

GATULINE® EXPRESSION



FAST TRACK SMOOTHING

The fight against the appearance and deepening of wrinkles remains the legitimate crusade of the cosmetic industry which needs raw materials offering **security** and **proven efficacy**.

Facial skin is subjected to the emotions and various forms of environmental stress and is marked by so-called “expression” lines. These lines result from **thousands of daily involuntary micro-contractions of the facial muscles**. They lead to the appearance of real deep wrinkles, the inevitable consequence of movements and pulling on the skin.

Besides the solutions proposed by plastic surgery and other invasive techniques, GATTEFOSSÉ proposes a **safe plant-based alternative** that meets the principal requirement of a skincare product: **rapid results**.

GATULINE® EXPRESSION

*A targeted anti-wrinkle ingredient:
the reliable option for smoother skin.*

Extracted from a tropical plant, GATULINE® EXPRESSION provides an effective solution to the demand for rapid reduction of facial wrinkles:

- **Quick action** shown *in vitro* and *in vivo*, as GATULINE® EXPRESSION **immediately limits** micro-contractions that create then aggravate facial wrinkles.
- Spectacular **reduction of wrinkles** leading to a **significantly smoother skin**.



ORIGIN & COMPOSITION

A plant based active



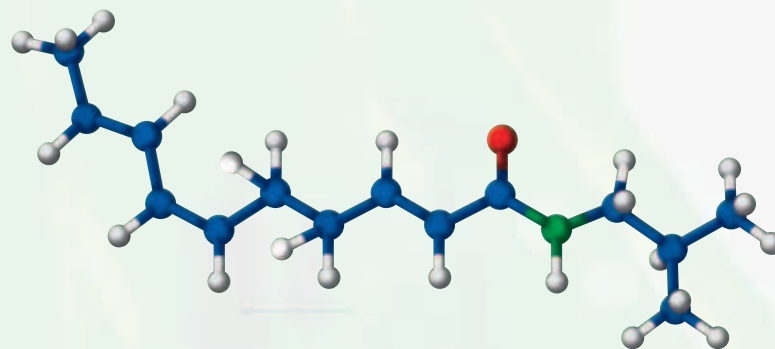
GATULINE® EXPRESSION is extracted from the upper parts of the *Acmella oleracea* plant belonging to the Compositæ family (*Compositæ-Helianthææ*). This small plant, which blossoms all year long, has a broad geographical footprint, covering the whole tropical zone in South America, Africa and Asia.

Originating from Peru and Brazil, *Acmella oleracea* is a cultivated non-endangered species, known and used for a very long time in Madagascar and La Réunion. Called “**Mafane**” in the Indian Ocean, this plant is used in food and as a medicinal plant. It is precisely in the wild region of La Réunion that GATTEFOSSÉ harvests it.

Composition

The bibliographic study has revealed a list of key majority compounds present in this plant. These are mainly isobutylamides of polyenic and polyenyinic acids. Of the dozen molecules identified, spilanthol (or (E,Z,E)-N-2-isobutyl-2,6,8-decatrienamide) is the molecule mainly responsible for the activity of GATULINE® EXPRESSION.

Fig. 1

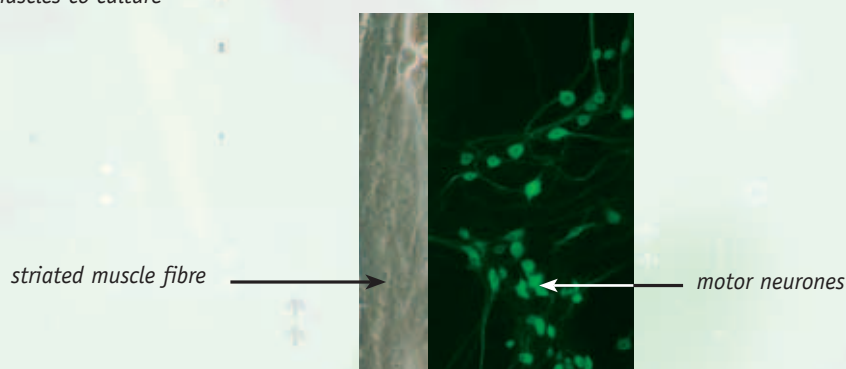


IN VITRO EFFICACY

Nerve-muscle co-culture model

The myorelaxing activity of the extract was first tested on a model reproducing muscle contractions. This model is produced by the co-culture of motor neurones with human muscle cells forming striated muscle fibres which, once innervated, spontaneously contract (fig 2).

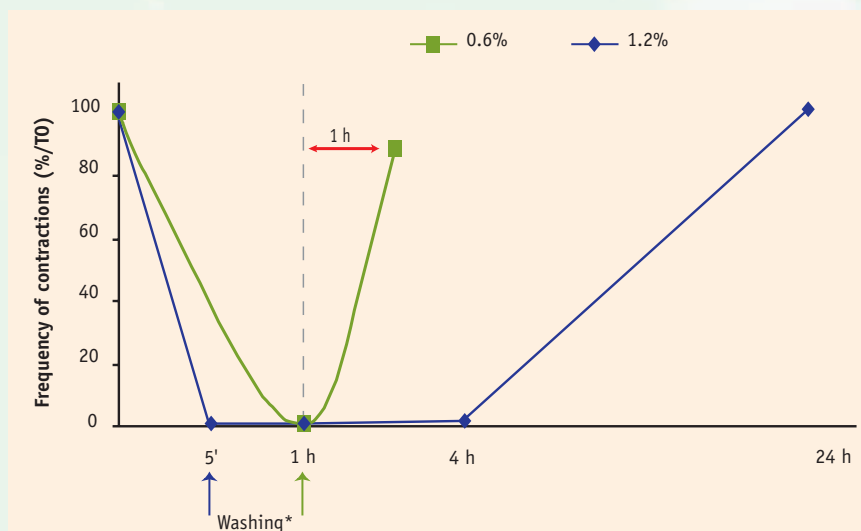
Fig. 2: Nerve-muscles co-culture



The muscle contractions were counted to prove that GATULINE® EXPRESSION blocked these contractions (fig 3). This blocking process is fully dependent on the concentration of the tested extract.

As such, it was demonstrated that **just 0.6% of GATULINE® EXPRESSION is enough for complete myorelaxation.**

Fig. 3: Activity of GATULINE® EXPRESSION on the cells



* (Change of the culture medium after complete blocking).

GATULINE® EXPRESSION shows a **fully reversible function** (complete recovery after 24 hours) and is thus positioned as a very safe extract while remaining highly effective.

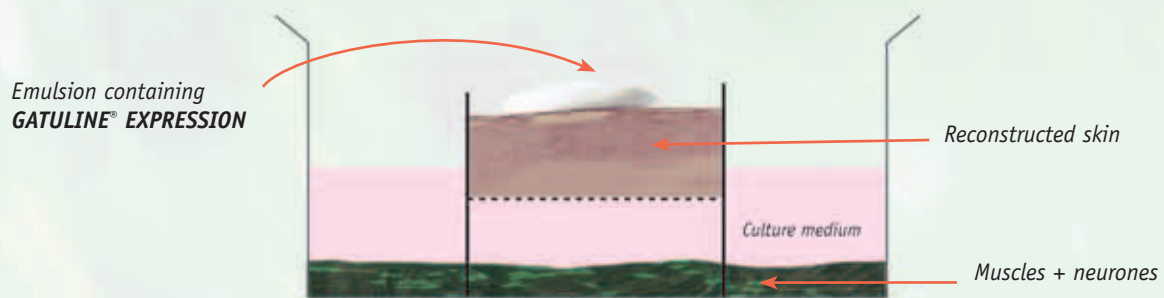
In a second test, the efficacy of GATULINE® EXPRESSION formulated in a cream was quantified using another innovative *in vitro* model.



Bioavailability

In order to make sure that GATULINE® EXPRESSION **does not deteriorate in the formulation or after topical application**, a new model was tested. This was a co-culture described in the previous page topped with reconstructed skin containing epidermis and dermis (fig 4).

Fig. 4: Schematic representation of the tridimensional model nerve-muscles-reconstructed skin



The efficacy of a standard formulation (O/W emulsion) containing GATULINE® EXPRESSION was evaluated against a placebo. Muscle contractions were counted to highlight the activity of the cream containing GATULINE® EXPRESSION on human skin and cells.

Fig. 5: In vitro activity of formulated GATULINE® EXPRESSION

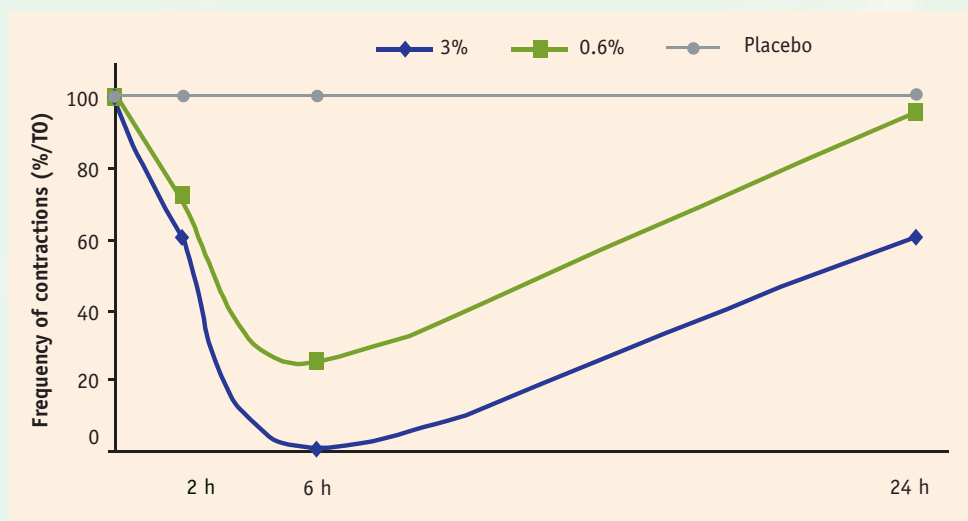


Figure 5 shows that GATULINE® EXPRESSION is a stable active ingredient, just as effective once formulated in a cream. Its **activity** is confirmed as **dose-dependent and reversible**.

GATULINE® EXPRESSION used in a standard formulation presents **good bioavailability**.

The 24 hour residual relaxing power of the cream containing 3% GATULINE® EXPRESSION allows us to expect an interesting **cumulative effect** when used daily.

IN VIVO EFFICACY

The *in vivo* smoothing efficacy of GATULINE® EXPRESSION has been demonstrated on “crow's feet” wrinkles.

Skin smoothing was assessed by topometric analysis using a hi-tech method: the **Fringe Projection** technique. This allowed GATTEFOSSÉ to demonstrate very precisely the benefits provided by daily application of GATULINE® EXPRESSION.

Fringe Projection, a purely optical method used to assess roughness of the skin, allows us to avoid artefacts due to contact with the skin.

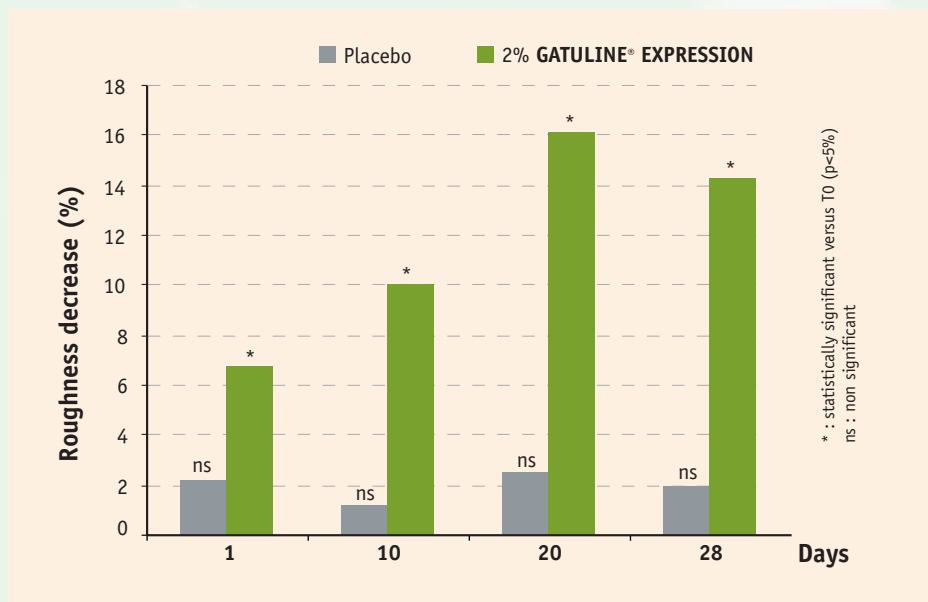
Tests were carried on two panels of volunteers (20 and 30 people) with twice-daily application for 28 days:

- 1 panel using a placebo formulation on half of the face and a formulation containing 2% of GATULINE® EXPRESSION on the other half
- 1 panel using a placebo formulation on half of the face and a formulation containing 5% of GATULINE® EXPRESSION on the other.

For the first panel, the roughness was quantified several times. This revealed the strong activity of GATULINE® EXPRESSION formulated at 2% (Fig 6).

75% of volunteers reacted very rapidly to the smoothing effect of GATULINE® EXPRESSION, the very next day after the first application.

Fig. 6: Average roughness on 15 people



The smoothing effect is visible and is reinforced during the first month of use.

The activity is therefore instant on the reduction of expression lines with only 2% of GATULINE® EXPRESSION.

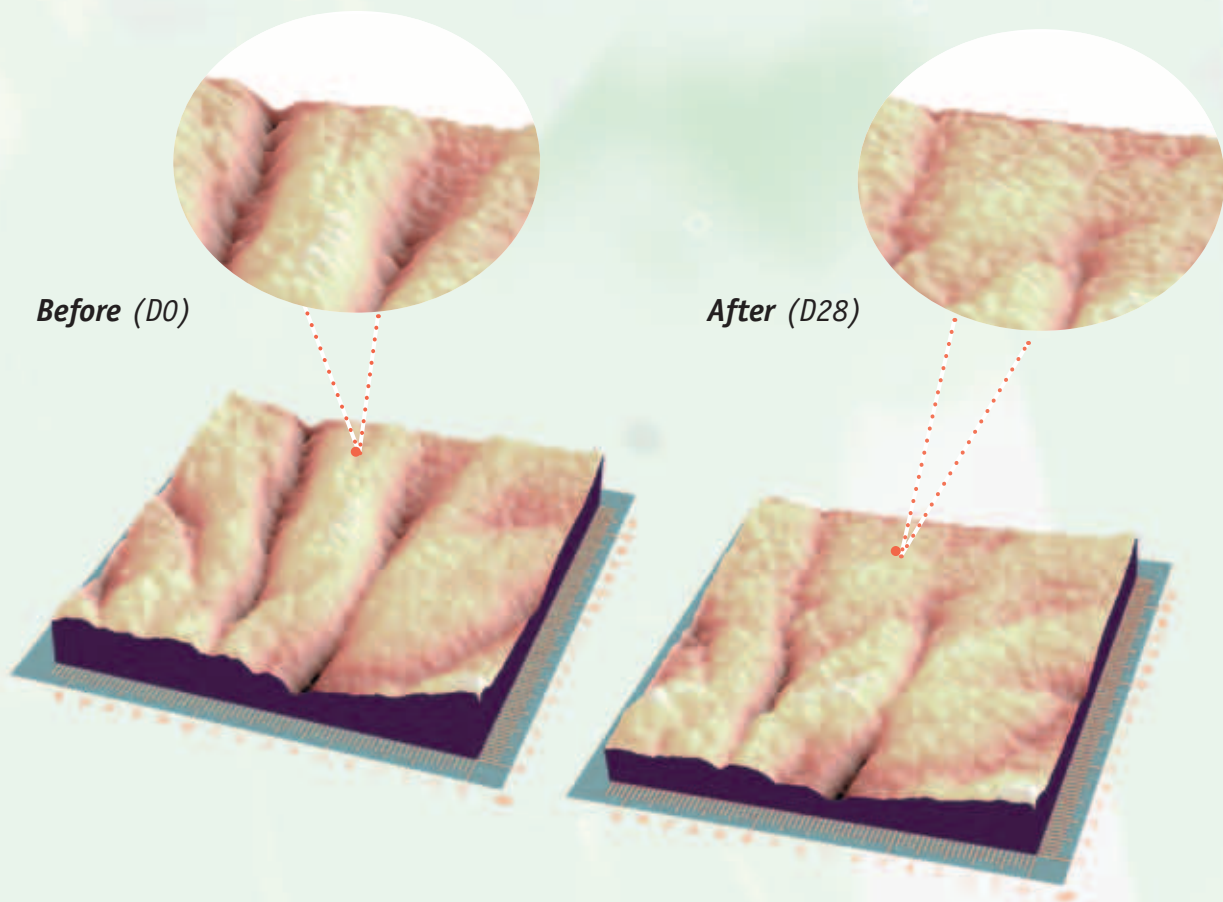


The results of the second panel confirmed the significant activity of the extract on wrinkle reduction.

With 5% of GATULINE® EXPRESSION, **more than 83% of volunteers** benefited from a reduction in crow's feet wrinkles.

Tested against a placebo, GATULINE® EXPRESSION offers very visible results on the skin of volunteers. Figure 7 shows that wrinkle depth is reduced, the skin is smoothed and looks younger.

Fig. 7: GATULINE® EXPRESSION activity at 5% in formulation, before treatment and after 28 days



GATULINE® EXPRESSION is therefore a key ingredient for the reduction of facial wrinkles.

➡ Very rapid effect in comparison with traditional anti-wrinkle ingredients.

Quality

The *Acmella oleracea* plant is harvested in a pollution free environment through a supply chain which guarantees full traceability.

Identified and measured by HPLC, the spilanthol molecule is guaranteed in all batches with a minimum concentration of 50 mg/l of GATULINE® EXPRESSION.

Intellectual property

A patent on GATULINE® EXPRESSION has been filed for targeted application on wrinkle smoothing.

CONCLUSION

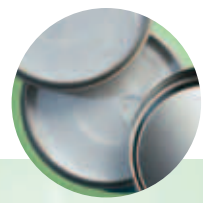
Expression lines result from the accumulated effect on the skin of movements constantly imposed by the subcutaneous muscles. GATTEFOSSÉ research has found a solution to attenuate these muscle contractions and thus delay formation and deepening of these wrinkles.

The **myorelaxing mechanism** has been clearly identified as being the cause of the activity of GATULINE® EXPRESSION.

In vitro tests conducted with GATULINE® EXPRESSION show that this *Acmella oleracea* extract **precisely and rapidly targets** the mechanism responsible for the formation of expression lines.

Finally, *in vivo* tests show that GATULINE® EXPRESSION **instantly and strongly reduces the wrinkled appearance** of the faces of a large majority of the panelists.

GATULINE® EXPRESSION is thus destined to become a key active ingredient for the next generation of anti-wrinkle cosmetics.



APPLICATIONS

GATULINE® EXPRESSION is the ideal active ingredient for **facial anti-ageing and anti-wrinkle care**, in particular aimed at smoothing out expression lines. This targets crow's feet, forehead wrinkles, frown lines between the eyebrows and the nasogenian fold.

This new active is precisely dedicated to skincare products and its **easy formulation** allows its use in emulsions, microemulsions, serums and gels.

The recommended concentration of use is between 2% and 5%.

SPECIFICATIONS

Organoleptic characteristics:

Aspect.....yellow to amber limpid liquid
Odour.....characteristic

Physico-chemical characteristics:

Specific gravity at 20°C (D20/4)0.87 to 0.91
Refractive index at 20°C 1.345 to 1.385
pH5 to 7
Dry extract.....> 0.5 g/100g
Solubility at 20°C soluble in water, insoluble in oils
Spilanthol content > 50 mg/l

Transport and storage conditions:

This product does not contain preservative. Prevent exposure to light. Store under nitrogen at room temperature.

Packing:

Industrial standard pack.....plastic packing of 800 g or 4 kg
Samples..... brown plastic bottle of 50 g

Regulatory:

INCI nameAlcohol (and) Water (and) Acmella Oleracea Extract
CAS n° 64-17-5/7732-18-5/90131-24-1
EINECS n° 200-578-6/231-791-2/290-335-0
Australia and Japan.....Approved for cosmetic use

Toxicological profile:

Local toxicity on the skin.....not classified
Local toxicity on the eyes well tolerated
Phototoxicity assay *in vitro*without phototoxic effect
Phototoxicity.....without phototoxic effect
Sensitizationwithout allergic effect
Photosensitization without photoallergic effect
Systemic toxicity LD50>2000 mg/kg not classified
Mutagenic effect (Ames test).....without mutagenic effect



FORMULAS

| "WRINKLE CORRECTOR" SERUM | | MM 8047/C |
|----------------------------------|---|-----------------------------|
| | INCI name | Trade name |
| I | GLYCERIN | |
| | BUTYLENE GLYCOL | |
| | <i>PRESERVATIVE</i> | |
| | DEMINERALIZED WATER | |
| II | ACRYLATE/C10-30 ALKYL ACRYLATE CROSSPOLYMER | CARBOPOL® ULTREZ 20 |
| III | ACRYLATES/ACRYLAMIDE COPOLYMER (and) MINERAL OIL (and) POLYSORBATE-85 | NOVEMER® EC-1 |
| IV | OCTYLDODECYL MYRISTATE | MOD |
| | ISOSTEARYL ALCOHOL (and) BUTYLENE GLYCOL COCOATE (and) ETHYLCELLULOSE | EMULFREE® CBG |
| V | DIMETHICONE (and) DIMETHICONOL | |
| VI | ACRYLATES/ACRYLAMIDE COPOLYMER (and) MINERAL OIL (and) POLYSORBATE-50 | NOVEMER® EC-1 |
| VII | ALCOHOL (and) WATER (and) ACMELLA OLEACERA EXTRACT | GATULINE® EXPRESSION |
| | <i>PRESERVATIVE</i> | |
| | CI-15985 (0.5 SOL.) | |
| | | % |
| | | 4.00 |
| | | 4.00 |
| | | 0.50 |
| | | 79.90 |
| | | 0.10 |
| | | 0.05 |
| | | 2.00 |
| | | 1.00 |
| | | 2.50 |
| | | 0.45 |
| | | 5.00 |
| | | 0.20 |
| | | 0.30 |
| | | 100.00 |

Sprinkle Carbopol® Ultrez 20 over I. Leave to stand. Add III. Mix well. Under rapid mixing (rotor stator), add IV, then V to I + II + III. Continue rapid mixing for 10 min. Add VI and the components of VII. Continue moderate stirring for 15 min.

| ANTI-WRINKLE SMOOTHING EMULSION | | JB 1954/C |
|--|--|--------------------------------|
| | INCI name | Trade name |
| I | CETYL ALCOHOL (and) GLYCERYL STEARATE (and) PEG-75 STEARATE (and) CETETH-20 (and) STEARATEH-20 | EMULIUM™ DELTA |
| | ISOSTEARYL PALMITATE | |
| | TOCOPHERYL ACETATE | |
| | CALOPHYLLUM INOPHYLLUM (SCAVENG) OIL | |
| | PPG-3 MYRISTYL ETHER | |
| | HYDROGENATED POLYDECENE | |
| | <i>PRESERVATIVE</i> | |
| | CETOSTEARYL ALCOHOL | |
| | ISOSTEARYL ISOSTEARATE | ISOSTEARATE ISOSTEARYLE |
| | DIMETHICONE | |
| II | DEMINERALIZED WATER | |
| | GLYCERIN | |
| III | CARRAGEENAN | |
| IV | HYDROGENATED POLYISOBUTENE | |
| V | ACRYLATES/ACRYLAMIDE COPOLYMER (and) MINERAL OIL (and) POLYSORBATE-85 | NOVEMER® EC-1 |
| VI | HDI/TRIMETHYLOL HEXYLACTONE CROSSPOLYMER (and) SILICA | |
| VII | ALCOHOL (and) WATER (and) ACMELLA OLEACERA EXTRACT | GATULINE® EXPRESSION |
| | <i>PERFUME</i> | |
| | CI-42090 (0.1 SOL.) | |
| | | % |
| | | 4.00 |
| | | 3.00 |
| | | 0.50 |
| | | 1.00 |
| | | 2.00 |
| | | 5.00 |
| | | 0.70 |
| | | 0.50 |
| | | 2.00 |
| | | 2.00 |
| | | 65.77 |
| | | 5.00 |
| | | 0.30 |
| | | 3.00 |
| | | 1.00 |
| | | 2.00 |
| | | 2.00 |
| | | 0.20 |
| | | 0.03 |
| | | 100.00 |

Under stirring, disperse Carrageenan into II. Heat I and II + III to 75 °C. Under rapid mixing (rotor stator 3000 rd/min), add I to II + III, mix for about 5 min. Add IV then V and maintain rapid mixing for about 5 min. Cool under planetary stirring and at about 35 °C, add the other ingredients, one by one.

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GATTEFOSSÉ is an independent, multinational company headquartered in France which creates, manufactures and distributes speciality products used as ingredients by the cosmetic and pharmaceutical industries.

Present in almost 50 countries worldwide, GATTEFOSSÉ enjoys a strong know-how and position in lipochemistry, biology and extraction from natural sources.

GATTEFOSSÉ offers the cosmetic industry a variety of high performance products classified as:

- **BASES & ADDITIVES:** emulsifiers, coemulsifiers, emollients, dispersers, solubilizers, thickeners...
- **TRADITIONAL PLANT EXTRACTS**
- **SUBSTANTIATED ACTIVE INGREDIENTS** from vegetable, mineral and marine origins.

