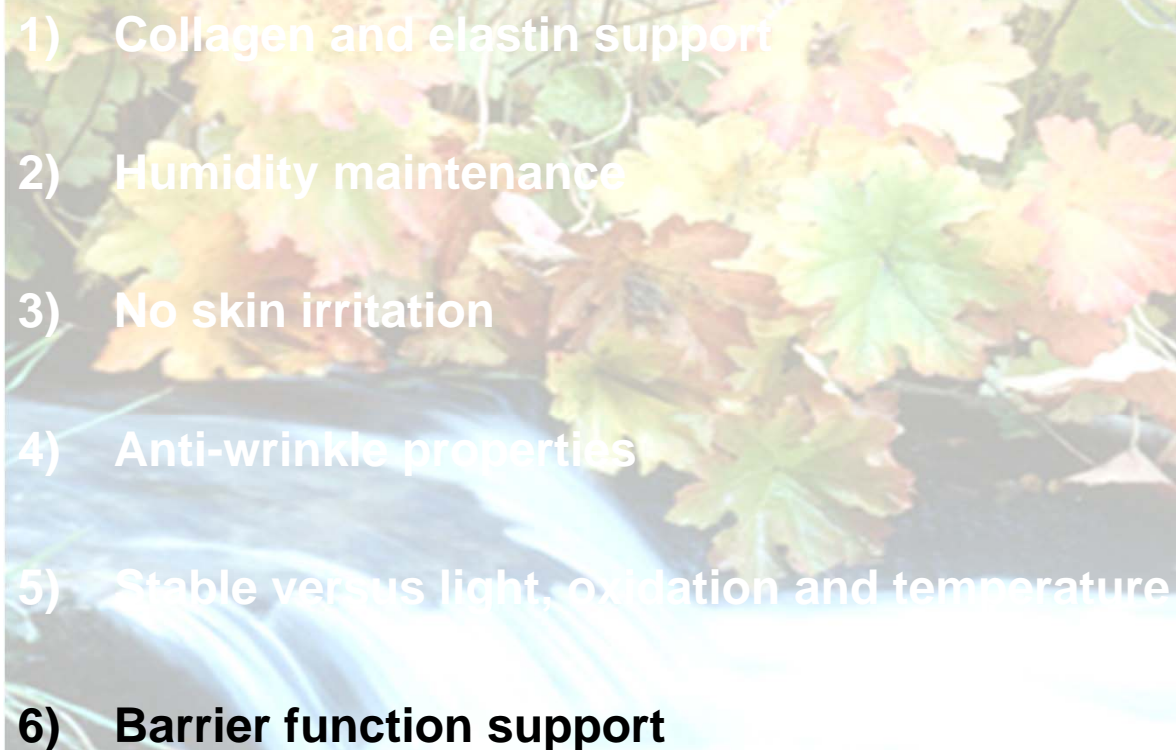
5) Stable versus light, oxidation and temperature

- **Light stability**
 - ⇒ **No decomposition**
- **Oxidation with H₂O₂**
 - ⇒ **No oxidation** after 24 and 48 hours
- **Storage investigations at different temperatures**
 - ⇒ **No degradation**



The active in RonaCare[®] Luremin[®] shows
excellent stability in powder form and in solution!

Claims fulfilled by RonaCare® Luremin®

- 
- 1) Collagen and elastin support
 - 2) Humidity maintenance
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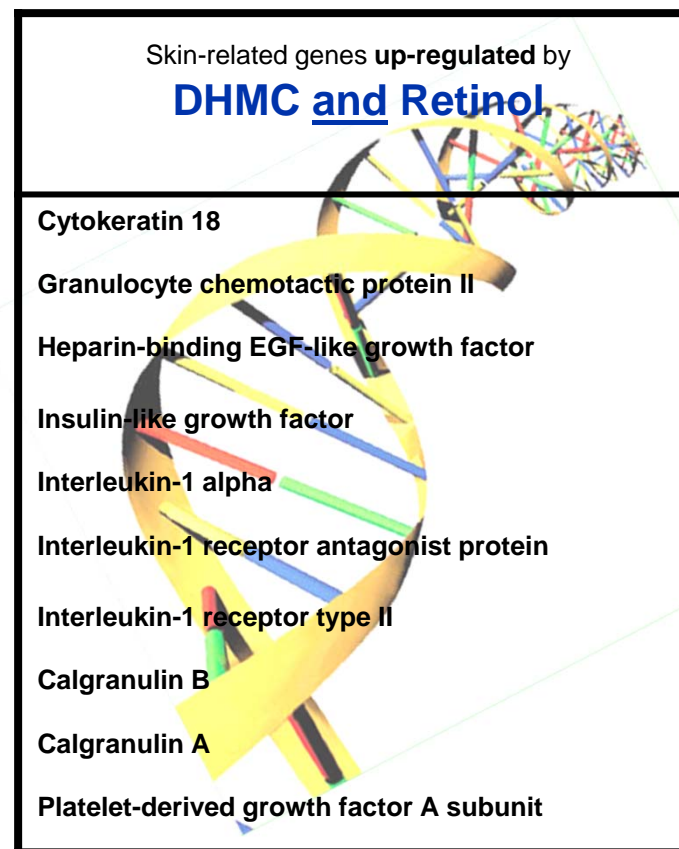
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6) Retinol-like activity

- **cDNA technology** determines whether a substance activates or inactivates genes in the cell nucleus.
- Depending on the resulting activation pattern the possible influence on the skin can be deduced.

10 up-regulated genes are in common with retinol to support the retinol-like activity of DHMC.

Skin-related genes **up-regulated** by **DHMC and Retinol**



- Cytokeratin 18
- Granulocyte chemotactic protein II
- Heparin-binding EGF-like growth factor
- Insulin-like growth factor
- Interleukin-1 alpha
- Interleukin-1 receptor antagonist protein
- Interleukin-1 receptor type II
- Calgranulin B
- Calgranulin A
- Platelet-derived growth factor A subunit

Picture: http://1in100.files.wordpress.com/2009/06/dna_500.jpg

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6) Retinol-like activity – Involucrin

Involucrin

- Protein precursor of the epidermal cornified envelope.
- It is cross-linked to other membrane proteins via Transglutaminase and **helps in the formation of an intact skin barrier.**
- It shows a positive regulative influence on the **keratinization process.**



The active of RonaCare® Luremin® (DHMC) stimulates 3.5 times the production of m-RNA of Involucrin.

Retinol is known to show no effect!

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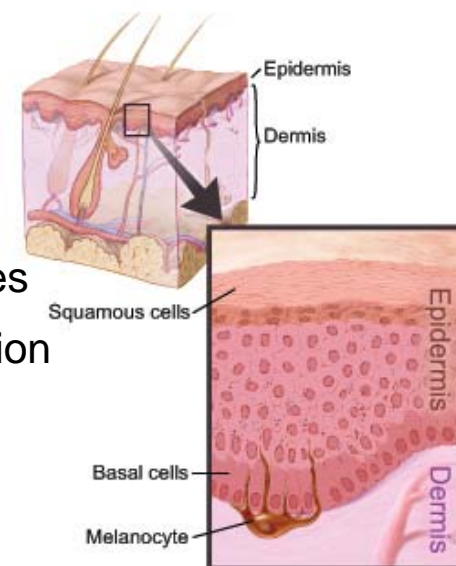
6) Retinol-like activity – Transglutaminase

Transglutaminase – a cross linking enzyme

- Catalyses the formation of covalent bonds between Lysine and Glutamine residues
= **biological glue to build up a highly molecular protein structure**

In case of up-regulation of **Transglutaminase**

- Increase the resistance of the skin to environmental influences
- Improvement of the skin structure, in particular for the formation of smooth skin
- Ameliorated barrier function



<http://www.caring4cancer.com/go/skin/basics/what-is-nonmelanoma-skin-cancer.htm>

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6) Retinol-like activity – Transglutaminase

In vitro Transglutaminase (TGK) activity assay:

- Retinol ($1 \cdot 10^{-6}$ M) **reduces** the activity of TGK
- The active in RonaCare® Luremin™ ($4 \cdot 10^{-2}$ mM) **increased** the activity of TGK .

It indicates a **different efficacy mechanism than retinol!**

RonaCare® Luremin® has a positive regulative influence on the keratinization process and may normalize skin.

RonaCare® Luremin®

It offers

- **Tightening**
- **Refreshing**
- **Rejuvenating and smoothing**
- **Stability and non irritation**

Challenge

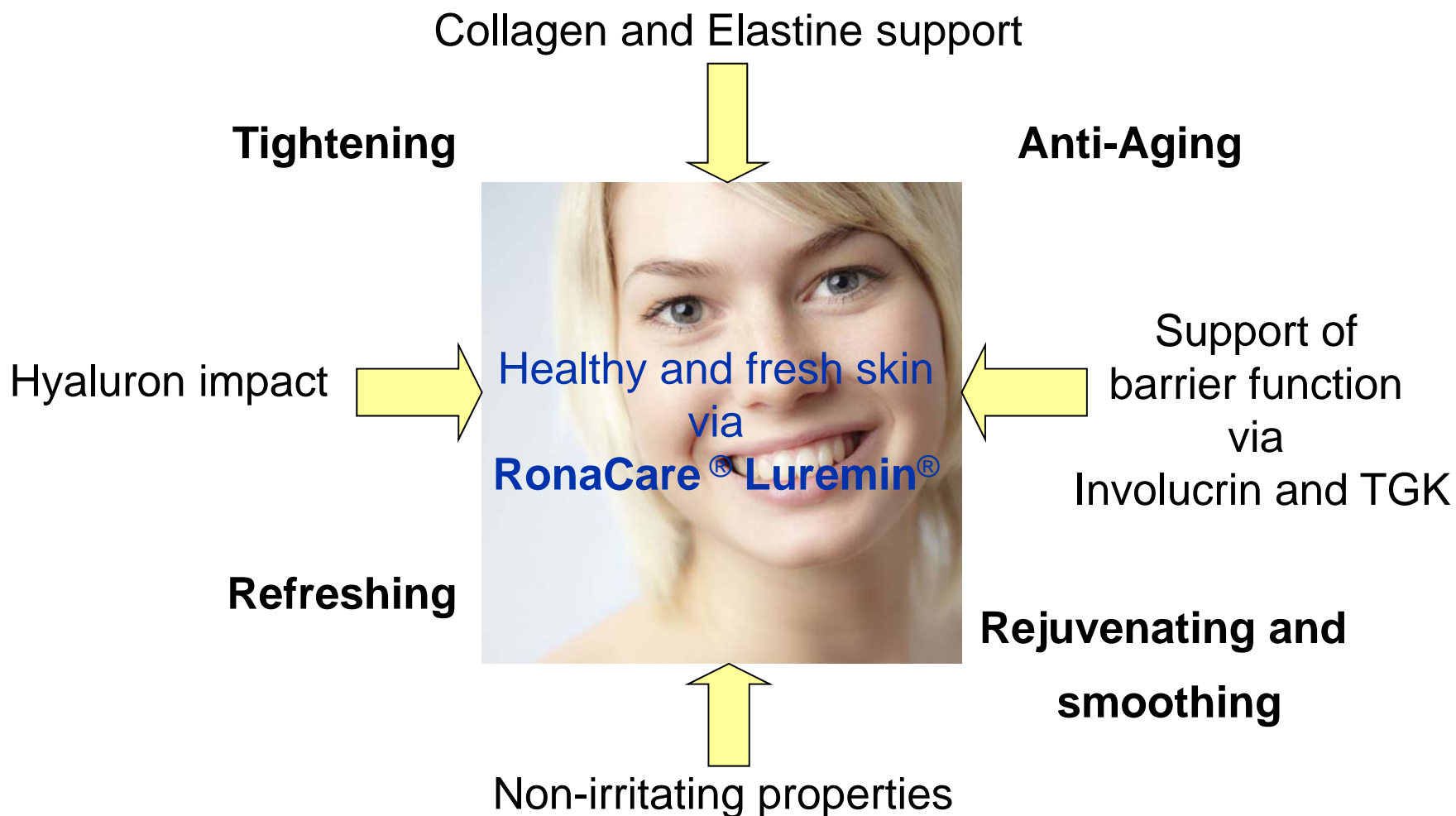


RonaCare® Luremin®

– **efficient and reliable** –

RonaCare® Luremin® is nature-identical and readily biodegradable.

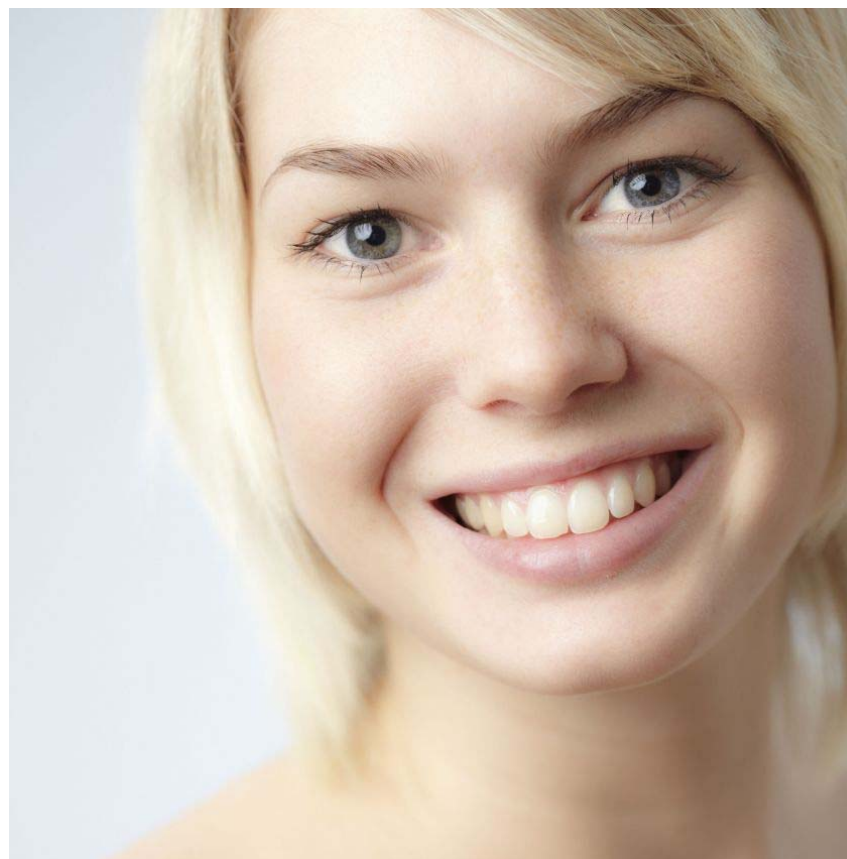
A complete solution !




RonaCare® Luremin®

- **Suggested applications**

- Anti-aging products
- Anti-wrinkle products
- Sun care products
- Dermocosmetic products



RonaCare® Luremin® Further information

- Use concentration 1 – 2 %  0.05 – 0.1 % of active **DHMC**
- Concentrations of 1 – 2 % of **RonaCare® Luremin®** will not affect the color of the formulation.
- Use in the water phase of an emulsion.
- Dispersion can be improved by surface active agents
- Stable within standard cosmetic pH ranges



RonaCare® Luremin®

Nice formulation with UV Protection, e.g.

MDA-S-42-01 **Anti Aging Face Cream with Sun Protection**

- Combination of UV-filters including RonaCare® UV-Pearls® OMC and RonaCare® AP and RonaCare® Luremin®
- Expected SPF value: 10
- Excellent touch, luxurious sensation

Further formulations available:

- Formulation booklet



RonaCare® Luremin®

offers

a **nature-identical approach**

to rejuvenate your skin in the most gently loving way!



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