

# SEPICALM™ VG

*A new lightening mode of action*

*So White, So Calming*

*and So easy to use !*

*SEPPIC Patent*



Active lightening ingredients must fit **3 main needs** in the cosmetic field :

**1.**

**Good  
Biological  
EFFICACY**

**2.**

**Excellent  
TOLERANCE  
level even on  
sensitive skin**

**3.**

**Very easy to  
use in all  
FORMULATIONS**

### SEPICALM VG

## Association of Palmitoylproline with a Water Lily Flower Extract for a NEW GENERATION OF LIGHTENERS

### So White ....

**POLYVALENT  
EFFICACY**

**New concept and new  
mode of action**

Decreases pigmentation  
induced by INFLAMMATION  
or AGEING

*In vitro & in vivo tested*

### So Calming ....

WELL  
**TOLERATED**  
and ADAPTED  
TO SENSITIVE  
SKINS

Soothes

### So easy to use....

**VERY EASY TO  
FORMULATE**

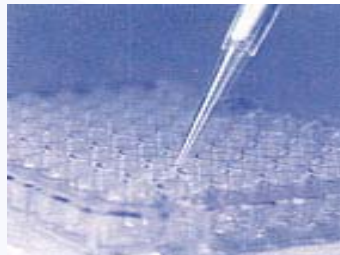
Stable, not colored



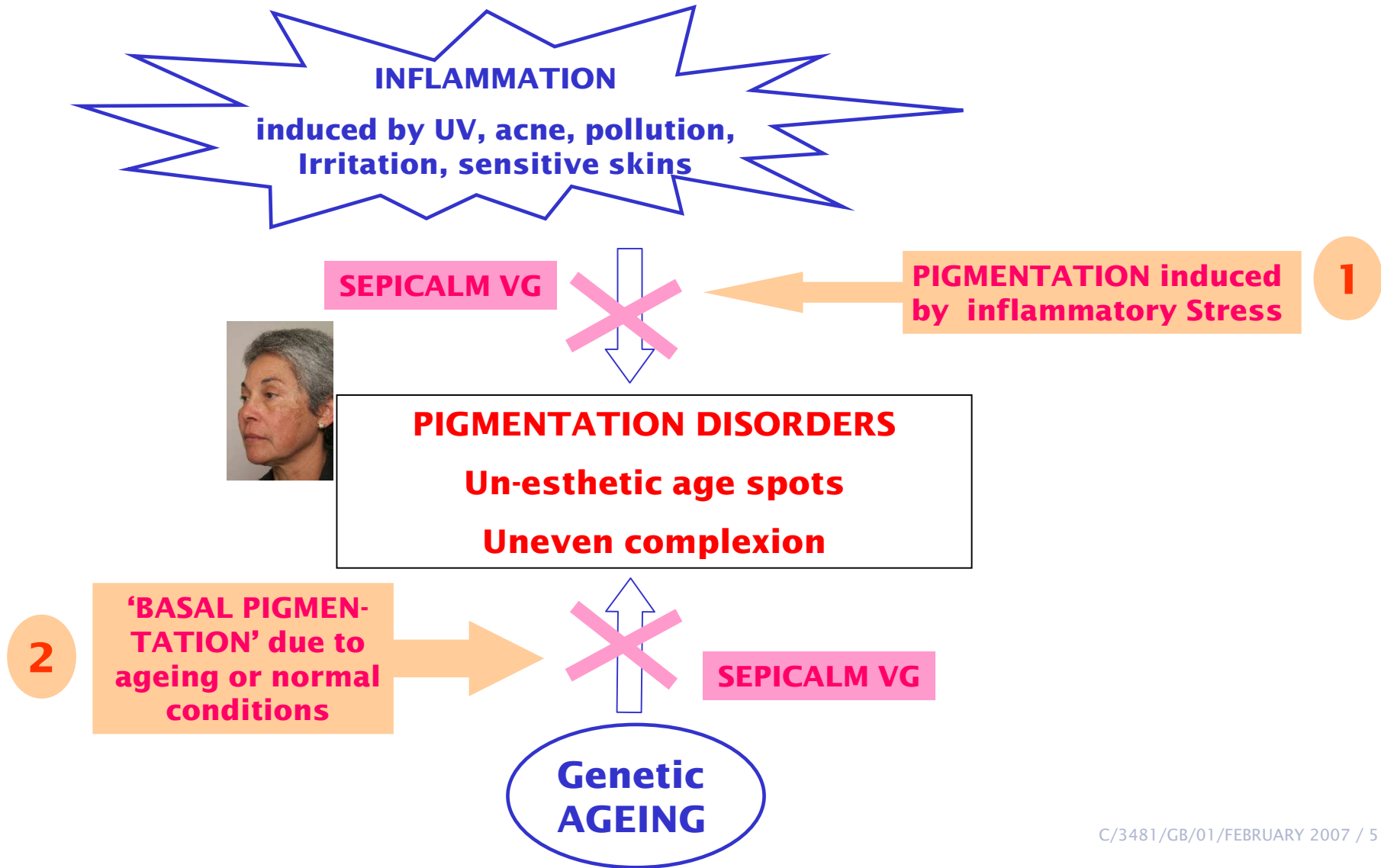
*Inci name : sodium palmitoylproline and nymphaea alba flower extract*

# 1. So white ...

***A new concept in lightening efficacy***  
***(proven in-vitro and in-vivo efficacy)***

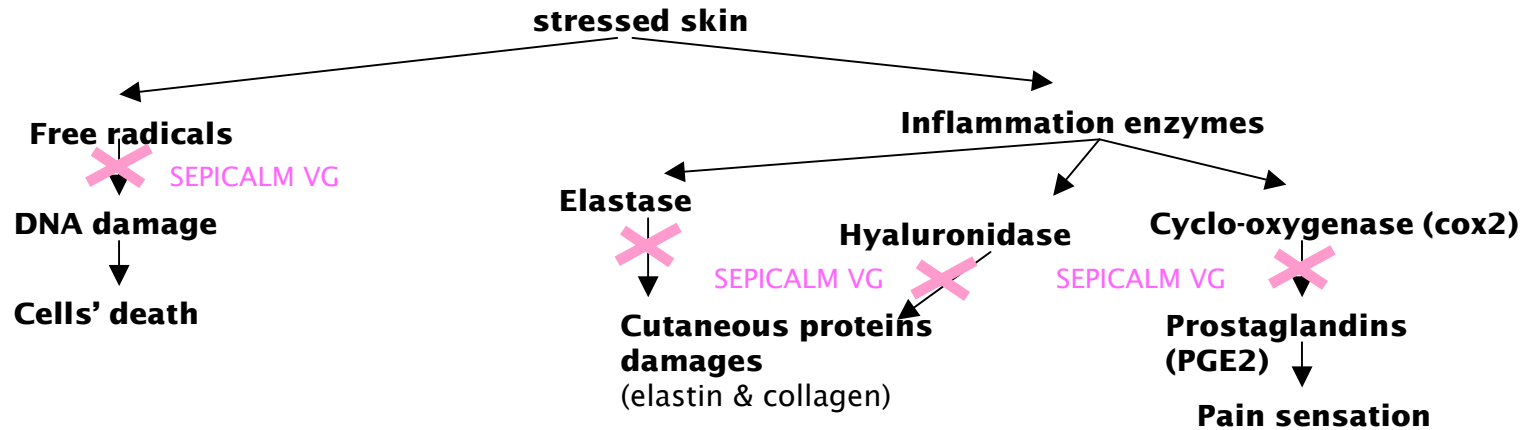


### Necessity to fight against different causes of pigmentation for an effective lightener



**SEPICALM VG** already used in the cosmetic field :

Known for its **modulation of inflammation** cascade (in vitro tested)



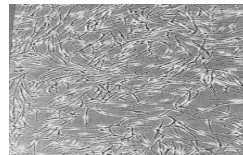
+ Known for its **soothing effect** - tested on volunteers



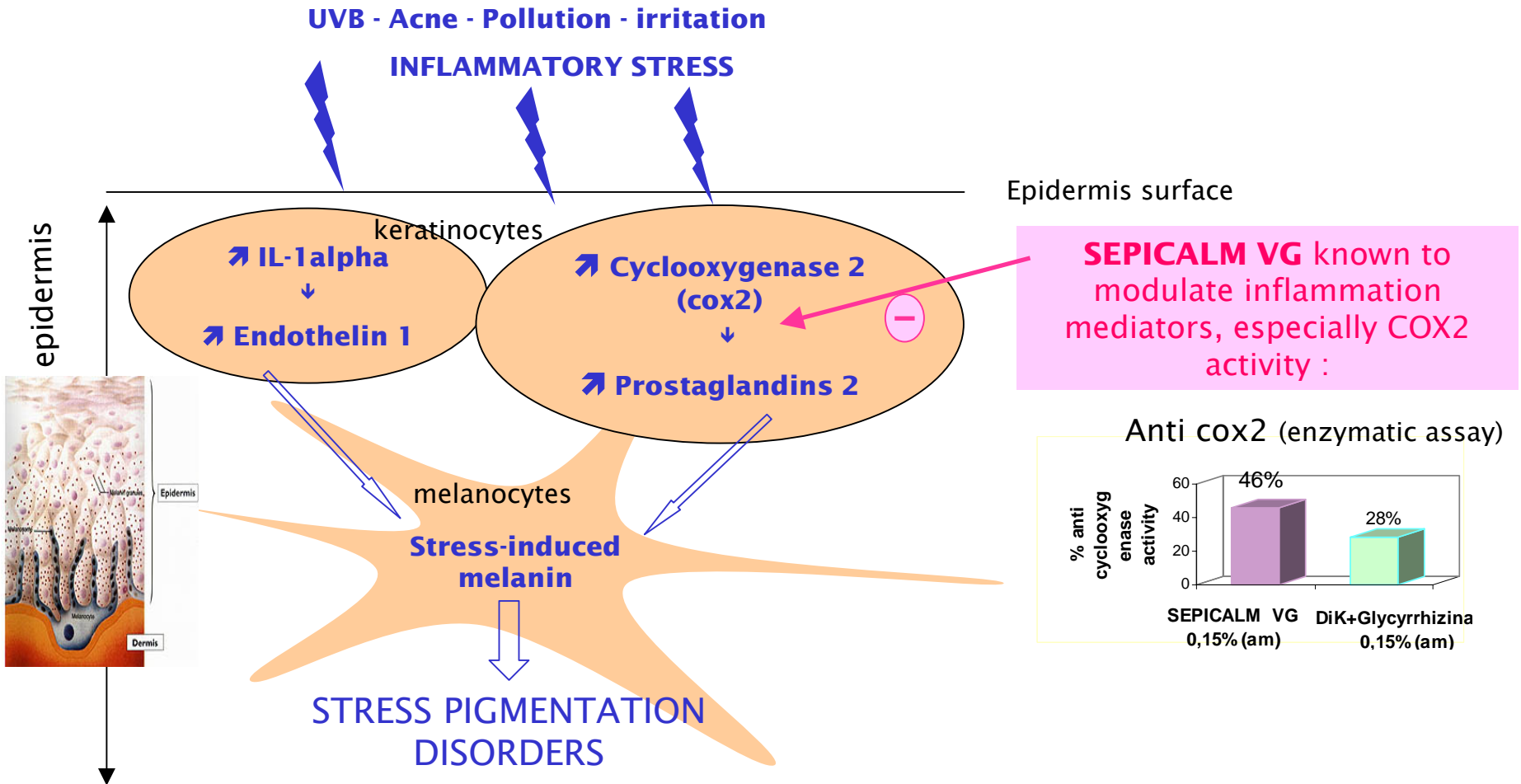
***=> SEPICALM VG could be a good candidate to reduce inflammation mediators responsible for Stress-induced Pigmentation ...***

# 1. So white ...

## ***1.1 Lightening effect of SEPICALM VG on Pigmentation induced by inflammatory stress :***



1. How Inflammation could be responsible for pigmentation ?



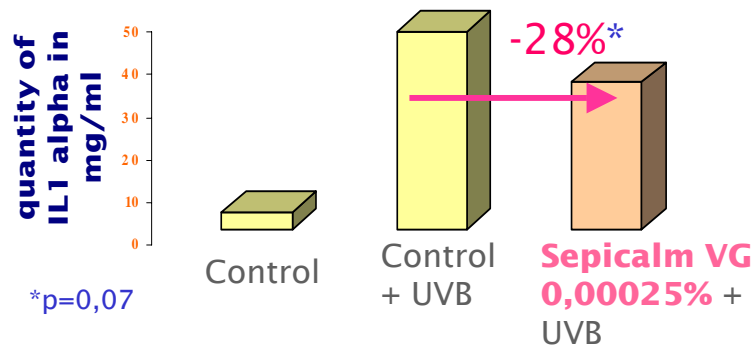
**=> Action of SEPICALM VG on IL-1 $\alpha$  and endothelin1 following stress ?**



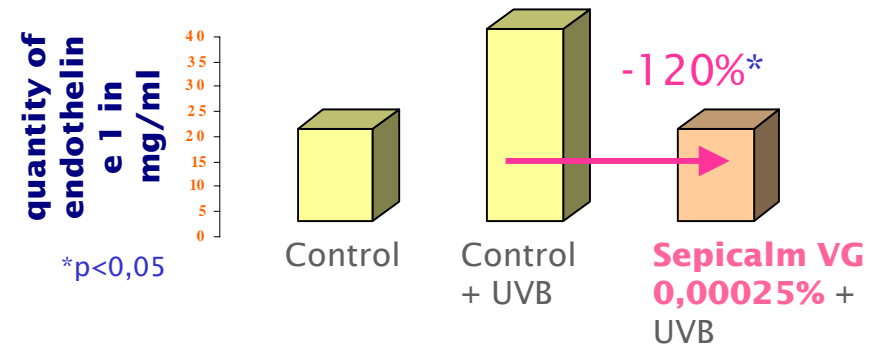
### 2. Reduction of keratinocytes IL-1 $\alpha$ and Endothelin 1 after a UVB stress :

**Protocol:** quantification of IL-1 $\alpha$  and endothelin 1 in normal human **keratinocytes** cultivated in different conditions (with or without 30 mJ/cm<sup>2</sup> UVB, with or without SEPICALM VG) :

#### a. IL-1 $\alpha$ reduction in keratinocytes :



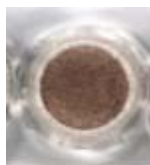
#### b. Endothelin 1 reduction in keratinocytes :



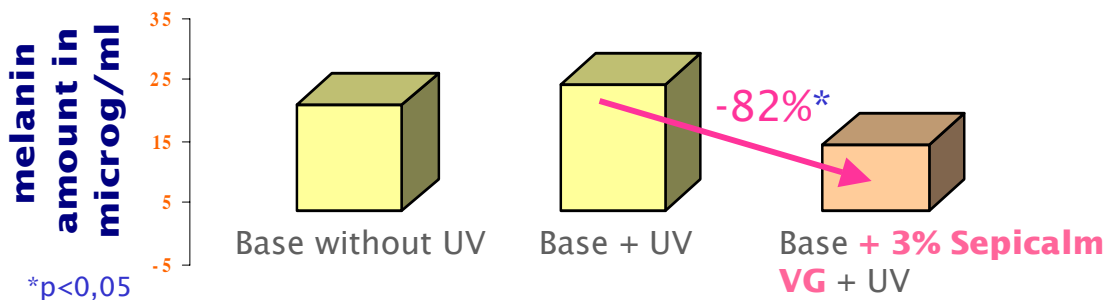
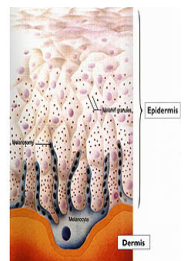
Besides its modulation of cox2 activity, SEPICALM VG also reduces keratinocytes IL-1 $\alpha$  and endothelin 1, key mediators of Stress-Induced Pigmentation

### 3. Lightening effect via a reduction of 'Stress-Induced Pigmentation' in 3D skin model after 7 days :

**Protocol:** Application of Base alone or Base +3% SEPICALM VG on **3D model Skinethic™ pigmented epidermis** (Phototype IV) – **submission to UVB 50 mJ/cm2 and UVA 1J/cm2 irradiations**– Lightening effect evaluated after 7 days by intracellular melanin dosage.



Lightening effect on pigmented epidermis after 7 days :

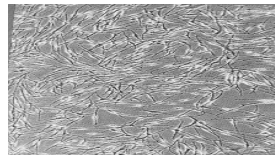
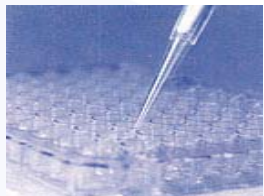


SEPICALM VG significantly reduces 'Stress-Induced Pigmentation' on epidermis via its modulation of inflammation mediators (IL-1 $\alpha$  , endothelin 1, Cox 2).

**SEPICALM VG inhibits skin pigmentation induced by inflammatory stress.**

# 1. So white ...

## ***1.2 Lightening effect of SEPICALM VG on Basal Pigmentation***



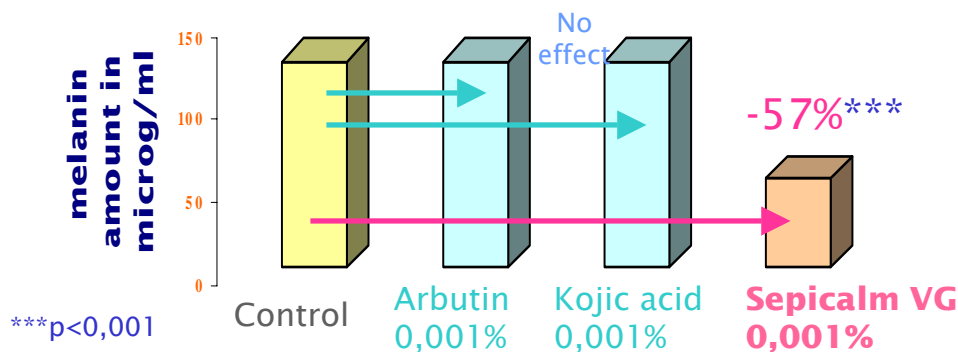


MELANOCYTES

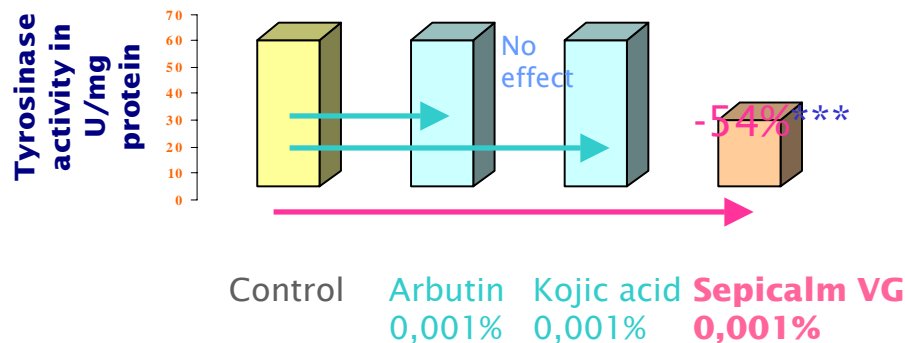
### 1. Spontaneous Lightening effect on melanocytes

**Protocol:** B16 melanocytes cultivated with or without SEPICALM VG in comparison with arbutin and kojic acid as positive references. Lightening effect evaluated after 72 hours of incubation by melanin amount and tyrosinase activity measurements.

#### a. Reduction of melanin pigments:



#### b. Inhibition of tyrosinase activity:



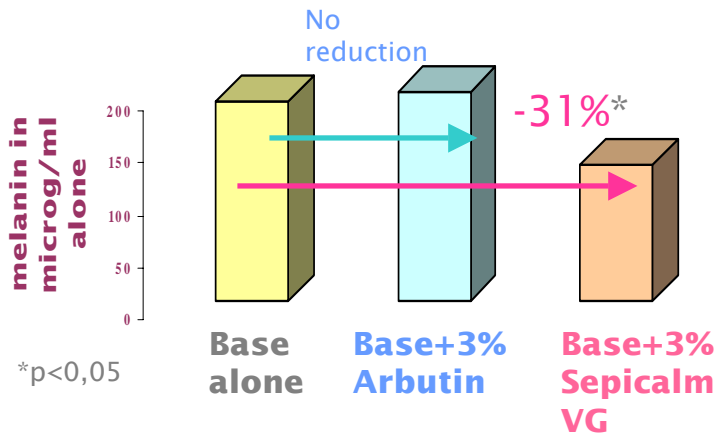
SEPICALM VG can also have a spontaneous lightening effect explained by an inhibition of the basal melanin and the tyrosinase activity.

Note : SEPICALM VG does not have any direct inhibition on tyrosinase activity *in tubo* (without cells) which could be explained by a genetic or a metabolic mode of action on tyrosinase rather than a competitive inhibition.

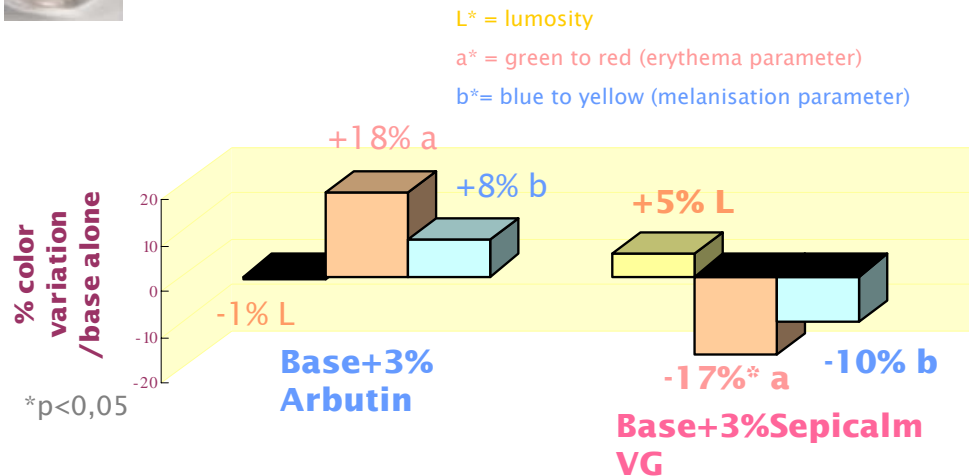
### 2. Lightening effect on 3D pigmented skin model after 7 days :

**Protocol:** Application of Base alone or Base +3% SEPICALM VG or base +3% Arbutin on **Skinethic™ pigmented epidermis** (Phototype VI) – Lightening effect evaluated after 7 days by **melanin amount** and **skin surface colometric measurement** (chromameter).

#### a. Melanin reduction :



#### b. Skin surface color reduction (in comparison to the base alone) :



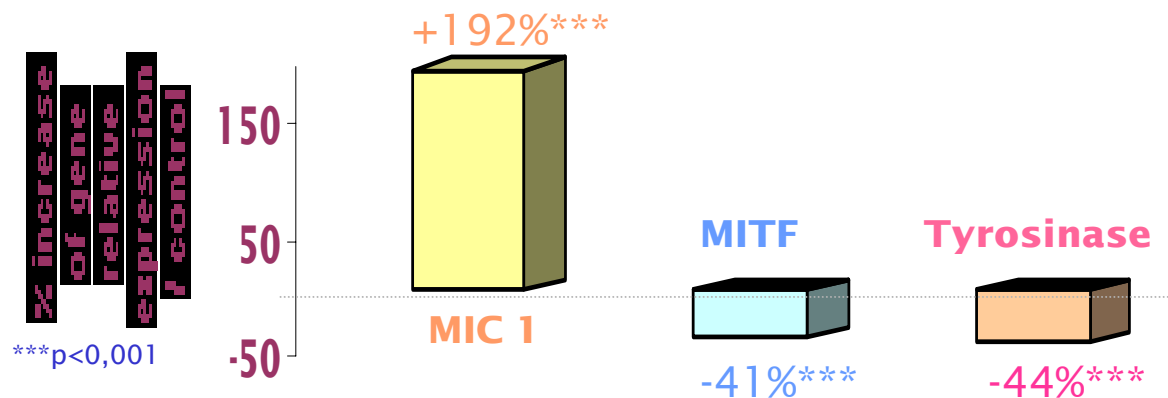
Only SEPICALM VG induces a lightening effect on skin surface (↗L\* ↘a\* ↘b\*) confirmed by a reduction of melanic pigments.

=> Better efficacy than arbutin, thanks to its lipoaminoacid structure (amphiphilic)

### 3. Analysis of key melanocytes gene expression : *molecular biology tests*

**Protocol:** Normal human melanocytes cultivated or not in the presence of SEPICALM VG - Differential expression of key **genes** involved in **basal pigmentation** : semi quantitative analysis (screening by a DNA micro-array method, 64 genes analysed) and confirmation by quantitative real time PCR.

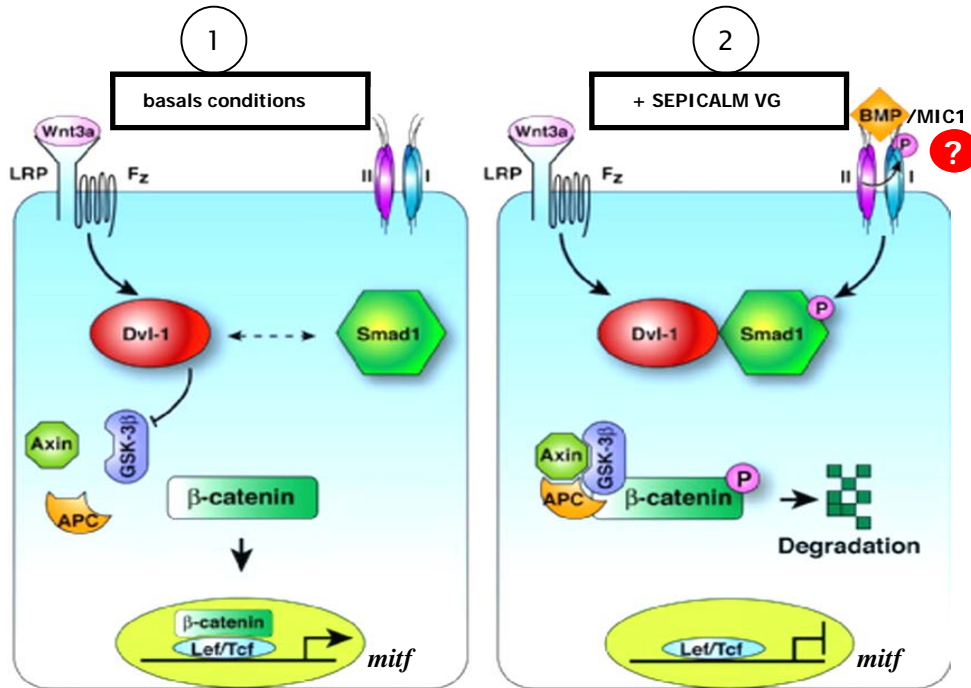
#### a. Induction of key melanocytes gene expression involved in basal melanogenesis :



SEPICALM VG induces a significant **increase of MIC1** gene expression and a significant **decrease of MITF and Tyrosinase** gene expression.

=> **Explanation of a new genetic mode of action acting on early steps of melanogenesis.**

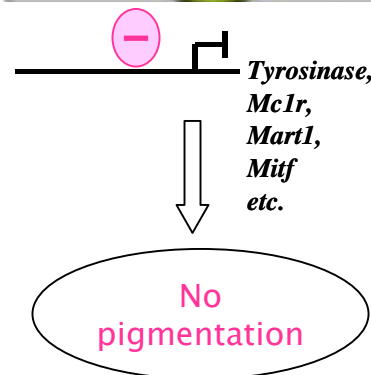
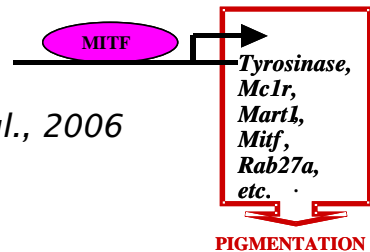
4. A new upstream mode of action, acting at the early stage of melanogenesis :



=> Sepicalm VG : A possible antagonist of Wnt signalling pathway leading to a decrease of tyrosinase gene expression

1. Wnt signalling pathway leads to the translocation of β-catenin, an indirect activator of MITF gene leading to the Tyrosinase gene expression => ↗ BASAL PIGMENTATION

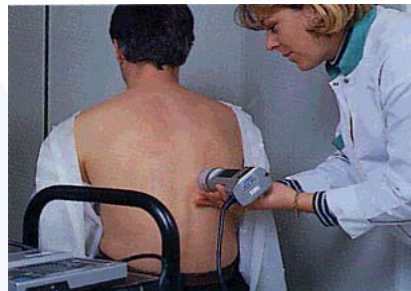
2. Sepicalm VG increases MIC1 gene expression known to belong to BMP protein family (known to disturb Wnt pathway )=> ↗ β catenin degradation => decrease MITF gene expression => decrease Tyrosinase gene expression => ↘ BASAL PIGMENTATION



Liu et al., 2006

# 1. So white ...

## ***1.3 In vivo lightening effect of SEPICALM VG (Study performed in Asia)***





### 1. Testing procedure :

- **SEPICALM VG at 3%** (formula 7057)

- **30 Asian volunteers**

- Application area: **Normal skin and ageing spots**

- **Evaluation before and after 2 and 3 months of treatment :**

1. **Skin color measurements**  
(Chromameter and Mexameter)

2. **Level of efficacy & comfort**  
(expressed by the volunteers)

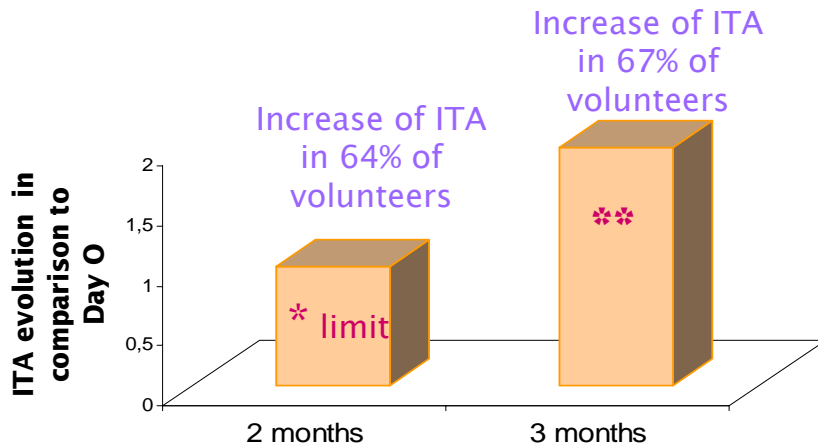
In vivo tested formula 7057 :

• <b>MONTANOV™ 68</b> (Cetearyl alcohol and Cetearyl glucoside - SEPPIC)	2.00 %
• <b>MONTANOV™ 202</b> (Arachidyl alcohol and behenyl alcohol and arachidylglucoside - SEPPIC)	2.00 %
• <b>LANOL™ P</b> (glycol palmitate - SEPPIC)	2.00 %
• <b>LANOL™ 99</b> (isononyl isononanoate - SEPPIC)	8.00 %
• Water	Up to 100%
• Chlorphenesin	0.30 %
• Magnesium aluminium silicate	1.00 %
• Cyclopentasiloxane	4.00 %
• <b>SIMULGEL™ EG</b> (Sodium acrylate/acryloyldimethyltaurate copolymer and Isohexadecane and Polysorbate 80 - SEPPIC)	1.00 %
• <b>SEPICALM™ VG</b> (Sodium palmitoyl proline & Nymphaea alba flower extract - SEPPIC)	3.00 %
• DL alpha tocopherol	0.05%
• Fragrance	0.30 %
• <b>SEPICIDE™ HB</b> (Phenoxyethanol & Methylparaben & Ethylparaben & Propylparaben & Butylparaben - SEPPIC)	0.70 %
• TEA	0.35 %

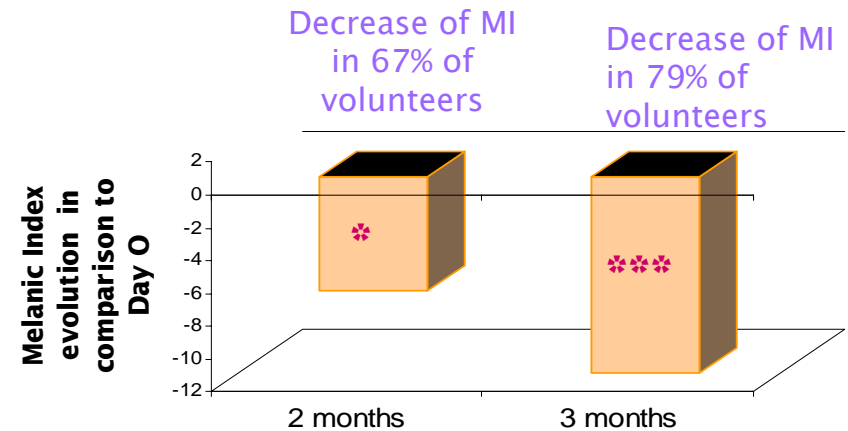
*Test performed in Thailand (Bangkok)*

## 1. Lightening effect of SEPICALM VG on normal skin => chromametric & mexametric measurements (Formula 7057)

### 1.1 Increase of Individual Typological Angle (ΔITA) in chromametry :



### 1.2 Decrease of Melanic Index (ΔMI) in mexametry :



ΔITA and Δ Melanin Index value = average calculated on 100% of the tested volunteers

$$ITA = \text{ArcTg} \left( \frac{L - 50}{b} \right) \times \frac{180}{\pi}$$

\*: p<0,05 in comparison to D0

\*\* : p<0,01 in comparison to D0

\*\*\*: p<0,001 in comparison to D0

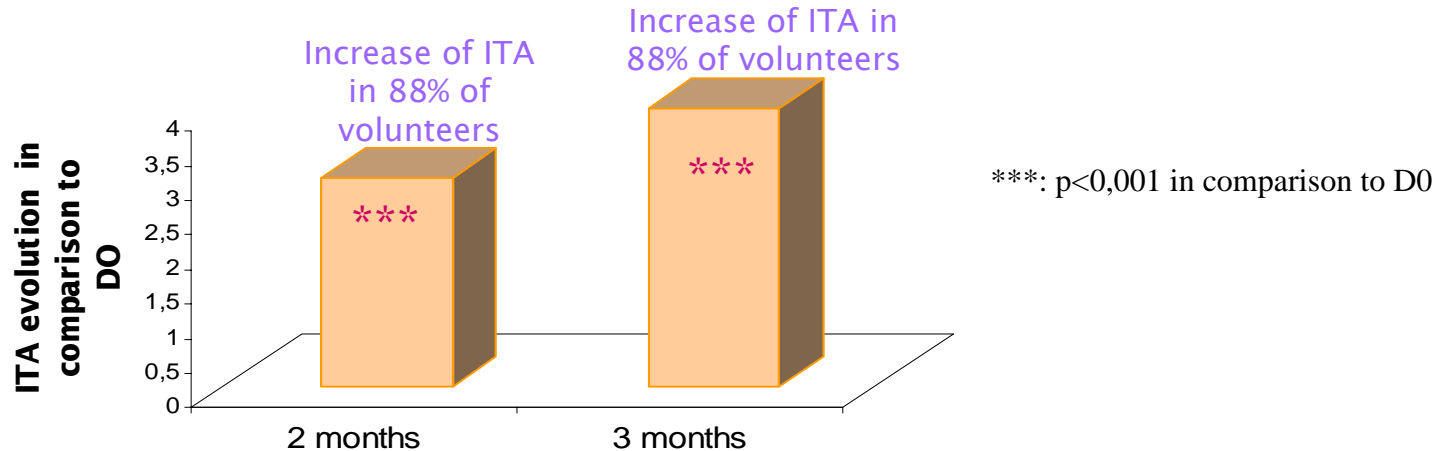
**By the second month of treatment, SEPICALM VG significantly lightens normal skin (↑ITA and ↓ Melanic Index), confirming its action on basal melanogenesis.**

**Complexion is brightened, more radiant.**

## 2. Lightening effect of SEPICALM VG on hyper-pigmented age spots

=> chromametric measurements (Formula 7057)

### Increase of Individual Typological Angle ( $\Delta$ ITA) in chromametry



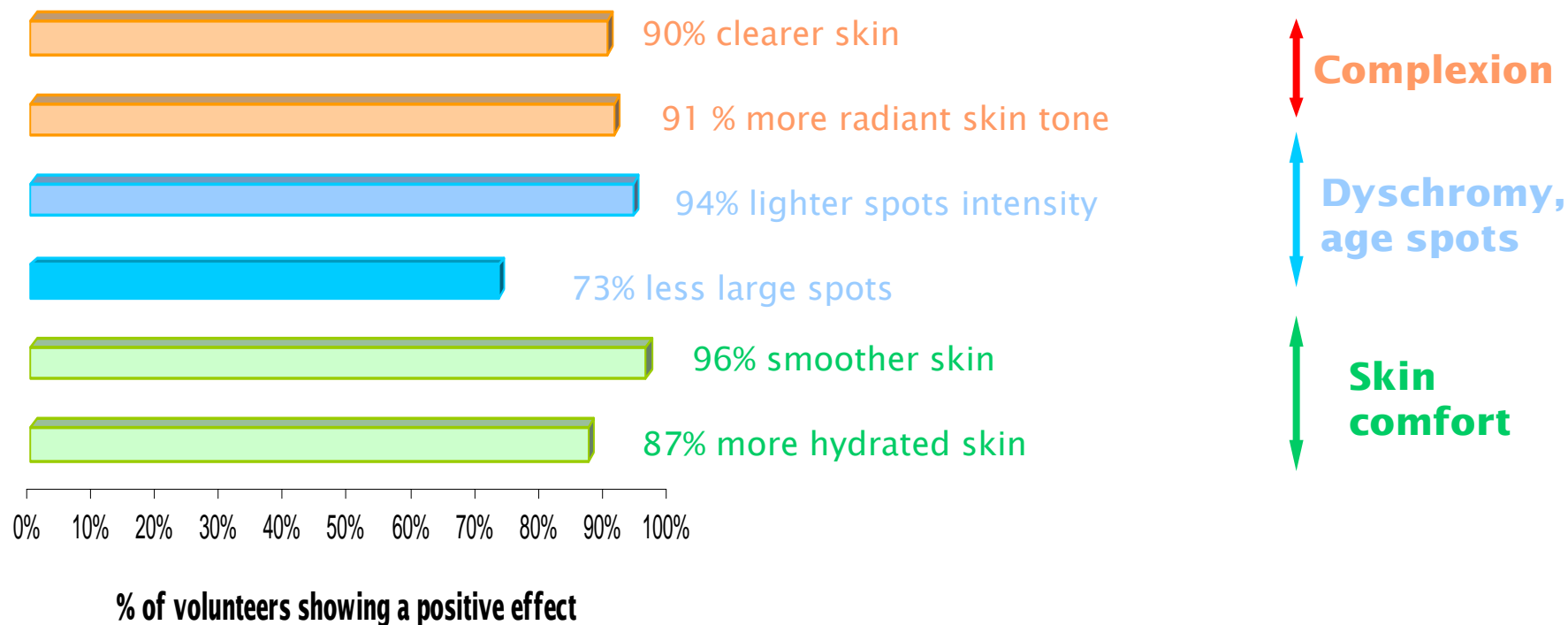
$\Delta$ ITA = average calculated on 100% of the tested volunteers

**By the second month of treatment, SEPICALM VG significantly decreases the pigmentation of ageing spots ( $\nearrow$ ITA).**

**Hyperpigmented spots fade away, skin tone becomes more uniform.**

## 3. Positive feedback from the volunteers after 3 months of treatment

(Formula 7057)



**Indication : 91% of the tested volunteers would have liked to continue the use of the formula 7057 and 77% would have liked like to buy it.**

**The tolerance level has been excellent on all the volunteers**

SEPICALM VG , so white ...

*Association of Palmitoylproline with a Water Lily Flower extract for a NEW CONCEPT OF LIGHTENER*

1

**Decreases Pigmentation induced by inflammatory stress**  
(UV, irritation, pollution, acne ...)

*How ? Fight against inflammation mediators induced by stress*  
(Interleukin 1 and Endothelin 1)

2

**Decreases 'Basal pigmentation'** due to normal condition or genetic aging

*How ? Upstream genetic reduction of tyrosinase expression via a new hypothetic biological pathway*

3

***Significant lightening effect on normal Asian skin and age spots after only 2 months of treatment***

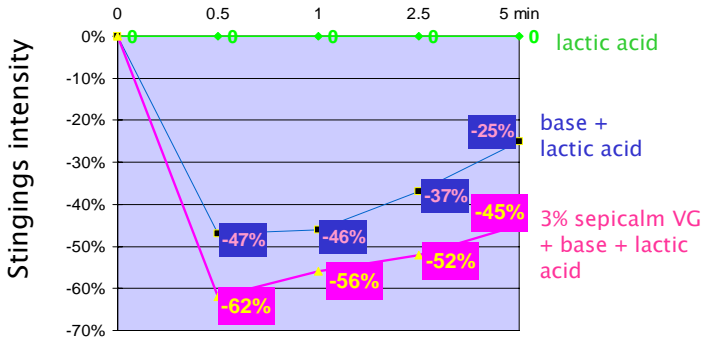
## **2. So calming ...**

***So adapted to sensitive skin,  
so well tolerated ...***

**SEPICALM VG, the first lightener with a soothing effect** (already used in the cosmetic field for its effective **soothing effect** due to a **modulation of inflammation mediators** induced by skin stress )

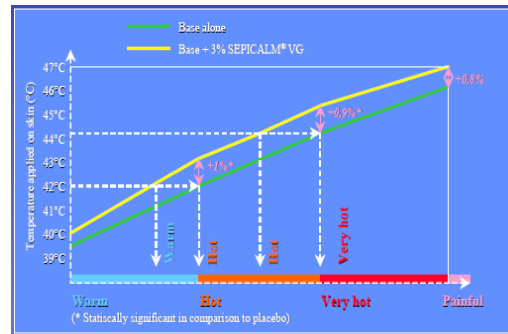
Immediate in vivo **soothing effect** of SEPICALM VG

**SEPICALM VG DECREASES STINGINGS Intensity felt by sensitive skin as a result of CHEMICAL irritations (AHAs)**



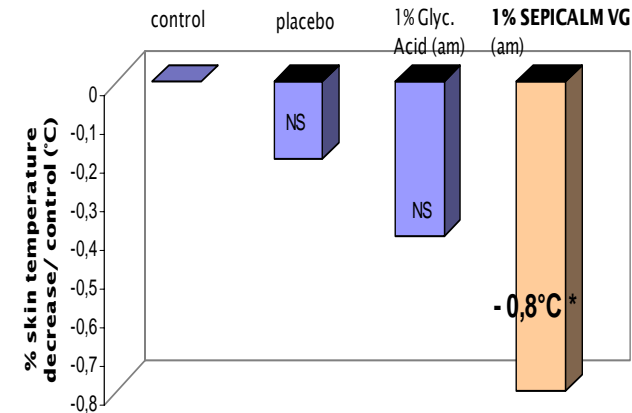
Stinging test

**SEPICALM VG DECREASES PAIN SENSATION felt after a THERMIC stress**



Thermal sensitivity test

**SEPICALM VG DECREASES Skin temperature after a UV stress**



Skin temperature test

## Good tolerance of SEPICALM VG at 3% :

- . **Well tolerated in occlusive patch 48 h**
- . **Well tolerated in normal usage condition** during 3 months (Asian panelist - *in vivo* test performed in Thailand – 2 applications per day)
- . **Non sensitizing** (Marzulli Maibach protocol)
- . **Non Mutagenic** (Ames test)

**Recommended dosage level : 3% for cosmetic application**



## 3. So easy to use ...

### *Formulation guidelines*



➔ **SEPICALM VG can be easily incorporated up to 3% in all types of whitening, lightening, and soothing projects**

Clear yellow liquid - Lipophilic

Color and odor stable over time.

Non-sensitive to heat and shearing.

Incorporation before emulsion (in the heated oily phase) or after emulsion.

May generate electrolytes during neutralization => Use of SEPIPLUS range polymers recommended.

Compatible with all classical whiteners and sun filters.

Compatible with all pH.



Suitable for White emulsions or cream-gels (with or without fragrance).

Advice : SEPICALM VG **must be heated at 40°C** before its use in formulation in order to liquify it - (can become paste at cold temperature).

### Formula

<b>A</b>	• <b>MONTANOV™ 68</b> ( <i>Cetearyl alcohol and Cetearyl glucoside - SEPPIC</i> )	2.00 %
	• <b>MONTANOV™ 202</b> ( <i>Arachidyl alcohol and behenyl alcohol and arachidylglucoside - SEPPIC</i> )	2.00 %
	• <b>LANOL™ P</b> ( <i>glycol palmitate - SEPPIC</i> )	2.00 %
	• <b>LANOL™ 99</b> ( <i>isononyl isononanoate - SEPPIC</i> )	8.00 %
<b>B</b>	• Water	Up to 100%
	• Chlorphenesin	0.30 %
	• Magnesium aluminium silicate	1.00 %
<b>C</b>	• Cyclopentasiloxane	4.00 %
	• <b>SIMULGEL™ EG</b> ( <i>Sodium acrylate/acryloyldimethyltaurate copolymer and Isohexadecane and Polysorbate 80 - SEPPIC</i> )	1.00 %
<b>D</b>	• <b>SEPICALM™ VG</b> ( <i>Sodium palmitoyl proline &amp; Nymphaea alba flower extract - SEPPIC</i> )	3.00 %
<b>E</b>	• DL alpha tocopherol	0.05%
	• Fragrance	0.30 %
	• <b>SEPICIDE™ HB</b> ( <i>Phenoxyethanol &amp; Methylparaben &amp; Ethylparaben &amp; Propylparaben &amp; Butylparaben - SEPPIC</i> )	0.70 %
<b>F</b>	• TEA	0.35 %

### Procedure (TRIMIX 8 kg)

Melt fatty components at 80°C ; Heat water in the main tank, then dissolve chlorphenesin (rotor stator 3000 rpm 5') and add magnesium aluminium silicate (planetary mixer + rotor stator 1000 rpm 10'). Add the warm fatty phase and start homogenizing at 3000 rpm. After 5' allow to cool. Introduce the silicon at 65°C then SIMULGEL™ while keeping homogenization 5' more. Stop the rotor stator and cool to 60°C. Then add SEPICALM™ VG . At 30°C add ingredients in D ; If required adjust final pH. After 60°C all steps are conducted under vacuum.

## **4. Summary of SEPICALM VG efficacy and future ...**



### SEPICALM VG

## Association of Palmitoylproline with a Water Lily Flower Extract for a NEW GENERATION OF LIGHTENERS

### 1. So White ....

**POLYVALENT  
EFFICACY with new  
mode of action**

Decreases pigmentation induced by INFLAMMATION or AGEING process

*In vitro & in vivo* tested

### 2. So Calming ....

First lightener  
VERY WELL  
**TOLERATED**  
and **ADAPTED  
TO SENSITIVE  
SKINS**

Soothing effect

### 3. So easy to use....

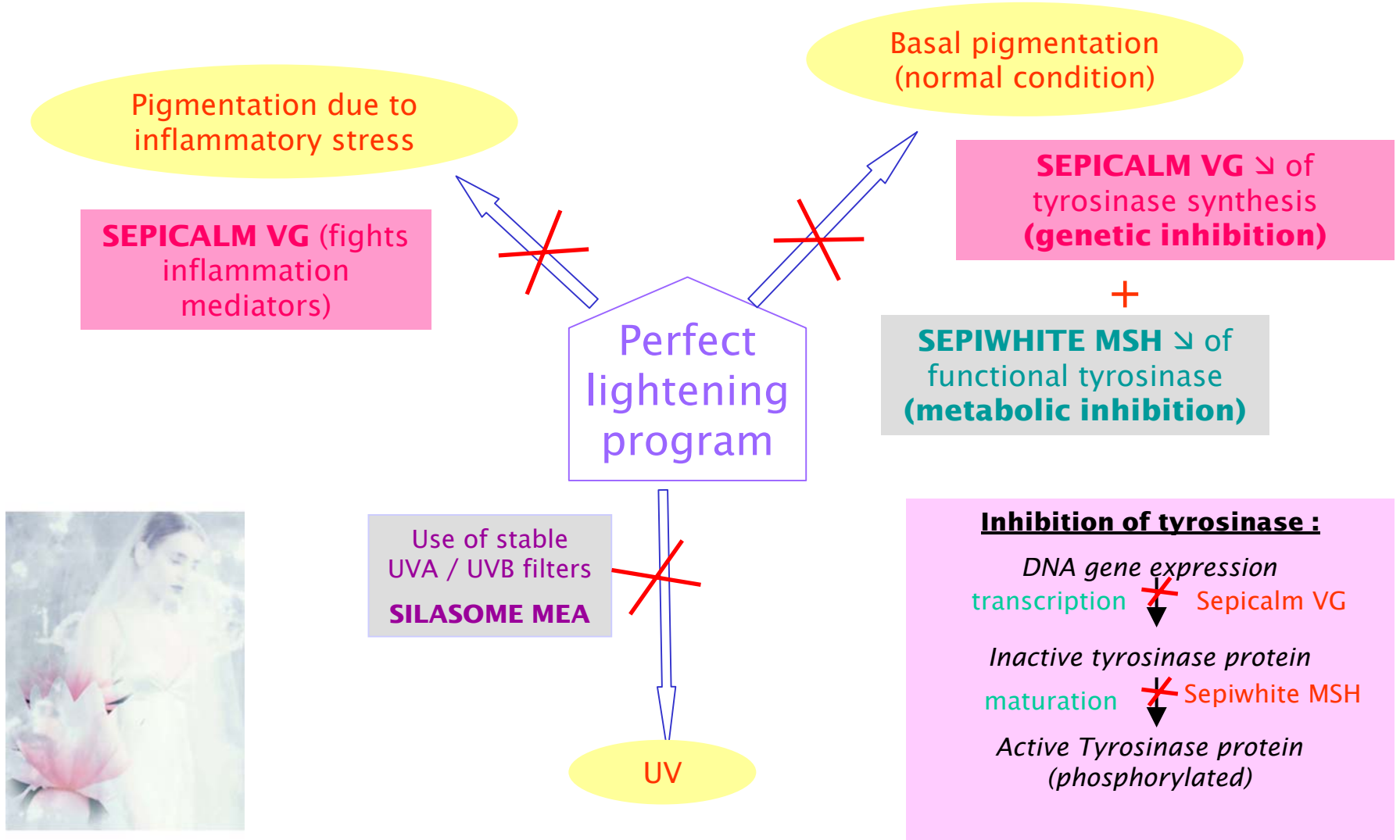
**VERY EASY TO  
FORMULATE**

Stable, not colored



*Inci name : sodium palmitoylproline and nymphaea alba flower extract*

**Necessity to fight against different causes of pigmentation to develop a perfect finished product**



### **Nota**

The analytical specifications warranted are only those mentioned on the certificate of analysis supplied with each delivery of the product.

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