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DARK SPOT & HYPERPIGMENTATION & RADIANT COMPLEXION CHALLENGE

Our **skin** is an **incredible factory** in perpetual activity to maintain **biochemical homeostasis** essential to the proper functioning of our **skin cells**.

The **challenge** here is to **understand** and **correct** the **mechanism**(s) disturbed by internal and / or external **aggression** in order to ensure an **improvement** of the condition of skin subject to **hyperpigmentation** and **loss of radiant complexion**.

A simple **aggression** is enough for our cells to trigger **cascades of cell defense** reactions. These mechanisms can then cause a **disruption** of our cells that **over-react** and **cause clinically visible damage** to our skin.

With our active ingredient, we alleviate dysfunctions related to cellular stress and stop hyperpigmentation. Internally, Ephyshine protects and strengthens the cellular and biochemical balance of the skin. Externally, Ephyshine improves the radiant complexion.

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HYPERPIGMENTATION

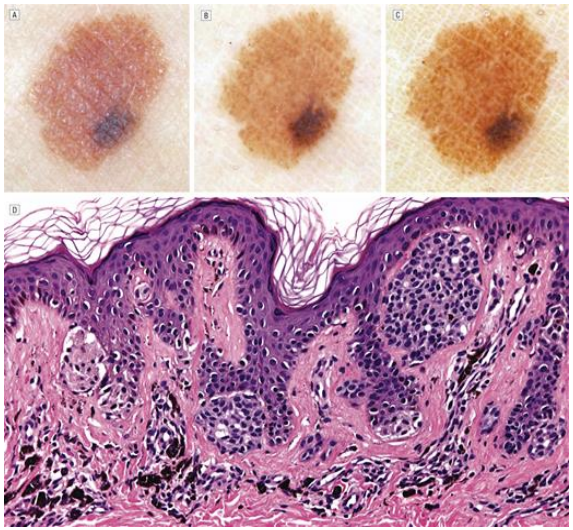
Postinflammatory hyperpigmentation (PIH) is an acquired **hypermelanosis** occurring after **cutaneous inflammation** or **injury** that can arise in all skin types, but more frequently affects skin-of-color people.

PIH results from the **overproduction of melanin** or an **irregular dispersion of pigment** after cutaneous inflammation. When PIH is confined to the epidermis, there is an **increase** in the **production** and **transfer** of **melanin** to surrounding keratinocytes.

This rise in melanocyte activity has been shown to be stimulated by **inflammatory mediators**. Multiple studies have demonstrated the **melanocyte-stimulating properties** with **leukotrienes** and others inflammatory mediators.

In addition, it is clearly demonstrated that **PIH** can **worsen** with **ultraviolet irradiation** or with **persistent** or **recurrent inflammation**.

The **management** of **PIH** requires limiting the emergence of inflammatory mediators, and the impact of skin stress specially with UV.



Hyperpigmentation and dark spots**

The dysfunction and the over-reaction of the cells cause the appearance of dark spots and affect the radiant complexion

*J Clin Aesthet Dermatol. Postinflammatory Hyperpigmentation. A Review of the Epidemiology, Clinical Features, and Treatment Options in Skin of Color. Erica C. Davis, MD[a] and Valerie D. Callender, MD[a,b]. Jul 2010.

**_Arch Dermatol._ Morphologic Changes of Acquired Melanocytic Nevi With Eccentric Foci of Hyperpigmentation ("Bolognia Sign") Assessed by Dermoscopy. Maria A. Pizzichetta, MD; Cesare Massone, MD; Giorgio Grandi, MD; et al. April 2006.

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Origin

Ephyshine is an active ingredient derived from an equatorial tree.

This plant is collected by pygmies in the context of a solidarity economy program.

- Tribes uses :

This **mucilaginous** plant is consumed **exceptionally** and associated with a **unique** and **rare event** (such as birth, ceremony, rite, etc.) with a **spriritual** dimension.

- Ephyla wants to preserve the **integrity** of the plant :

Use of a **seed** pool of the tree → **sustainable** production, **no deforestation** and **regenerated** plant

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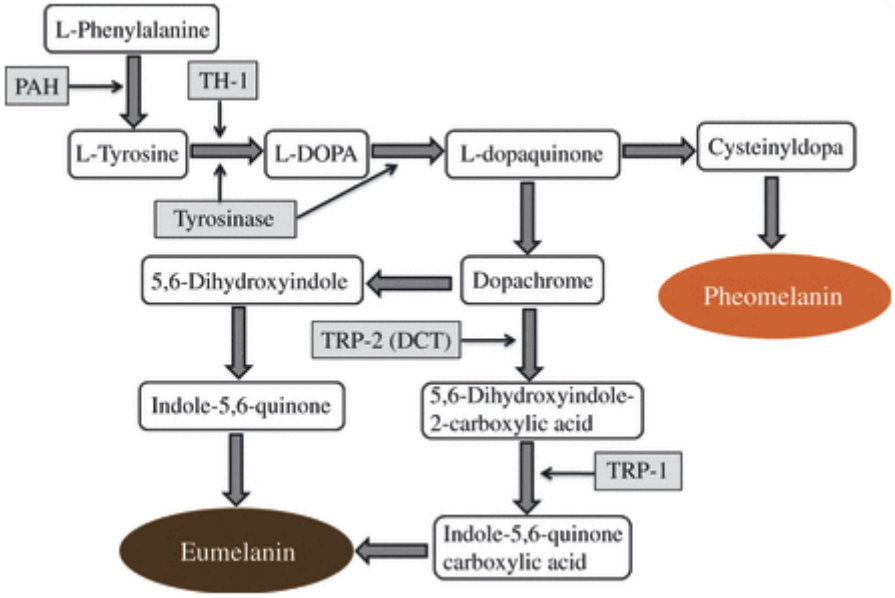
MELANOGENESIS

Phenotypic diversity of pigmentation

Phenotypic diversity of pigmentation is due to the size and number of **melanosomes**, the amount and type of **melanin**, and melanin transfer and distribution in **keratinocytes**.



Types of melanin

There are two types of melanin: **eumelanin**, brown-black or dark insoluble polymer and **pheomelanin**, red-yellow soluble polymer.

Key enzyme of melanogenesis

Tyrosinase is a glycoprotein located in the melanossomal membrane, with an **internal**, a **transmembrane**, and a **cytoplasmic** domain. It catalyzes the conversion of **L-tyrosine into L-DOPA**, the rate-limiting stage in melanin synthesis*.

An ingenious biochemical mechanism for UV cell protection

*An. Bras. Dermatol. vol.88 no.1. Mechanisms regulating melanogenesis. Inês Ferreira dos Santos Videira, Daniel Filipe Lima Moura, Sofia Magina. Rio de Janeiro Jan. Feb. 2013

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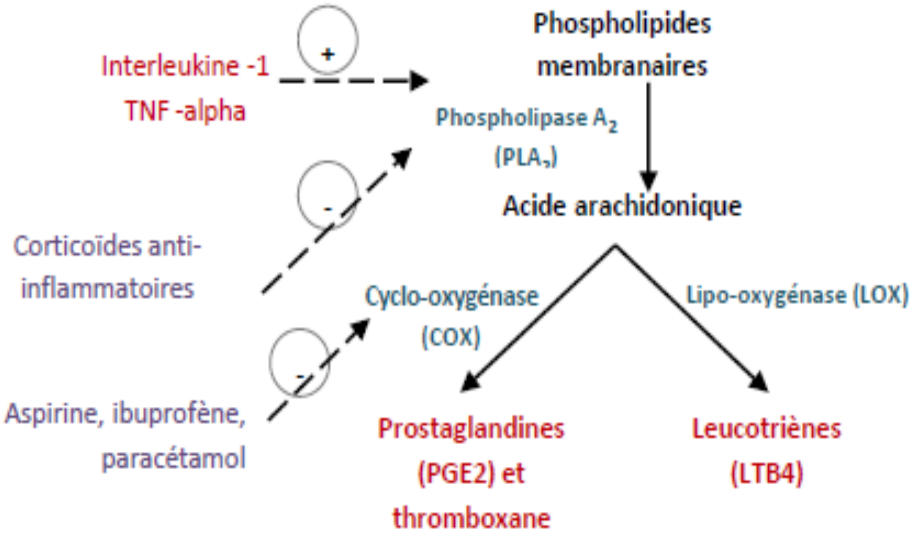
STRESS & INFLAMMATION

When a disturbance and/or inhibition of a biological mechanism occurs, a stress signal is perceived by the cell. It reacts by activating its defense mechanisms. One of the most important inflammatory processes is under the control of the enzymes of the arachidonic cascade :

Prostaglandins, thromboxane and leukotrienes are the main inflammatory **mediators** of this synthesis pathway. Especially, **leukotrienes** are molecules of **stress signal amplification** which allow to initiate the **cellular reactions**.



Inflammatory cascade

The cellular response to stress for a return to the basal balance

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Overall Highlighting and Attenuation of dark spots

D0 **D+28**

1% ephyshine after 28 days of use
Reduction of the dark spots visibility: -22%*

*n= 20, statistically significant results

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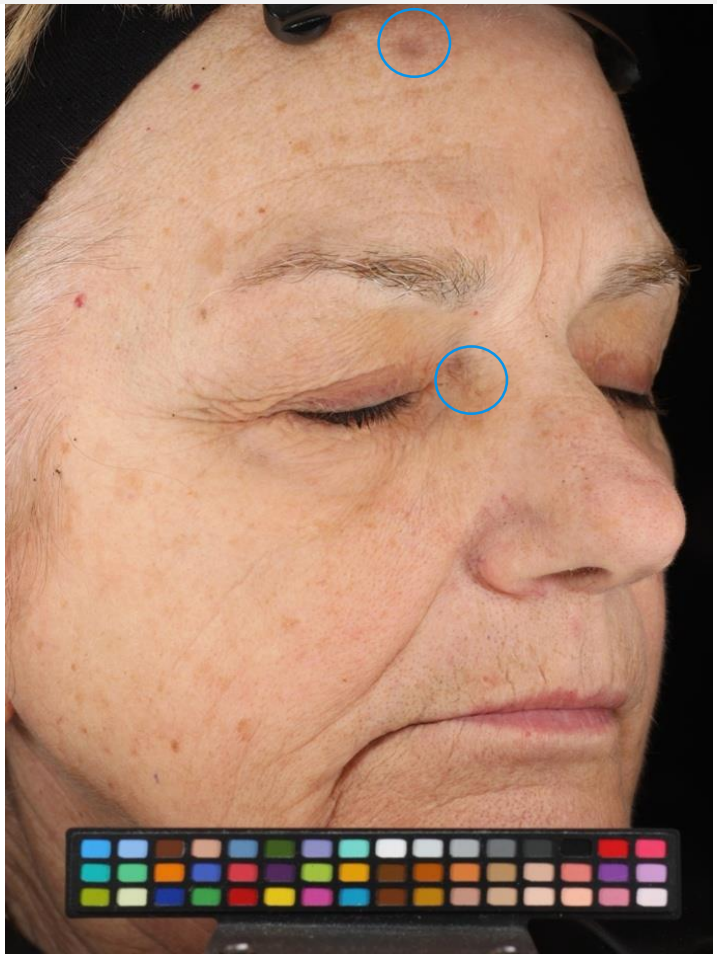

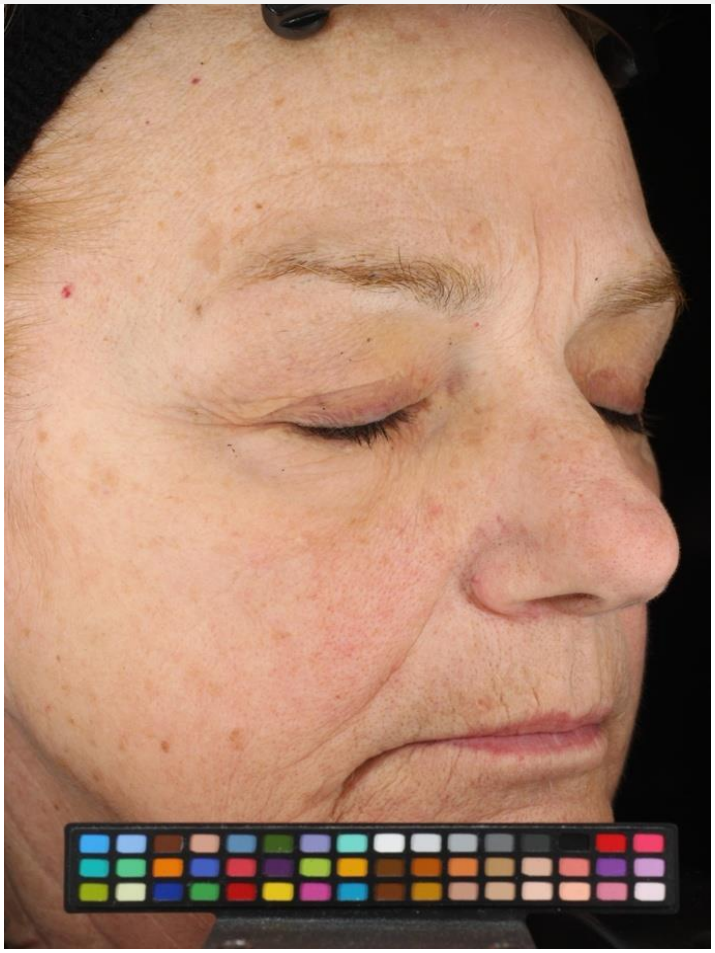

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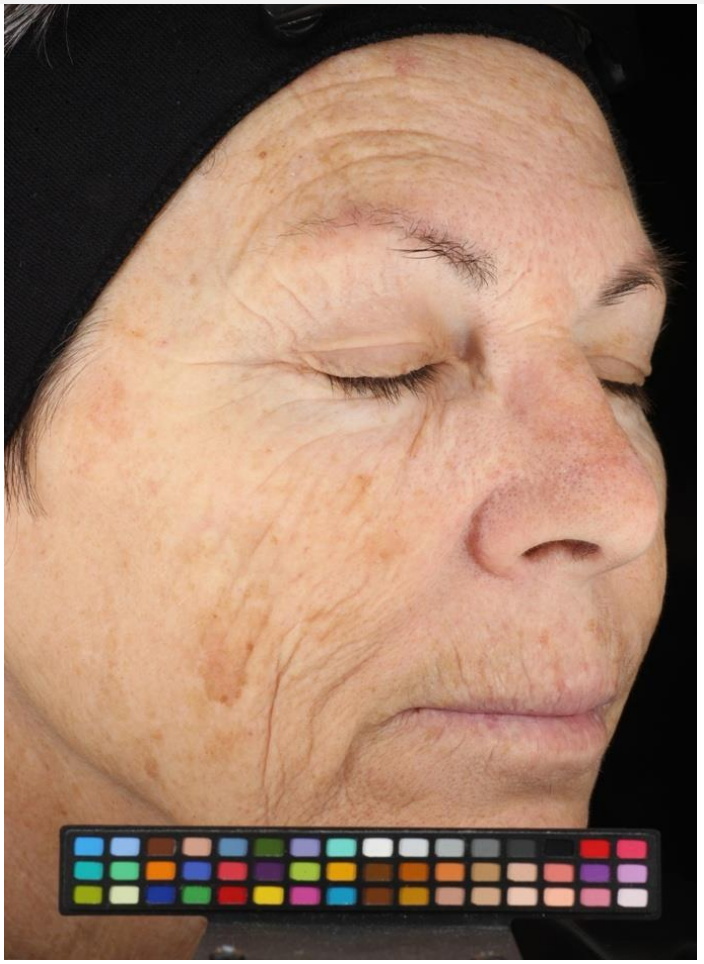

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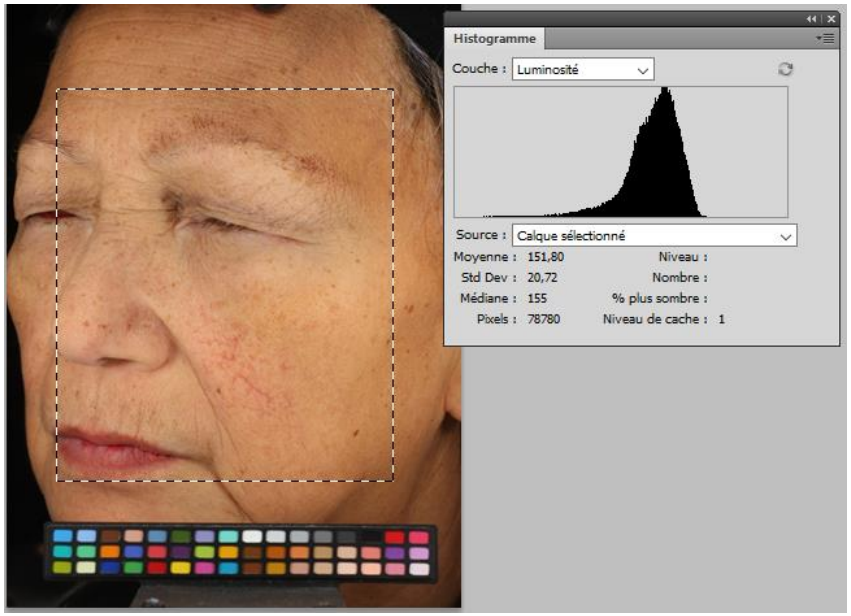
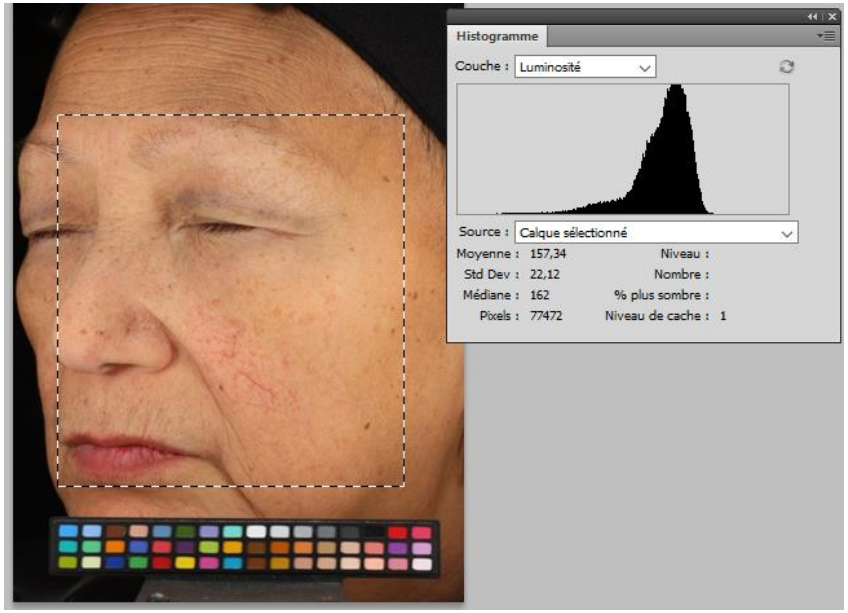
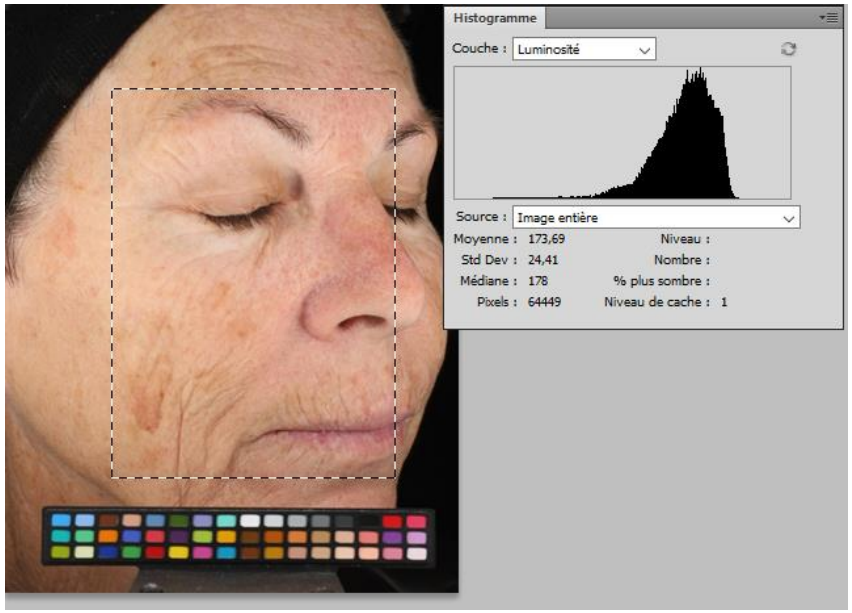
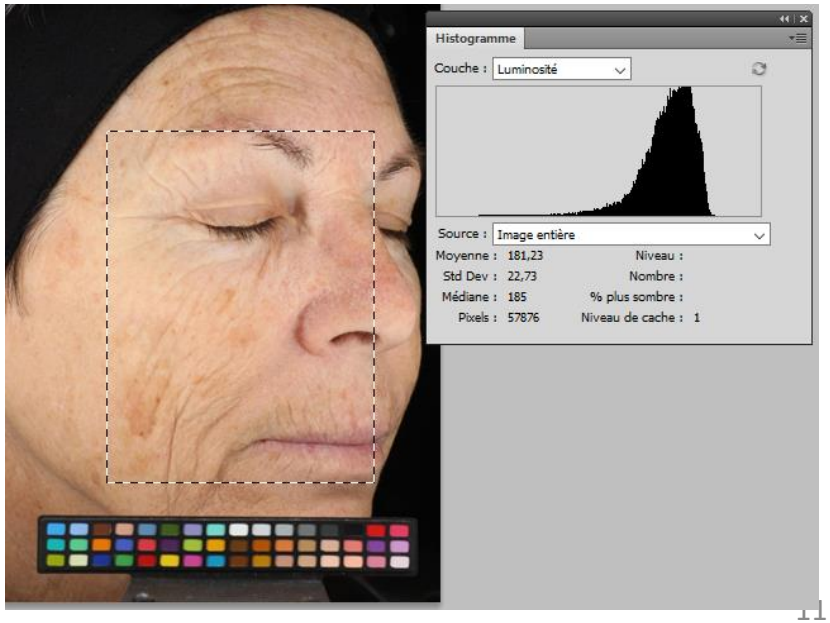

Histogramme
Couche : Luminosité
Source : Calque sélectionné
Moyenne : 151,80
Std Dev : 20,72
Médiane : 155
Pixels : 78780
Niveau :
Nombre :
% plus sombre :
Niveau de cache : 1


Histogramme
Couche : Luminosité
Source : Calque sélectionné
Moyenne : 157,34
Std Dev : 22,12
Médiane : 162
Pixels : 77472
Niveau :
Nombre :
% plus sombre :
Niveau de cache : 1


Histogramme
Couche : Luminosité
Source : Image entière
Moyenne : 173,69
Std Dev : 24,41
Médiane : 178
Pixels : 64449
Niveau :
Nombre :
% plus sombre :
Niveau de cache : 1


Histogramme
Couche : Luminosité
Source : Image entière
Moyenne : 181,23
Std Dev : 22,73
Médiane : 185
Pixels : 57876
Niveau :
Nombre :
% plus sombre :
Niveau de cache : 1

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In Vitro: ephyshine takes over and boosts cellular protection against UV

MATERIAL AND METHOD :

Experimental set up

Normal human keratinocytes were obtained from an Abdominoplast performed on a 76-years-old woman. The cells were grown until reach about 80% confluence. The media were then "enriched" with stem cells according to the method of Goodell et al[1]

The cells were preincubated for 24 hours at 37 ° C, in a humid atmosphere and 5% CO_2, in the absence (control) or in the presence of the reference product. At the end of the preincubation period, the cells were irradiated with UVB (30 mJ / cm²) and then incubated for 6 days at 37 ° C., under a humid atmosphere and 5% CO_2, in the absence (control) or in the presence of the active ingredient.

The viability of primary cells is achieved by Blue Alamar test.

ephyshine at very low level is able to protect 92% of the most UV-sensitive cells against UV stress.

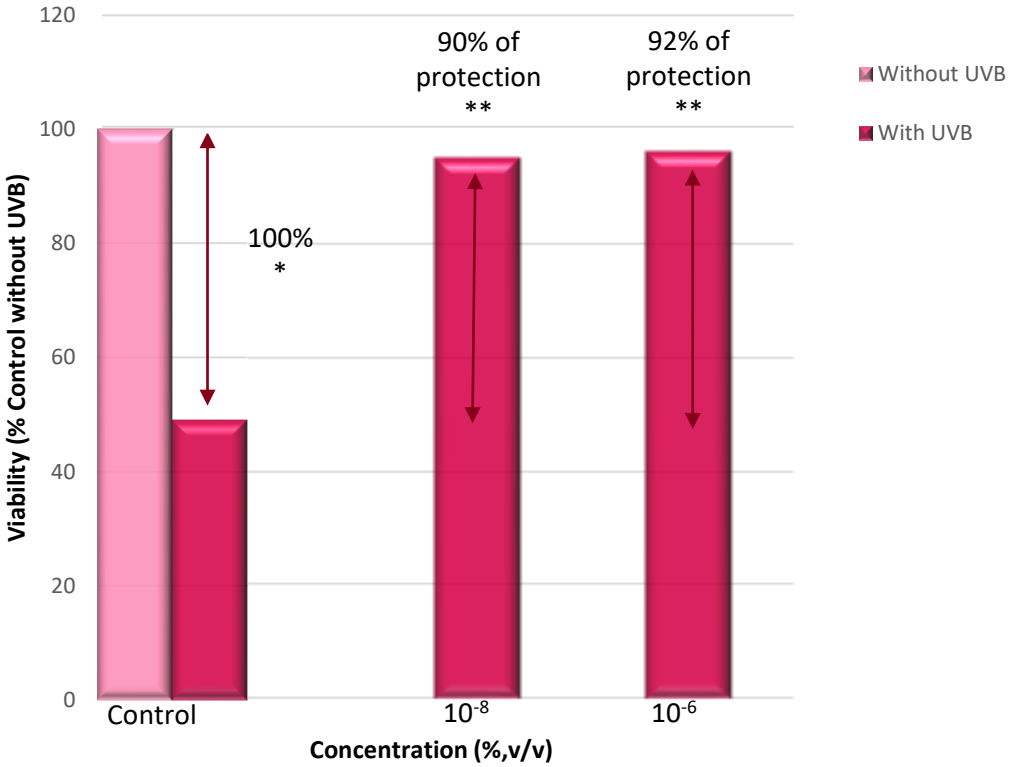

Figure 4 : % of cell viability = f(ephyshine concentration)

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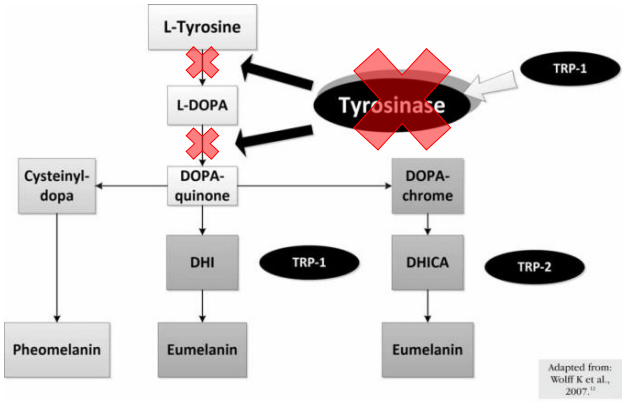
In vitro : Inhibition of the Tyrosinase (Anti dark spots mechanism)

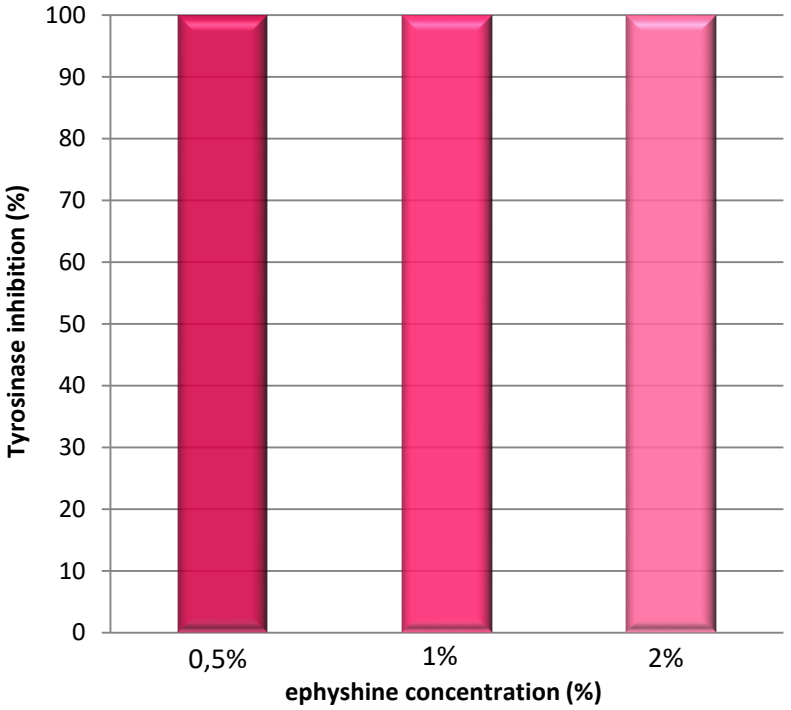
MATERIAL AND METHOD :

A lightening effect is possible when the inhibition of Tyrosinase, the key enzym of melanogenesis, is demonstrated.

The activity of Tyrosinase is studied by enzymatic analysis

ephyshine inhibits 100% the tyrosinase activity, the key enzyme of melanogenesis.





ephyshine corrects enzymatic over-activation of melanogenesis to reduce visible skin signs

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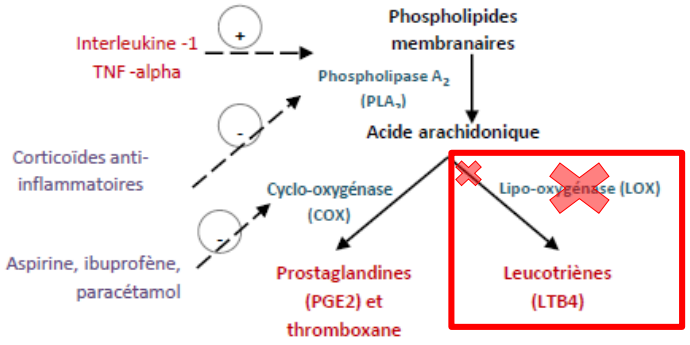
In vitro : Anti-inflammatory action

MATERIAL AND METHOD :

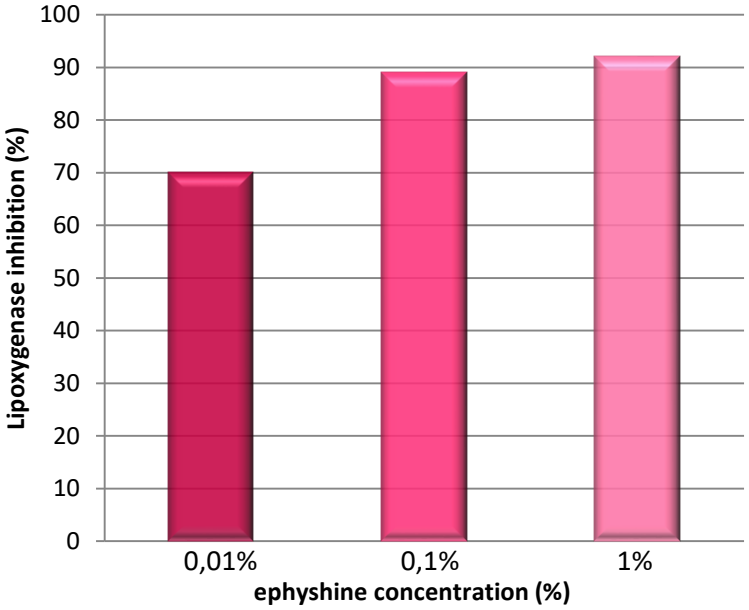
A destressing (anti-inflammatory) action can be demonstrated by the inhibition of the enzymes involved in the cascade of arachidonic acid, in particular Lipoxygenase.

The inhibitory activity of Lipoxygenase is studied by enzymatic analysis



Ephyshine at a dose of 0.01% inhibits by almost 69% the activity of Lipoxygenase, the key enzyme of the inflammatory process. At 1% Ephyshine inhibits 91% of this Lipoxygenase. These results reflect an **inhibition** of the **amplification** of the **inflammatory signal**. **ephyshine** does not prevent the initiation of the biochemical mechanism of inflammatory reaction but **inhibits** the **activity of Lipoxygenase**, a **key mediator** of the inflammatory cascade. Thus, **ephyshine** does not trigger **any side effects**

ephyshine calms and soothes the cellular reaction triggered during stress



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ephyshine, technical data sheet

- INCI: Dimethyl Isosorbide & Propanediol & Aqua & *Caesalpinia sappan* extract
- CAS: 5306-85-4 & 504-63-2 & 7732-18-5 & ND
- EINECS: 226-159-8 & 207-997-3 & 231-791-2 & ND
- COSMOS READY
- CHINA COMPLIANT
- APPEARANCE, liquid beige to brownish
- FORMULATION: hydrosoluble / lipodispersible
- STORAGE CONDITIONS: 18 months in a dry and well-ventilated place
- DOSAGE : 1%
- TOLERENCE:
    - Cutaneous: non-irritant at 1%
    - Ocular: insignificant cytotoxicity at 1% (eye irritation potential)
    - Non-phototoxic
    - Non-mutagenic

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Conclusion

1. **Curative effect**
    - ephyshine is an "anti-dark spot" active ingredient and an overall lightening. The results are visible in only in 1 month, **the skin is radiant.**
        - Average decrease of dark spot : 22% at 1 month
        - Inhibition of Tyrosinase : 100%
2. **Preventive effect**
    - ephyshine inhibits the activity of Lipoxygenase, the key enzyme of the stress signal, thus avoiding propagation of one of the main hyperpigmentation mechanism.
        - De-stressing and soothing power : 69%

ephyshine is a unique active ingredient possessing more than one function, a triple action:

Illuminates the skin while **protecting it from UV** rays and **soothing our skin cells**.

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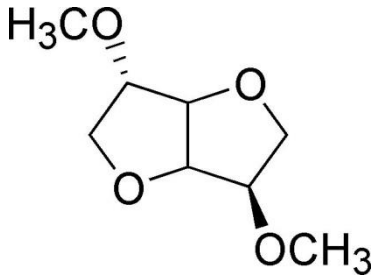
Vector

- **Ephyshine's vector is 100% natural, it is synergy between Dimethyl Isosorbide and the Propanediol.**
- **The Dimethyl Isosorbide is a liquid crystal. It surrounds, preserves and protects the active ingredient and avoids interactions between solvent and the active.**
- **It facilitates the absorption of the active and it is a skin penetration vector that does not affect or damage the active ingredient.**



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