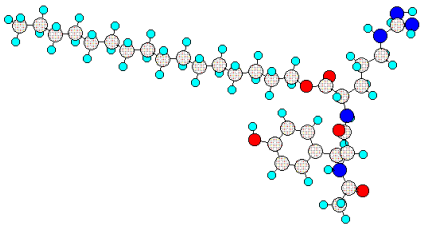
Face Make-up

Patent N° WO 98/07744

CALMOSENSINE™



Lipo-dipeptide Arg-Tyr

Function:

Messenger of happiness and muscle relaxation, Calmosensine™ helps prevent the appearance of first wrinkles.

Definition:

Lipopeptide with the sequence N-Acetyl-Tyrosyl-Arginyl-Hexadecyl Ester solubilised in a hydroglycolic excipient

Properties:

Calmosensine™ stimulates the release of pro-endorphins, providing an exhilarating effect in the skin, and inhibits muscle contractions responsible for the appearance of expression wrinkles.

Characteristics:

Calmosensine™ is derived from a peptide naturally present in the body

INCI name:

Butylene Glycol - Aqua (Water) - Laureth-3 - Hydroxyethylcellulose - Acetyl Dipeptide-1 Cetyl Ester

Applications:

Creams, gels, emulsions, make-up foundation... aimed at preventing the appearance of first wrinkles (expression lines)

Formulation:

Water-soluble
Incorporation at room temperature

Recommended use level:

3%

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CLAIM SUBSTANTIATION

Effect on neurotransmitter release

Neurotransmitter for relaxation

β-endorphin and met-enkephalin are neuropeptides involved in the down-regulation of nerve and muscle activity.

Human keratinocytes are incubated for 24 hours with lipo-Arg-Tyr. The RT-PCR technique determines the stimulation of the gene expression of POMC (Pro-opiomelanocortin), the precursor of β-endorphin and met-enkephalin.

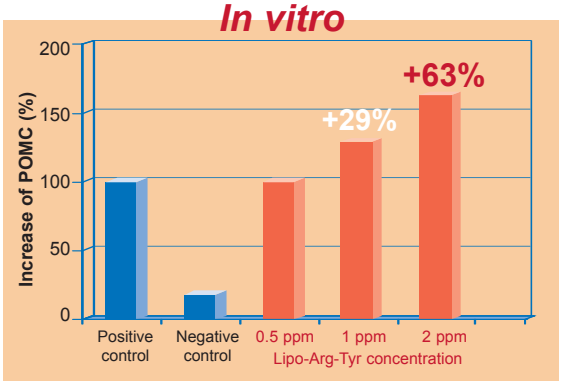
Neurotransmitter for contraction

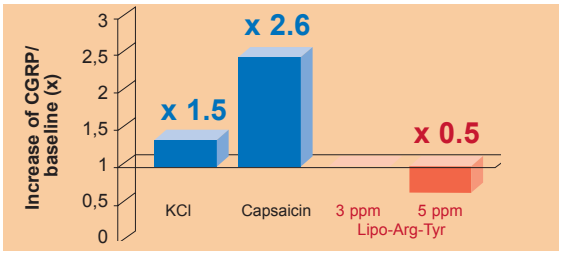
Calcitonin Gene Related Peptide (CGRP) is a neuropeptide involved in the stimulation of muscle activity and sensitization.

Nerves in culture are incubated with Lipo-Arg-Tyr, KCl or capsaicin. CGRP released in the culture medium is measured by an ELISA test.

Calmosensine™ modulates the release of certain neurotransmitters: stimulation of relaxation messengers and lessening of contraction messengers.

In vitro



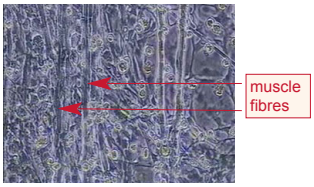


Effect on muscle relaxation

The variation of muscle contraction frequency with the presence of various products (Lipo-Arg-Tyr, positive and negative control) is studied with an *in vitro* model of nerve-muscle co-culture containing axons and neuromuscular junctions (BET, France). Contraction frequency is recorded and analysed by computer processing.

In vitro

Decrease of contractions	Calmosensine™ 1 ppm 5 min incubation	Calmosensine™ 1 ppm 2h incubation	Positive control	Negative control
Fibre 1	> 20%	Total inhibition	Total inhibition	-
Fibre 2	-	Total inhibition	Total inhibition	-
Fibre 3	-	Total inhibition	Total inhibition	-



Nerve-muscle co-culture

Calmosensine™ can progressively decrease muscle contraction frequency until total inhibition within 2 hours.

Formulation

Age Prevention Cream with CALMOSENSINE™

Indicative formula Ref : SED0403437D

Part A	%
Water deionised	qs 100
Ultrez 10 *(Carbomer)*	0.20

Part B	%
Crodamol CAP *(Cetearyl Ethylhexanoate, Croda)*	5.00
Crodafos CES *(Cetearyl Alcohol - Dicetyl Phosphate - Ceteth 10 Phosphate, Croda)*	5.00
Crodamol GTCC *(Caprylic/Capric Triglyceride, Croda)*	10.00
Crodamol STS *(PPG 3 Benzyl Ether Myristate, Croda)*	5.00

Part C	%
Glycerin	5.00
Nipagine	0.20

Part D	%
Potassium sorbate	0.10

Part E	%
Water deionised	4.00
Sodium Hydroxyde 30%	0.45

Part F	%
CALMOSENSINE™ *(Sederma)*	3.00

Part G	%
Fragrance	0.10

Protocol

Phase A: disperse Ultrez 10 and let swell for 15 minutes. Heat Part B at 75°C. Heat Part C until dissolution and add Part A. Heat A+C at 75°C. Pour B into A+C. Extemporaneously add Part D. At 50°C, add Part E. At 35°C add Part F and Part G.

Non-guarantee

This formulation has been subjected to limited stability tests and has been shown to perform well. However formulators adopting this approach should ensure to their own satisfaction long term stability and functionality. It is good practice to conduct safety tests on all final formulations prior to marketing. Suggested uses should not be taken as an inducement to infringe any existing patents.

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