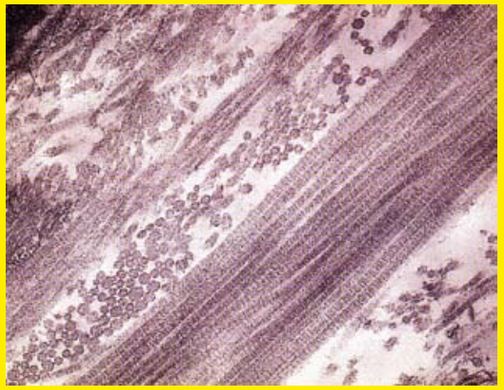

RAFFERMINE®

ELASTICITY AND CUTANEOUS RESISTANCE TO THE TEST OF TIME

The different components of the dermis (cells and matrix) interact ones with the others to give birth to a functional tissue which maintains the upper layers of the skin. In the course of aging, this elastic tissue undergoes deep deteriorations pointed up by cutaneous slacking and wrinkles.

Just as the cell walls of soybeans – structurally and functionally speaking – RAFFERMINE®, rich in glycoproteins and purified polysaccharides, favors the reorganization of the three - dimensional matrix network:

➢ It revitalizes the renewal of the ECM by stimulating: the synthesis of collagen I, of fibrilline-1, and of GAGs, highly hydrophilic molecules involved in the moisturizing and the plasticity of the skin.

➢ It stimulates the contraction capacities of fibroblasts and enhances the cell-matrix adhesion by boosting the synthesis of fibronectin.

On account of the fact that it increases the functionalities of the dermis network and reinforces the biomechanical properties of the skin, RAFFERMINE® is recommended for face and body toning skin care.

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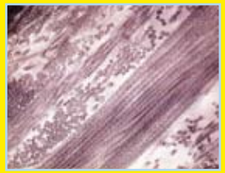
Engineering natural active ingredients



RAFFERMINE®

Rich in glycoproteins and polysaccharides of soybean membranes

Stimulates the synthesis of the extracellular matrix

- Boosts the synthesis of collagen I fibers
- Increases the synthesis of GAGs
- Enhances the synthesis of fibrillin-1

Favors the reorganization of the matrix network

- Augments cell-matrix interaction
- Improves the contractile properties of fibroblasts

Improves skin tone and elasticity

FIRMING EFFECT - ANTI-WRINKLE EFFECT

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RAFFERMINE®

GENERAL PRINCIPLES

RAFFERMINE® is a plant active substance obtained from soybean membranes. Rich in glycoproteins and structural polysaccharides, it reinforces the three-dimensional network of the dermis and improves firmness of the skin:
- by revitalizing programs for the synthesis of components of the extracellular matrix (ECM),
- by stimulating the adhesion and contraction capacities of fibroblasts to boost the functioning of the dermal network.

➤ RAFFERMINE® stimulates the synthesis and reorganization of the ECM

RAFFERMINE® revitalizes fibroblasts metabolism and boosts the synthesis of constitutive macromolecules of the ECM: collagen I, glycosaminoglycans and fibrillin-1. RAFFERMINE® thereby favors the renewal of the ECM.

RAFFERMINE® enables the continual remodeling of the ECM:
- via its direct action, by preserving the contractile properties of fibroblasts
- via its indirect action, by stimulating the synthesis of fibronectin, an anchoring glycoprotein, mediator of cell/matrix adhesion.

After 28 days of treatment, RAFFERMINE® improves skin tone and elasticity. Wrinkles in the crow's feet and nasolabial fold decrease significantly.

TECHNICAL SHEET

- **Latin name:** *Glycine soja*
- **I.N.C.I. name:** Hydrolyzed Soy Flour
- **Cas N° :** 9010-10- 0

Form
- Aqueous solution
- Aspect: limpid liquid
- Odor: weak
- Color: amber

Analytical features
- Dry matter: 12 - 18 g/l
- Proteins (Kjeldhal method): 4 - 7 g/l
- Carbohydrates (Dubois method): 5 - 9 g/l
- pH: 6.0 to 7.0
- Hydroxyproline: > 4000 µg/g of proteins
- Uronic acids: > 2.5 g/l
- Preservative: 0.29% phenoxyethanol, 0.11% parabens

Bacteriology
- Sterile product
- No yeast and mould present
- No pathogenic germs present

Packaging
Sterile 1L and/or 5 L plastic container

Storage
Store preferably at +20°C

Use
- Fully soluble in aqueous medium
- Solubility in ethanol: soluble up to 20/80 ethanol/water (v/v)
- Can withstand temperatures up to 80°C for at least two hours
- Stable with pH > 5
- Recommended amount: 2 to 5%

Innocuousness

✓ Determination of irritant potential on caucasian skin: Non irritant
✓ No mutagenecity according to Ames' test
✓ No phototoxic
✓ Non cytotoxic
✓ Evaluation of sensitizing capacity on human volunteers with normal skin: Hypoallergenic
(Marzulli-Maibach method)

COSMETIC EFFICACY

IN VITRO STUDIES

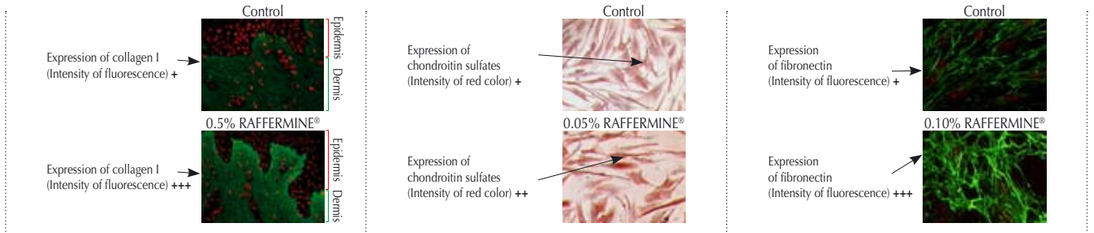
Effect of RAFFERMINE® on the synthesis and reorganization of the ECM

1/ Quantification of the effect of RAFFERMINE® at 0.1% on the components of the ECM - normal human fibroblasts -

	Collagen I	Fibrillin-1	Fibronectin
Method	Elisa	Quantitative PCR	Elisa
Result	+693%*	+24%	+159%

* Effect comparable to that obtained with vitamine C at 0.5 µg/ml - Significant result according to Student's test (P<0.05)

2/ Visualization of the effect of RAFFERMINE® on the components of the ECM

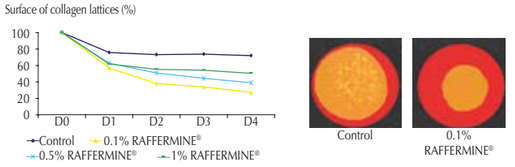


RAFFERMINE® stimulates the synthesis of constitutive macromolecules of the ECM.

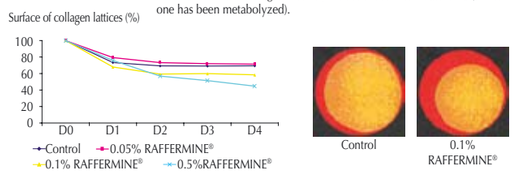
3/ Evaluation of the effect of RAFFERMINE® on the dynamic properties of fibroblasts grown in an equivalent dermis

Growing fibroblasts in a 3-dimensional collagen network (equivalent dermis) enable the study of the effect of RAFFERMINE® on their dynamic properties in a physiological environment mimicking *in vitro* the cell-matrix interactions that exist *in vivo*.

➤ ***Direct effect*** Treatment of fibroblasts grown in a collagen matrix with RAFFERMINE®.



➤ ***Indirect effect*** Pretreatment of fibroblasts with RAFFERMINE® during 5 days. Then, inoculation in the collagen matrix (indirect effect of RAFFERMINE®, which one has been metabolyzed).



RAFFERMINE® stimulates the mechanism of contraction of equivalent dermis caused by fibroblasts. The results obtained suggest that RAFFERMINE® boosts (direct effect) the contractile capacity of fibroblasts and favors their attachment to collagen fibers. The existence of an « indirect » effect suggests that RAFFERMINE® acts on the synthesis of proteins or glycoproteins such fibronectin, involved in the cell-matrix adhesion.

IN VIVO STUDIES

Effect of RAFFERMINE® on the biomechanical properties of the skin: elasticity and tone

Cutometer study on 20 female volunteers, mean age 55 ± 11 years.

	R2 : gross elasticity	R5 : net elasticity	- X : Tone
Facial skin	+10%* (P=0.0486)	+12%* (P=0.0062)	+19%* (P=0.0107)

* significant results (P<0.05)

After 28 days of twice daily application and compared to the placebo, RAFFERMINE® formulated at 4% in an emulsion increases the parameters characteristic of skin elasticity and tone. 70% of the volunteers presented a clear-cut improvement of elasticity and 75% an improvement of skin tone.

Effect of RAFFERMINE® on anti-wrinkle properties

Profilometer study on 20 female volunteers.

* Significant results according to Student's test (P<0.05)
** Significant result according to Student's test (P<0.10)

	Crow's feet *53 ± 9 years*	Nasolabial fold *55 ± 11 years*
Number of wrinkles	-11%* (P=0.0413)	-8%** (P=0.0569)
Total wrinkled surface	-19%* (P=0.0353)	-28%* (P=0.0006)
Total length of wrinkles	-12% (P=0.1122)	-13%* (P=0.0260)

Tested at 4%, RAFFERMINE® possesses anti-wrinkle properties after 28 days of treatment of the crow's feet and nasolabial fold in 72% and 90% of volunteers, respectively.

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