Active Beauty
Scientific File

Redens'In™
In-depth skin redensifier

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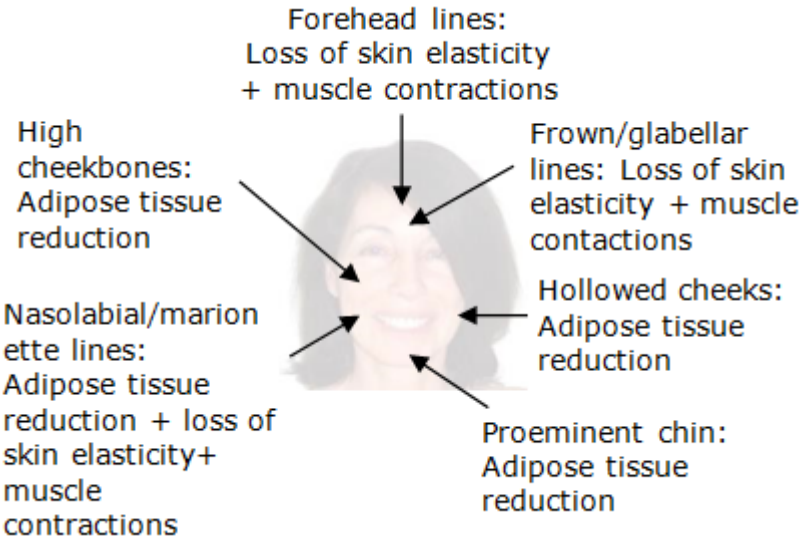
1. Skin and ageing

Ageing is a natural and non reversible phenomenon which concerns all tissues. Major symptoms are adipose tissue reduction and extracellular matrix alterations that lead to ageing signs: wrinkles, hollowed cheeks, alteration of the facial feature harmony.

Nowadays, surgery solutions have been developed to limit subcutaneous loss of volume, such as injectable fillers. These operations are more and more popular, but they are still expensive and painful.

Givaudan Active Beauty has launched a non invasive cosmetic solution that mimics injection. This active is a cosmetic alternative to plastic surgery. It resculpts the face from within thanks to a volumizing effect. Its action is optimized by a unique patented technology of vectorization.
Ageing signs are mainly due to the alteration of the extracellular matrix (ECM) composition, leading to a loss of skin elasticity, and change in adipose tissue distribution. Consequences of both of these events are reinforced by the effect of gravity.



Ageing and lipoatrophy
Children's adipose tissue is abundant with a homogenous distribution. However, it undergoes several modifications with age. The ageing process starts at 20, with visible signs appearing at 30 years old.

Lipoatrophy is a decrease of fat tissue volume. It mainly concerned the face area.

This mechanism is due to several biological imbalances:

- Decrease of adipocyte size;
- Alteration of adipocyte function ;
- Impaired fat cell differentiation;
- Fat distribution.

Ageing signs appear progressively and chronologically. Lipoatrophy affects first temples, jowls, and then chin.

Ageing and loss of skin elasticity
Ageing is responsible for a decrease of the connective tissue quality. Numerous component contents, such as collagen, elastin and glycosaminoglycans (GAG) decrease with age.

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Hyaluronic acid is the major GAG of the human skin. Total HA content in adult body is approximately: 15g. This high molecular weight polymer, thanks to its viscoelastic properties, is responsible for extra cellular matrix structure and in water balance.

HA is the ground substance of the ECM. Free form HA is implicated in ECM structure. Besides, HA may be bind to some tissue proteins called hyaladherins.

Scientific study was performed to highlight age- related decrease of HA content. It has been proven that it was due to:

- an increase of HA bound forms ;
- an imbalance between HA synthesis and degradation.

This phenomenon leads to a loss of skin mechanical properties.

Wrinkle filling, a new stake for the cosmetic industry?
Young face tends to be convex, with nice curves: fleshy and smooth lips, full cheeks. With age, these lines are altered and become concave: hollowed cheeks, prominent chin…

Adipose tissue reduction and extracellular matrix modifications are responsible for these age- related alterations.

Restoring volume in specific area of the face (around the eyes and the mouth…) seems to be necessary to prevent ageing sign appearance.

Replumping the skin from within offers new perspectives to fight against ageing signs.
Nowadays, this mechanism is becoming a major stake for the cosmetic industry. Givaudan Active Beauty takes part of this trend by developing Redens'In™, a cosmetic alternative to aesthetic surgery.

2. Origin and composition

Redens'In™ is a vectorized blend of two actives:

- Hyaluronic acid, a high molecular weight natural polymer
- *Commiphora mukul* extract which increases adipose tissue volume.

2.1. Hyaluronic acid

Hyaluronic acid is a key component of the Extracellular matrix. Each HA molecule is composed of n repeating disaccharide units (Sodium glucuronate and N-acetyl-glucosamine).

Origin
HA is obtained from a biotechnological process using vegetable substrate and lactic bacteria. Givaudan Active Beauty has developed an environment-friendly process based on renewable resources.

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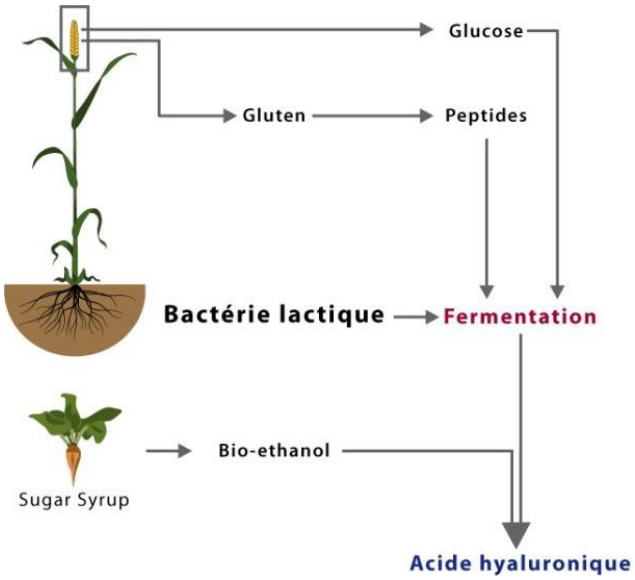

2.2. *Commiphora mukul* extract

Ethnobotanical data

Commiphora mukul is a tree from the Burseraceae family. This shrub grows in rocky and arid regions in Western India and in Arabic peninsula.

Uses

Commiphora mukul secretes a resin known as Bdellium in the Bible. It is one of the most ancient perfumed substance. Similar to myrrh, it has been exported during centuries by caravans along the Arabic Incense Road. Bdellium belonged to the gifts of Queen She-ba to King Salomon.

The oleoresin is obtained by incision of the *Commiphora mukul* bark. Under this form, it is known as “Guggul” and has been used for centuries in Ayurvedic medicine.

Redens’In™ is composed of an oleoresin extract.

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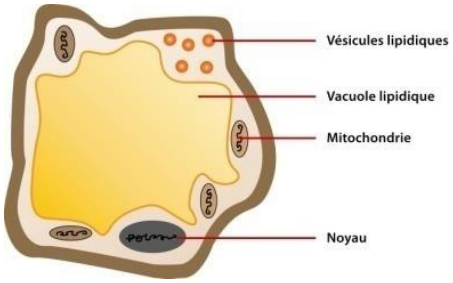
3. Mechanism of action

3.1. Hyaluronic acid

Hyaluronic acid is transferred to the deep layers of the skin thanks to the Spherulite technology and alleviates HA content decrease due to ageing. It plumps the dermis and prevents loss of skin tonicity and elasticity.
Redens'In™ fills up wrinkles by mechanical effect.

3.2. *Commiphora mukul* extract

Lipid storage is realized in specialized cells of the hypodermis called adipocytes.



During lipogenesis, these extensible cells store the lipids as triglycerides in vacuoles.

Commiphora mukul extract acts on two synergistic mechanisms to limit lipolysis and enhance lipogenesis:

- G3PDH activation: triglyceride synthesis in adipocyte need the presence of glycerol under its activated form called glycerol-3-Phosphate.
- Glycerol 3-phosphate deshydrogenase (G3PDH) is a key enzyme for glycerol-3-Phosphate formation.
- cAMP inhibition: Adenosine Mono-phosphate cyclique (AMPc), synthesizes form ATP with Adenylate Cyclase, is responsible for proteine kinase A activation. This enzyme is involved in tryglyceride degradation in fatty acids and glycerol.

This extract increases triglyceride storage in adipocytes by physiological effect.

***Commiphora mukul* extract increases adipocyte volume and thus limits wrinkles appearance by physiological action.**

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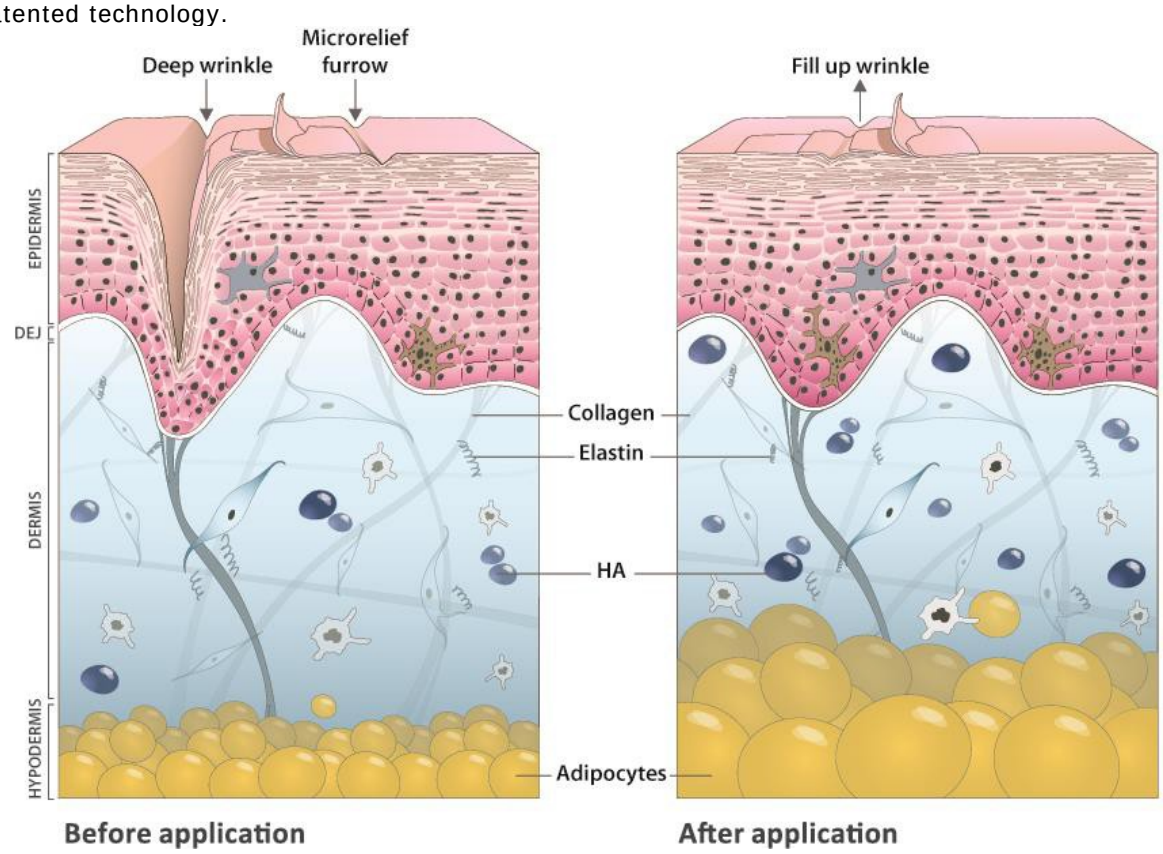
3.3. Redens'In™

Redens'In™, optimized blend of HA and *Commiphora mukul* extract, has a volumizing effect on the dermis and the hypodermis.

Redens'In™ fills up wrinkles from within by mechanical and physiological effects. It limits subcutaneous volume loss. This active is vectorized toward specific facial areas thanks to a unique patented technology.



4. Test

4.1. Skin elasticity and wrinkle appearance, *in vivo* test

Skin is subject to ECM and adipose tissue age-related alterations. These modifications lead to the loss of skin elasticity and wrinkle appearance.
21 female volunteers, from 45 to 65 years old, with crow's feet.

- Treatment: application of Redens'In™ at 2% in a cream, twice a day (morning and night) during 28 days on the crow's feet area.
- Conditions: volunteers haven't used any topic or systemic treatment likely to interfere with the study.

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Phase	Components	%
A	Emuliance Cetearyl wheat bran glyco-sides (and) Cetearyl alcohol Caprylic/capric triglyceride Preservative	5% 12% QS
B	Water Propylene glycol	QSP 100% 7.5%
C	Redens'In™ Water	2% 1%
D	Fragrance	QS
E	Sodium hydroxide	QS pH 5

To highlight Redens'In™ efficacy, three analysis have been processed:

- Quantitative evaluation of the skin appearance using Skin Image Analyzer®, with Quantiride® software
- Photography analysis
- Evaluation of the perceived efficacy by the panel through a questionnaire.

4.1.1. Quantitative evaluation by image analysis

The objective is the depth wrinkle evaluation before and after treatment with Redens'In™ at 2% in a cream on the crow's feet.
Quantitative evaluation of the skin relief variations is realized with a specific software: Skin Image Analyser® - MONADERM.
This usual method analyzes shadows obtained from crows feet silicone prints exposed to oblique lighting (35°).

Parameters:

- Total wrinkle surface
- Microrelief furrow number (< 55 µm) and median wrinkle number (55-110 µm

Protocol

- Silicone prints are taken on the treated zone at DO and at the end of the treatment;
- Prints are lighten by oblique light (35°), and shadows are then observed by digital camera linked to a computer;
- Quantitative analysis of the skin relief by Quantirides®

All furrows with a minimum of 0.03mm2 are detected.

Results

After a 4 week treatment, the analysis has proven:

- A significant decrease of the microrelief furrow number (-37%);

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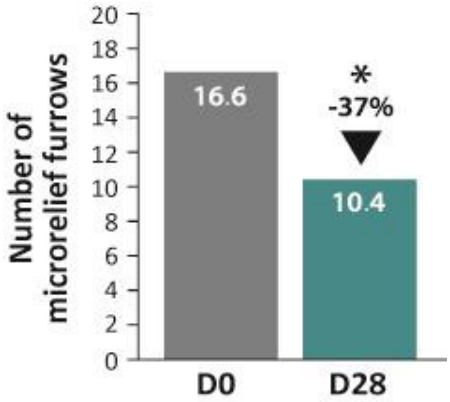
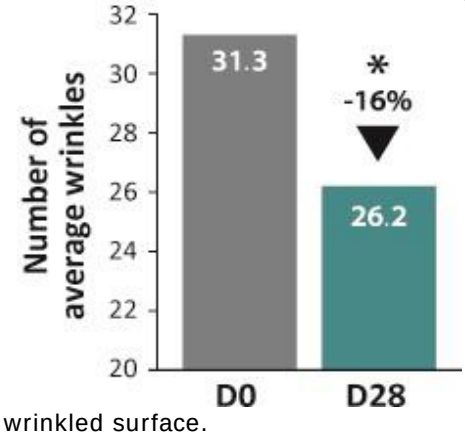


- A significant decrease of the average wrinkles number (-16%);



- A decrease of the total wrinkled surface.

At the end of the treatment, the skin is smoother.

4.1.2. Evaluation of the visual expected effect

Protocol
Visualization of Redens'In™ lifting effect, after a 4 weeks treatment with a cream formulated with 2% of the active.

Macrophotographies are taken with a digital camera in standardized conditions (light, distance, speed, aperture…).

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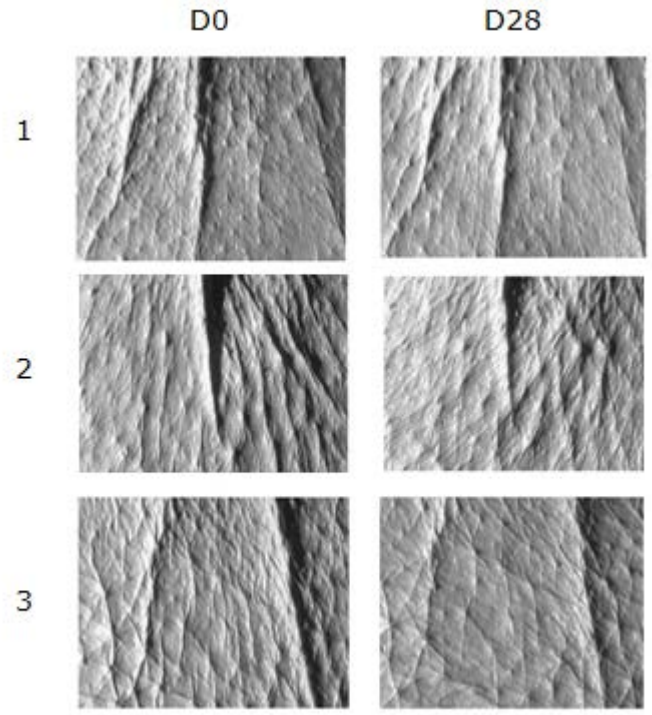

Redens'In™ visible reduces skin relief after 28 days.

4.1.3. Panel evaluation

Evaluation of the perceived efficacy of the cream by the panel, through a questionnaire.

Volunteers answer to a questionnaire at the end of the treatment.
Most of the volunteers consider that the product is efficient, with visible results.

4.1.4. Conclusion

Tests have proven, after a daily treatment with Redens'In™ at 2% in a cream:

- An outstanding anti-wrinkle effect by image analysis and photography;
- A customer satisfaction through a questionnaire, which lays stress on a perceived efficacy of the product.

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5. Cosmetic uses

By increasing dermis and hypodermis volume, Redens'In™ can be use in anti-ageing product range:

- Anti-wrinkle products
- Eye contour serums
- Lip contour products (serums, …)

6. Conclusion

Ageing signs are due to alterations of both dermis and hypodermis composition. Skin loses its mechanical properties and becomes thinner, leading to wrinkles appearance.

Redens'In™ is a cosmetic alternative to plastic surgery. It replumps the skin by increasing HA level and fat storage in specific area.

7. References

1.ALSTER. T, Lipoatrophy and Aging, Washington Institute of Dermatologic Laser Surgery, Georgetown University Medical Center, Washington DC.
2.SHIFFMAN A., KAMINSKI M., Fat transfer to the face, Technique and New concepts, Facial plastic surgery clinics of North America, vol 2, 2001.
3.ASKEN S., Microliposuction and Autologous Fat transplantation for aesthetic enhancement of the aging face, Dematol Surg Oncol, 1990.
4.GOSAIN K., KLEIN H., SUDHAKAR V., PROST W., A volumetric analysis of soft tissue changes in the aging midface using High Resolution MRI: Implication for facial rejuvenation, Volumetric analysis of aging midface, vol 115, 2004.
5.SEMERIA E., LEVY JL., Le vieillissement facial, analyse de la sémiologie esthétique et proposition de systématisation des traitements, Annale de chirurgie esthétique, Volume 44, N°6, 1999.
6.DONOFRIO M., Fat distribution: A morphologic study of the aging face, Dermatolog Surg, 1107-12, 2000.
7.ASCHER B., COLEMAN S., ALSTER T., BAUER U., BURGESS C., BUTTERWICK K., DONOFRIO L., ENGELHARD P., GOLDMAN P., KATZ P., VLEGGAAR D., Full scope of effect of lipofacial lipotrophy: a framework of disease understanding, Dermatolo surg, 32 : 1058-69, 2006.
8.MEYER J.M., STERN R., Age-dependent changes of Hyaluronan in human skin, The journal of investigative dermatology, vol 102, 1994.
9.MANUSKIATTI W., MAIBACH H., Hyaluronic acid and skin: wound healing and aging, International journal of dermatology, vol 35, 1996.
10.JUHLIN L., Hyaluronan in skin, Journal of internal medicine, 61-66, 1997.
11.MONHEIT G., COLEMAN K., Hyaluronic acid fillers, Dermatologic therapy, vol 19, 141-50, 2006.

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