EphyGENICS

EPHYLA
Natural Active Design

Inspired by **epigenetic therapy,** EPHYLA research is discovering new **active plant** ingredients that act on **skin gene expression.**

The advent of **epigenetics** has changed the way of thinking about cutaneous aesthetic defects by including the **environmental dimension**.

EphyGENICS are a range of epigenetic active ingredients that help your skin to **better adapt** to its environment and no longer suffer from its **genetic inheritance** in the face of stress or time.

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Beyond wellness, Wellbeing

EphySTEM

For all ages… and for all skin types…

Our work on epigenetic modification shares Oscar Wilde's view that « **one should not try to add years to one's life, but rather try to add life to one's years** ».

Thanks to **EphyGENICS :**
It becomes possible to optimize the **proper switching** and **use of genes** in skin cells.

The « Genics » of **EphySTEM :**

- **Action at the heart of the cells** (Genic 1)
  - Whispering in the ears of histones
  - Cuddle the stem cells
- **Superpowers** (Genic 1)
  - Restore Telomeres
  - Regenerate skin tissue
- **A lenitive Anti-Ox** (Genic 1)

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For all ages… and for all skin types…

We are all familiar with the signs of skin aging. At the biochemical level, aging is characterized by a reduced efficiency of mitochondria, **a shortening of telomeres** (the "caps" at the ends of chromosomes), as well as a lesser management of **free radicals** promoting oxidation and inflammation. This altered biochemical process is the negative consequence of epigenetic modifications on DNA or **Histones** [1].

Epigenetic modifications switch the use of genes in cells, moreover, they determine the quality of their transcription, which, consequently, impacts the **quality** and **performance** of functional and structural proteins [2]

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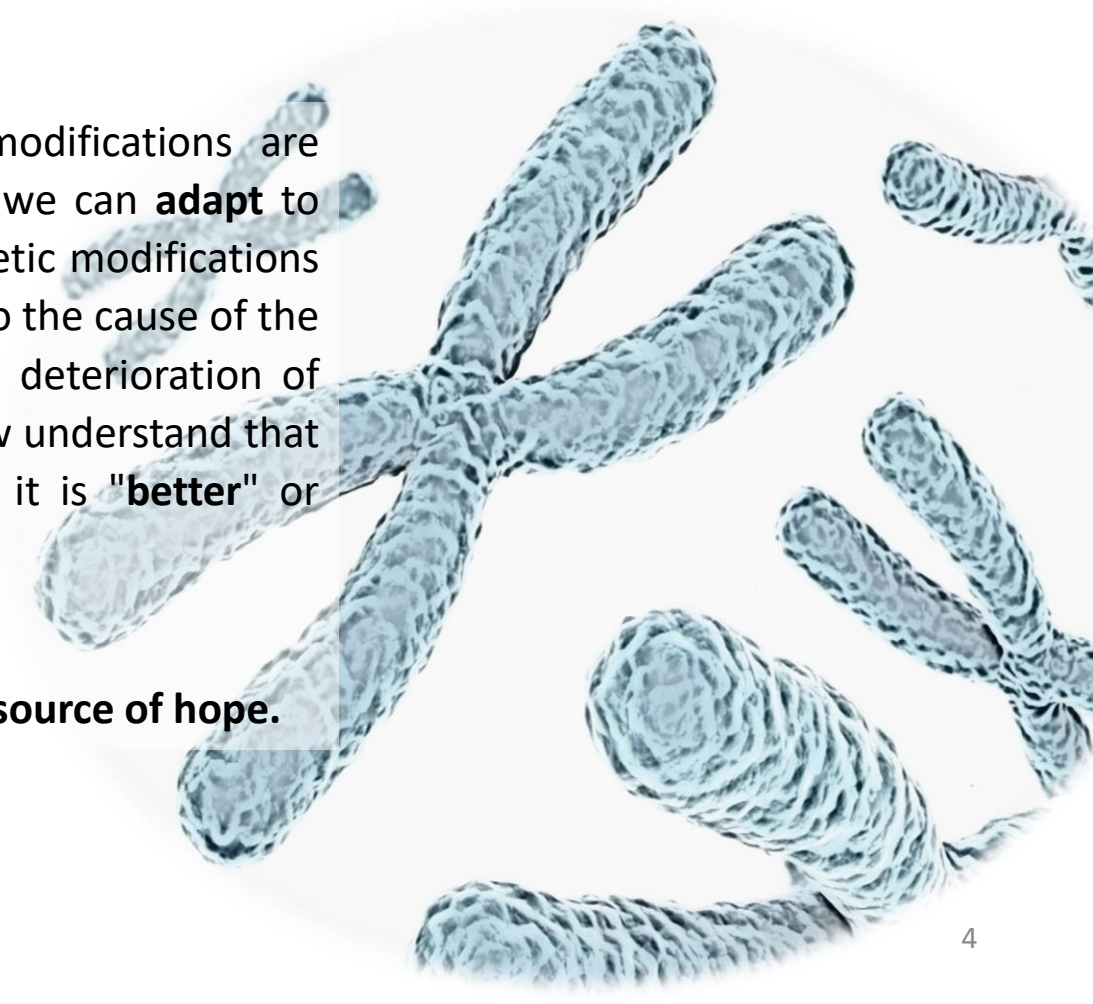
For all ages… and for all skin types…

We must understand that epigenetic modifications are constantly **evolving**, and thanks to them we can **adapt** to our **changing environment**. These epigenetic modifications are, in essence, **reversible** [3], they are also the cause of the **improvement** or, on the contrary, of the deterioration of our **metabolism**. With epigenetics, we now understand that nothing is definitively acquired, whether it is "**better**" or "worse".



This potential for improvement is a great source of hope.

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The plant at the heart of epigenetic action :

“Caesalpinia sappan" is a shrub native to southern Asia that now grows in the equatorial zone of Africa, particularly in Cameroon. In the mature seed, we draw a powerful **epigenetic** active ingredient that is particularly effective in **improving cellular and skin regeneration.**

The **Bakas** Pygmies, in the heart of the equatorial forest in eastern Cameroon, are collaborating with Ephyla on the supply chain.

The Bakas consume the seeds traditionally as a condiment for dishes.

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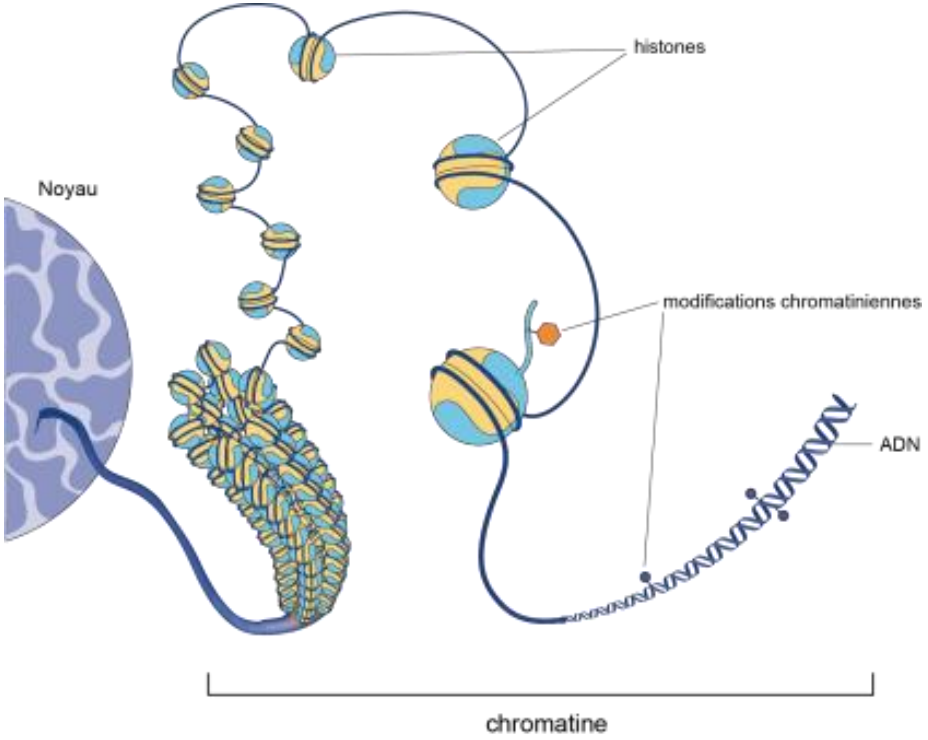
Genic 1

Whispering in the ears of HISTONES EphySTEM

EphySTEM acts in the heart of the cell nucleus, it maintains the **flexibility** of the chromosomes by stimulating the good winding of the chromatin around the **histones** (Stimulation of the activity of **HDAC** and in particular, of **Sirtuin I**).

This action preserves the **quality** of the genetic material when **chromatin deconds and opens up** by unwinding its DNA to express a **gene**.

It is then important that the DNA remains exposed to the numerous enzymes and molecules in the cell nucleus for **only a short time**.



Organisation de la chromatine dans le noyau d'une cellule (modifié de Probst et al., 2009)

***EphySTEM** acts directly on the **histones** at the heart of the skin cells to **optimize** the **winding/unwinding** of the DNA*

Genic 1

Whispering in the ears of HISTONES

EphySTEM

HDAC** activation to stimulate/initiate **deacetylation

HAT inhibition also leads to gene protection [4] mainly when gene expression is not required.

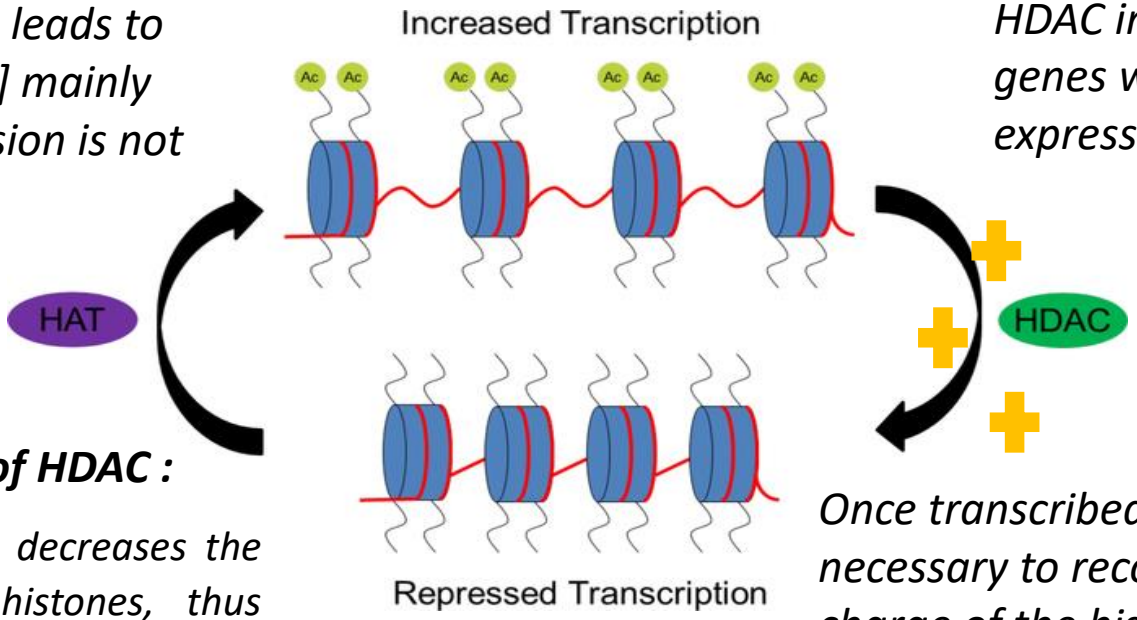


Figure adapted from Korzus E, Manipulating the brain with epigenetics. Nat. Neurosci 2010, 13, 405–406

HDAC inhibition protects genes when their expression is required.

Meaning and role of HDAC :

Acetylation of lysines decreases the positive charge of histones, thus decreasing the interaction with negatively charged DNA. This modification leads to an opening of the chromatin, thus allowing the transcription of genes.

Once transcribed, deacetylation is necessary to recover the positive charge of the histones thus increasing the interaction with the negatively charged DNA and condensing the chromatin again.

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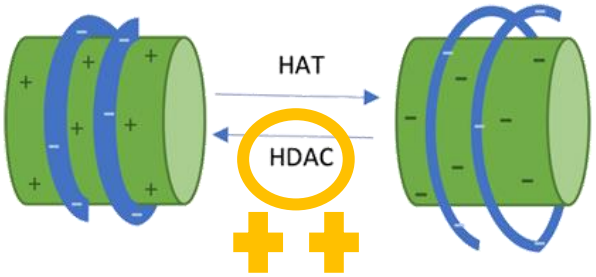
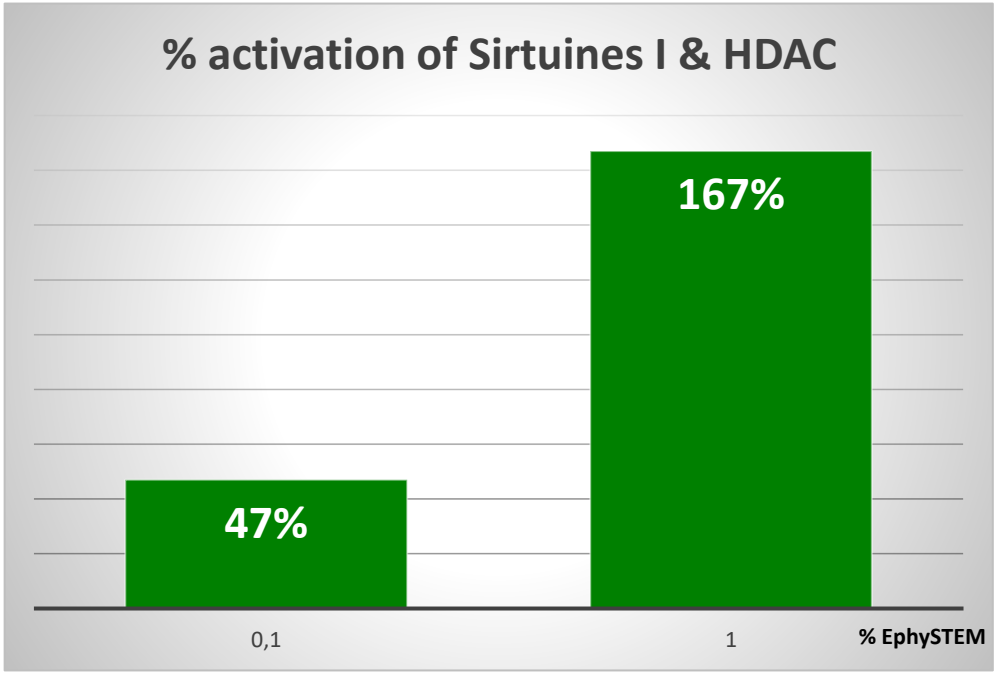
Genic 1

Whispering in the ears of HISTONES EphySTEM

Activate HDAC

The proper winding of DNA around histones is ensured mainly by HDAC (Histone deacetylases) and in particular, type Sirtuins I. The activity of these enzymes offers a high protection to the genetic material. The higher their activity, the more efficient and faster the chromatin condensation.





***Graphic 1 :* Enzymatic Test_** *In Tubo assessing the increase in basal enzyme activity (basal activity reduced to zero in this graph). Test carried out in triplicate with controls.*

EphySTEM at 1% stimulates HADCS activity (including SIRT I) by 167%, this stimulation is 47% with 0.1% EphySTEM.

EphySTEM acts on the optimization of DNA winding after gene transcription = ACTIVATION of HDAC (including SIRT I)

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Genic 1

Cuddle the Stem Cells

EphySTEM

« Feeling good from skin »

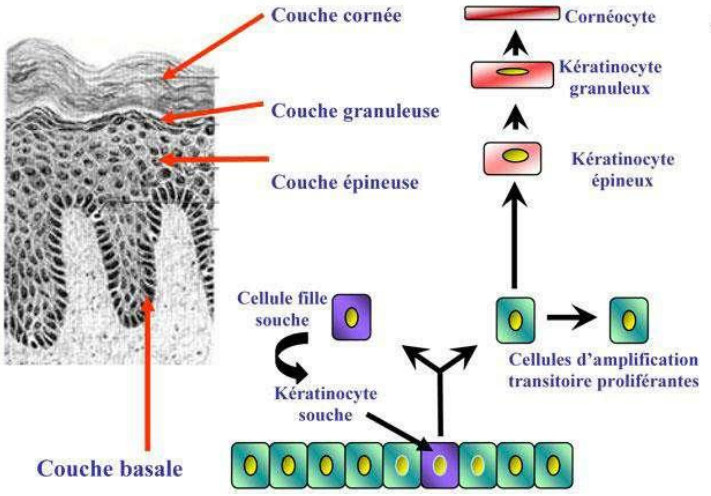
The ZEN attitude of Stem cells

The youthfulness of our skin lies in the pool of undifferentiated pluripotent **stem cells** that reside in the basal layer of the epidermis. The **genetic freshness** and proper cell renewal of our skin depend on this pool of stem cells. In essence, very fragile and extremely sensitive, stem cells are the first to be **impacted by stress** and cellular constraints.

EphySTEM, by its epigenetic action protects the genetic material of the differentiated cells, and maintains the youthfulness of the skin by **preserving the stem cells**.

In the event of environmental or endogenous stress, epigenetic action allows the skin's stem cells to **dodge stress** and **remain ZEN**.

The skin regenerates from the stem cells of the basal layer of the epidermis, as long as they remain ZEN !....



Stem keratinocytes (bottom) divide into two: one daughter cell retains the ability to divide while the other begins to differentiate. Gradually, this differentiation continues while reaching the outer layers of the skin. © I-Stem

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Genic 1

Cuddle the Stem Cells

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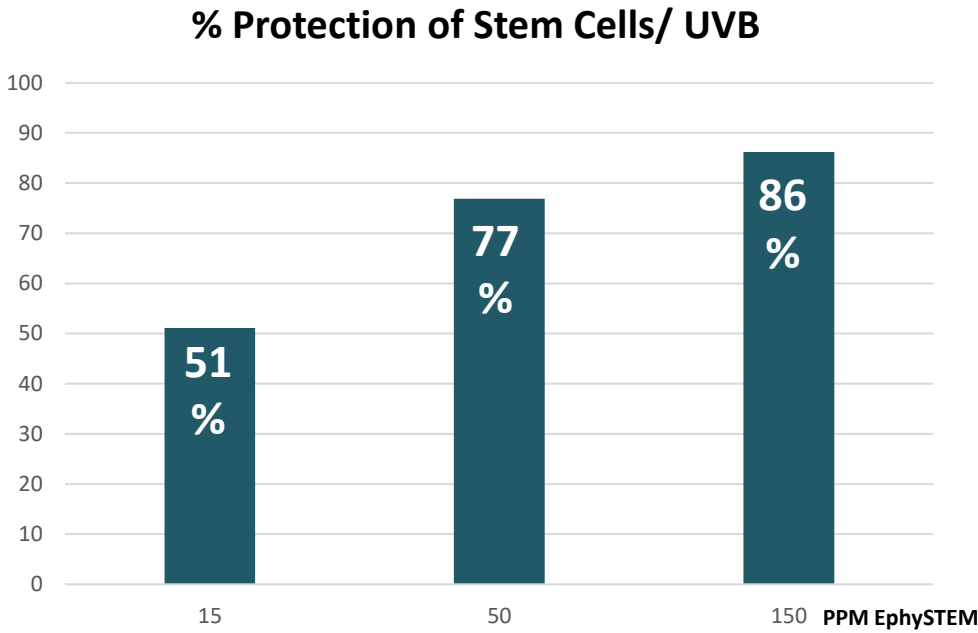
Stem Cells stay ZEN

The **epigenetic** action of the active **EphySTEM** brings a protective effect on the stem cells of the skin (basal layer).

EphysSTEM at a dose of **150 PPM** is able to avoid 86% of mortality during UV-induced cell stress

Capital Preserved
« Cellules souches »



Graphic 2 : In Cellulo test _*Normal human keratinocytes were obtained from a 50-year-old donor. The cells were grown to approximately 80% confluence. The media were then "enriched" with stem cells using the method of Goodell et al*. The cells were pre-incubated for 24 hours at 37°C in the absence (control) or presence of the reference product. At the end of the pre-incubation period, the cells were irradiated with UVB (30 mJ/cm²) and incubated for 6 days at 37°C in the absence (control) or presence of the active ingredient. The viability of the primary cells is obtained by the Blue Alamar test, performed in triplicate with control.*

**Hoescht 33342 HSC staining and stem cell purification protocol. (1996) J Exp Med 183, 1797-806*

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Epigenetic action

EphySTEM

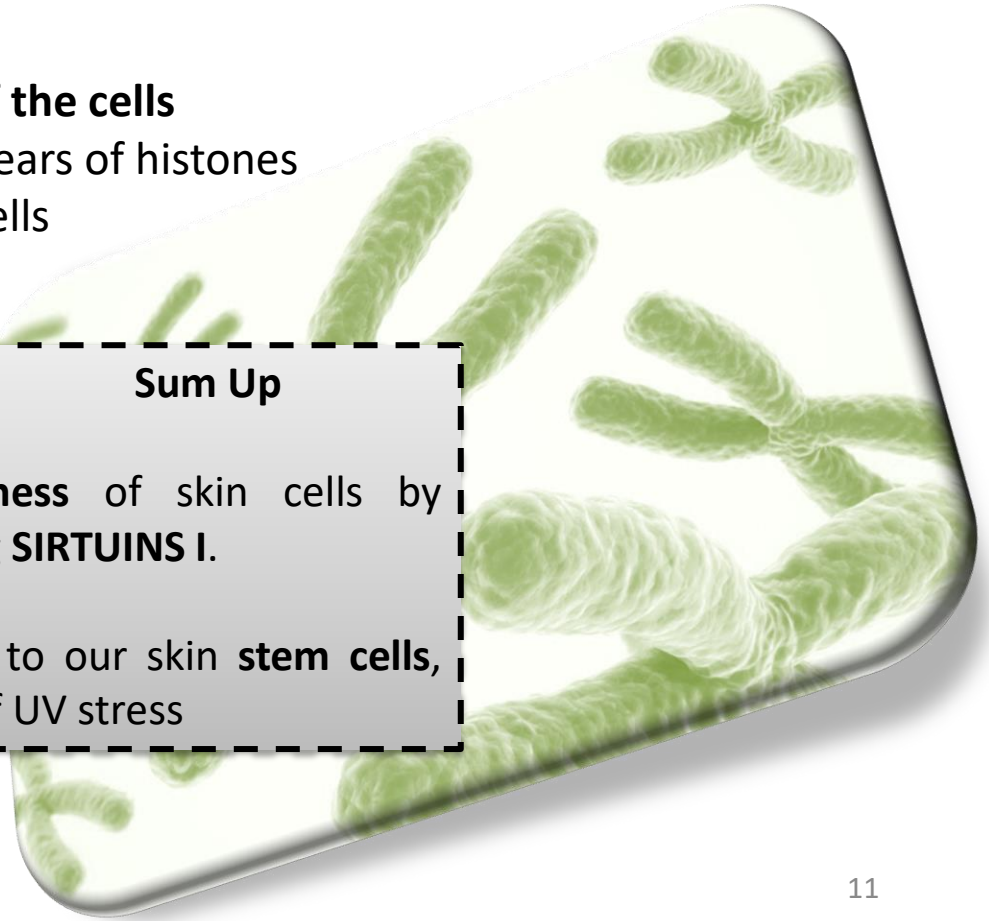
❖ **Action at the heart of the cells**
- Whispering in the ears of histones
- Cuddle the stem cells

Genic 1

Sum Up

✓ **Preserves the youthfulness** of skin cells by activating **HADC**, including **SIRTUINS I**.

✓ Provides **high protection** to our skin **stem cells**, particularly in the event of UV stress



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Genic 2

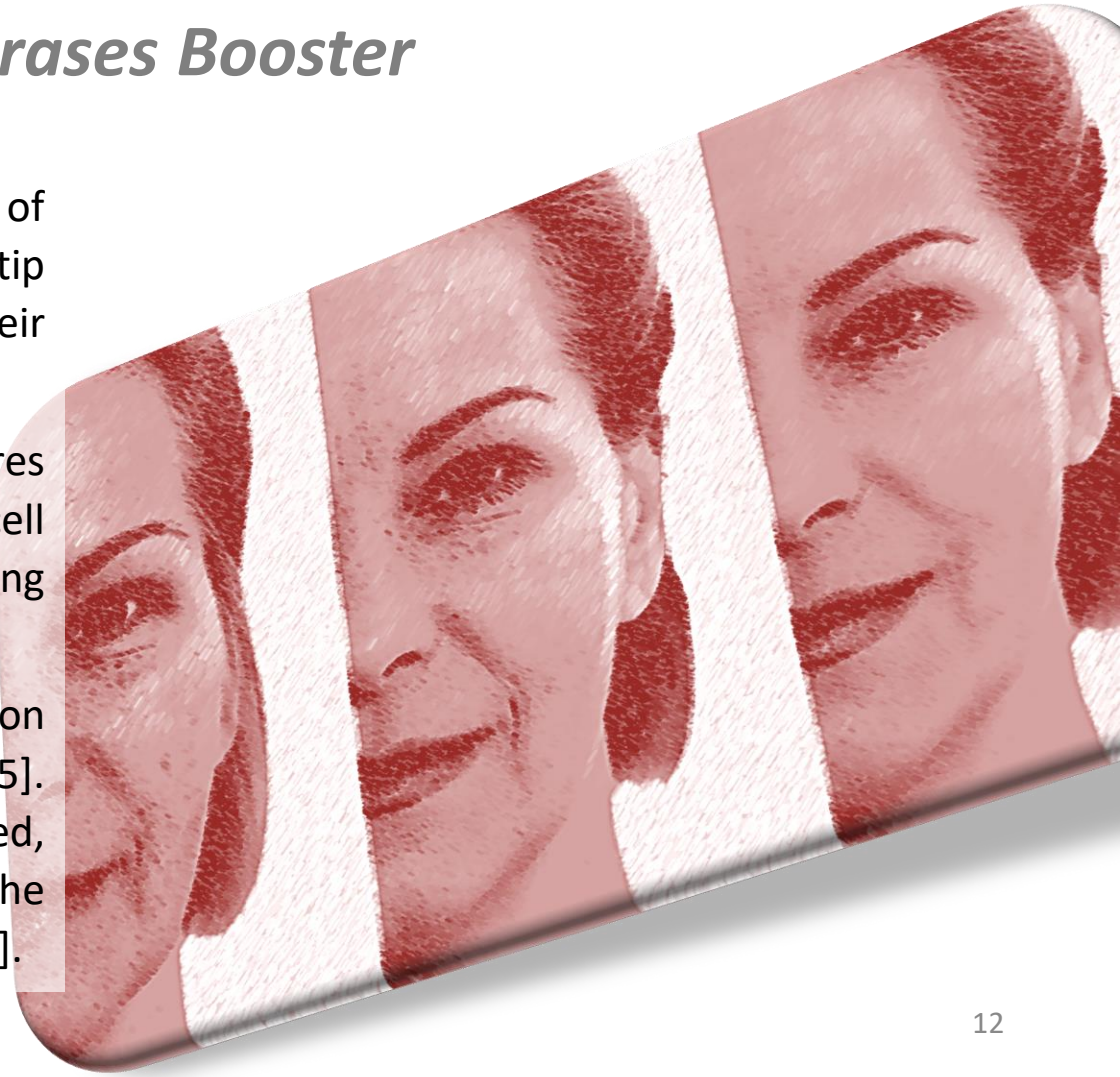
Superpower : Telomeres « Rescue » EphySTEM

Telomerases Booster

The beneficial epigenetic action of **EphySTEM** continues to work right to the tip of our chromosomes, at the level of their **protective "caps"...**

Indeed, these "caps" are called telomeres and they shorten at each mitosis (cell duplication) and this induces cell aging (senescence).

Slowing down telomere degradation effectively **reduces** cellular **senescence** [5]. For this, a key enzyme must be activated, **telomerase**, which is in charge of the nucleotide polymerization of telomeres [6].



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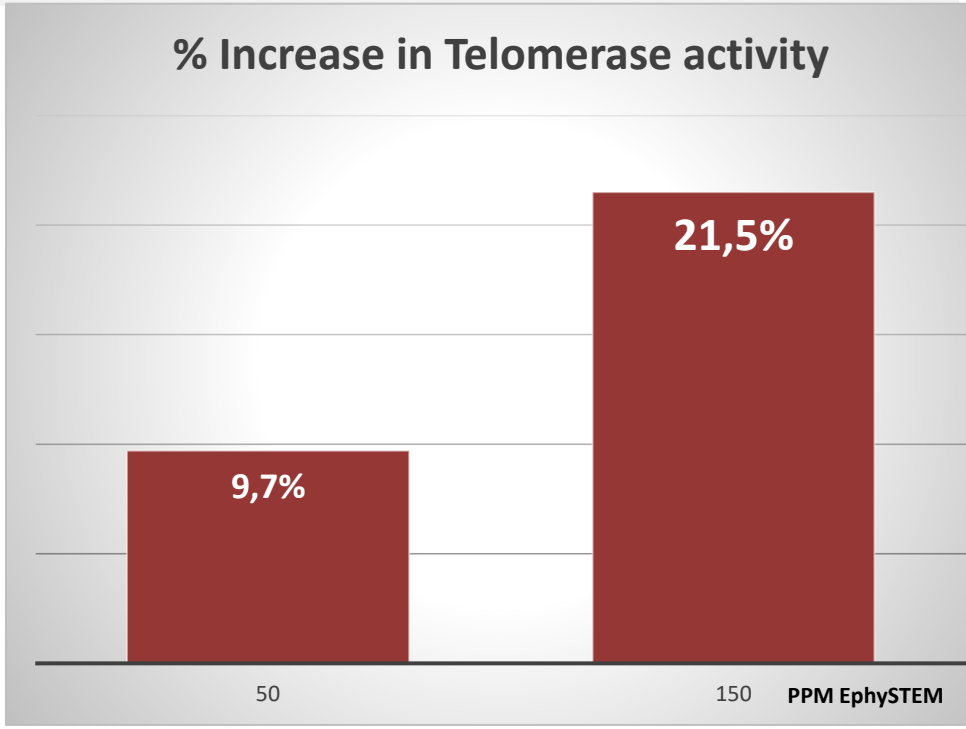
Genic 2

Superpower : Telomeres « Rescue » EphySTEM

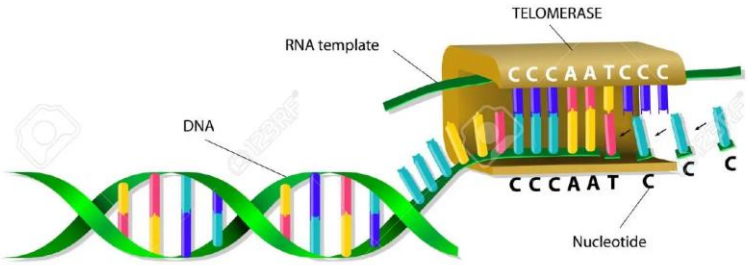
Telomerases Booster

EphySTEM acts at the tip of the chromosomes by increasing the basal activity of **telomerases**, thus increasing their polymerization capacity.

EphySTEM from the dose of **150PPM** is able to increase by 21.5% the activity of Telomerases in human skin cells



Graphic 3 : In Cellulo test_ *Normal human keratinocytes were cultured to approximately 75% confluence. The cells were preincubated for 24 hours at 37°C. At the end of the incubation period, telomerase was extracted from the cells and its activity was determined using a specific and sensitive kit. The principle of the telomerase activity kit couples a PCR step (in which telomerase elongates) with an ELISA step allowing the semi-quantitative determination of the quantities of telomerase elongation products. Test performed in triplicate with control controls.*



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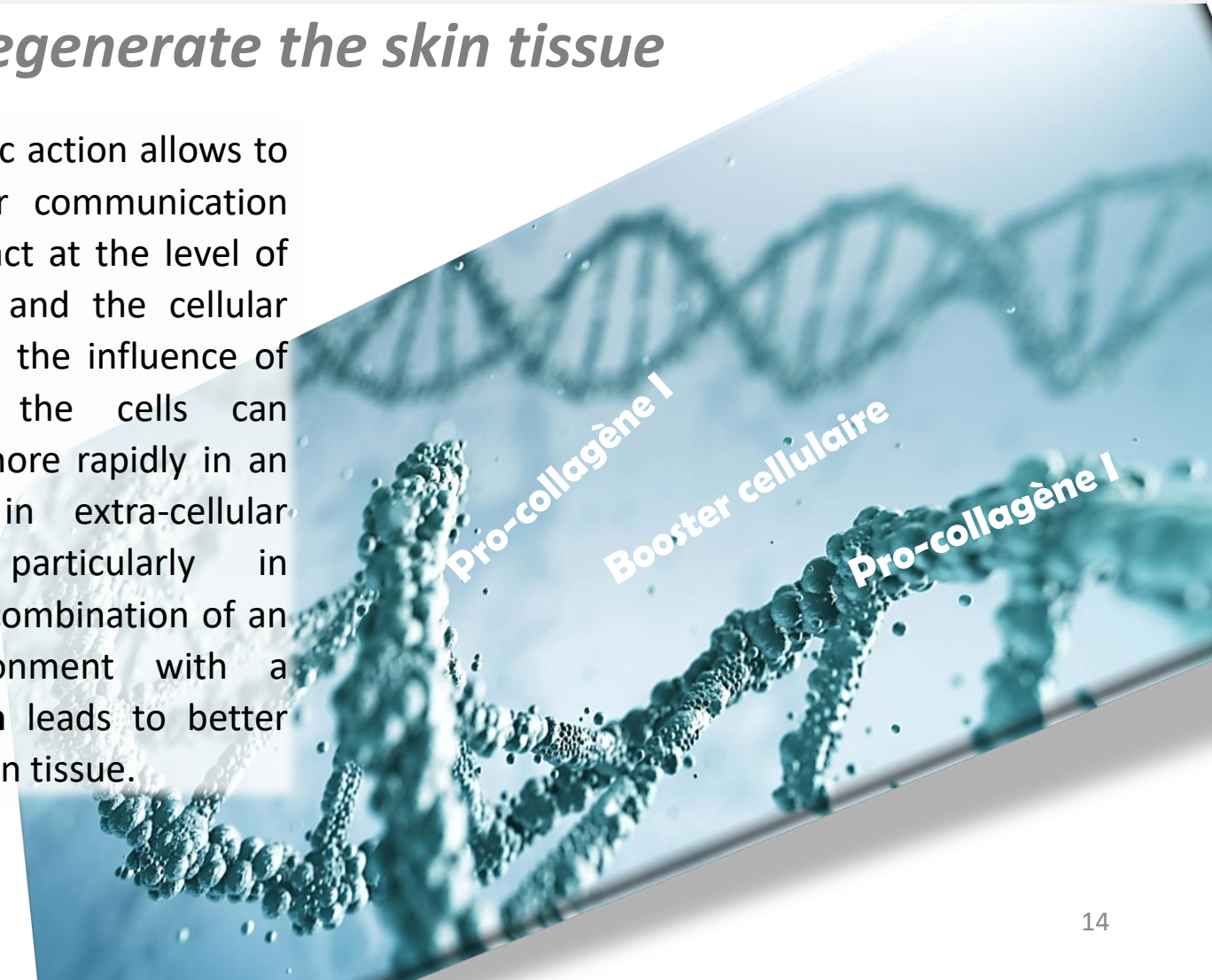
Genic 2

Superpower : Make skin new

EphySTEM

Regenerate the skin tissue

EphySTEM by its epigenetic action allows to increase the inter-cellular communication and more particularly to act at the level of the **extra-cellular matrix** and the cellular **regeneration**. Thus, under the influence of our active ingredient, the cells can reconstitute themselves more rapidly in an environment increased in extra-cellular matrix, and more particularly in **Pro_Collagen type I**. The combination of an increased matrix environment with a **boosted cell regeneration** leads to better renewal or repair of the skin tissue.



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Genic 2

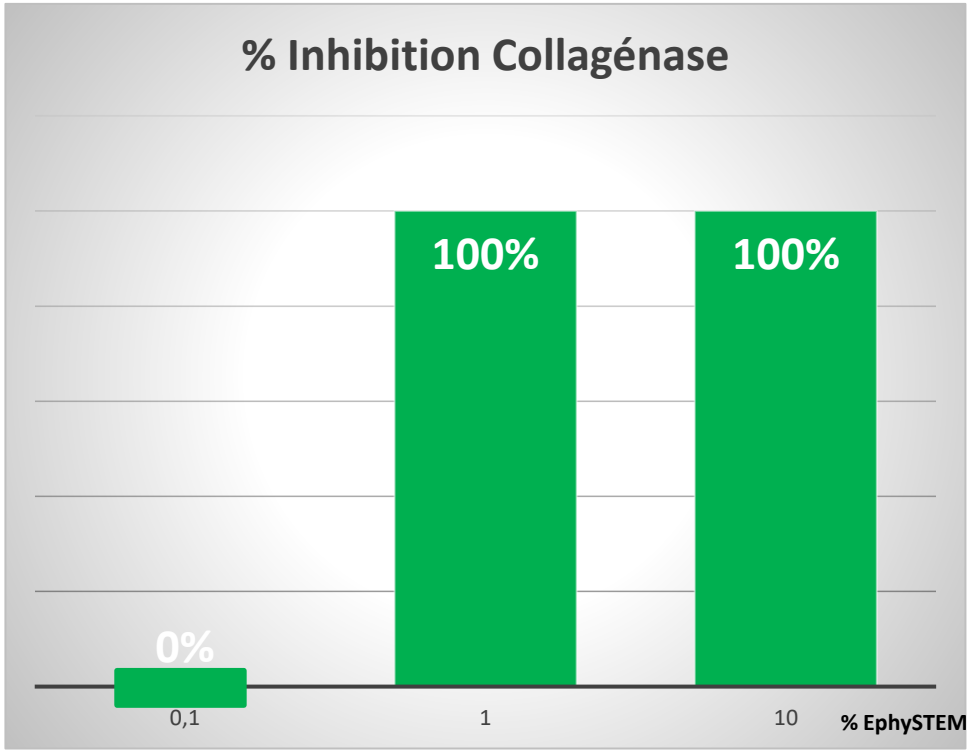
Superpower : Make skin new

EphySTEM

The preserved Matrix

EphySTEM acts at the heart of the skin matrix by **stopping the degradation** of collagen, so the extracellular matrix is **preserved** in the skin tissue.

EphySTEM, from the dose of 1%, is able to **INHIBIT by 100%** the activity of collagenase.



Graphic 4 : Enzymatic Test_ *In Tubo evaluating the inhibition of basal enzyme activity (basal activity reduced to zero in this graph). Test carried out in triplicat with controls.*

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Natural Active Design

Genic 2

Superpower : Make skin new

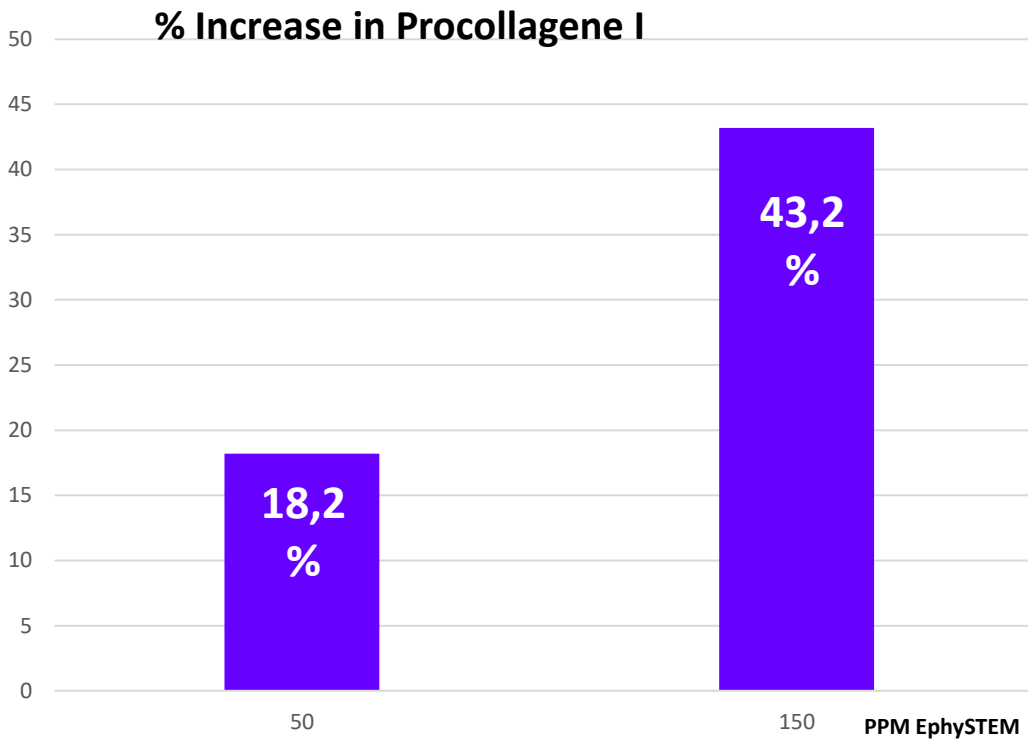
EphySTEM

The augmented Matrix

EphySTEM effectively protects collagen, but its epigenetic action is perceived at the heart of the skin matrix by boosting the production of **collagen I**.

Thus, with **EphySTEM**, the extracellular matrix **increases** in the skin tissue.

EphySTEM, from the dose of **150PPM**, is able to increase by **43.2%** the level of **pro-collagen I** produced by human skin cells.



Graphic 5 : In Cellulo test_ *Normal human fibroblasts from a 68-year-old donor were cultured to confluence. At confluence, the cells were incubated for 48 hours, in the presence or absence of the test products. At the end of the incubation period, Pro-collagen I was assayed with a specific Elisa kit and total proteins were determined by the Bradford spectro-colorimetric method. The test was performed in triplicate with controls.*

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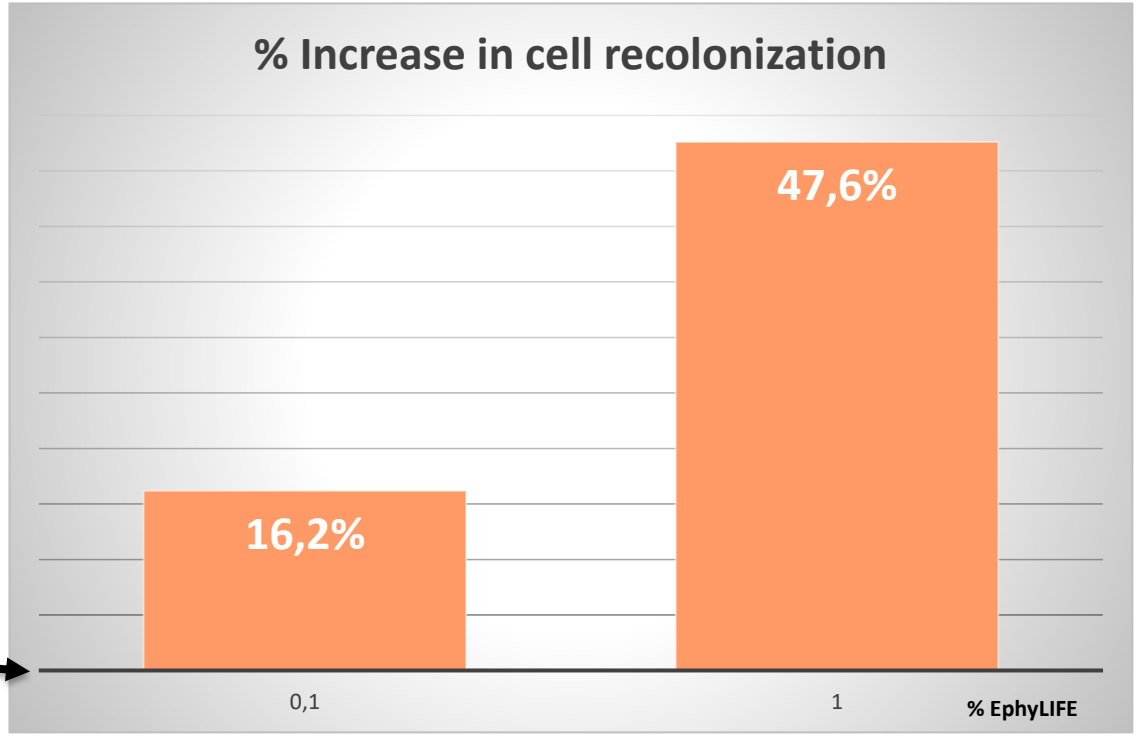
Genic 2

Superpower : Regeneration EphySTEM

Increase in the regeneration potential of skin cells



Basal rate of cell recolonization

EphySTEM at a dose of 1% is able to increase by more than **47%** the recolonization of the cell carpet

Graphic 6 : In Cellulo test _*From a culture of normal human fibroblasts incubated at 37°C in a humid atmosphere with 5% CO2. At confluence, the cell mats are scraped ("Scrap test") and the culture media are enriched with the controls and the test products for 24 hours. At the end of this incubation period, the recolonized surfaces are measured by image analysis.*

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Epigenetic action

EphySTEM

❖ **Superpowers**
- Restore Telomeres
- Regenerate skin tissue

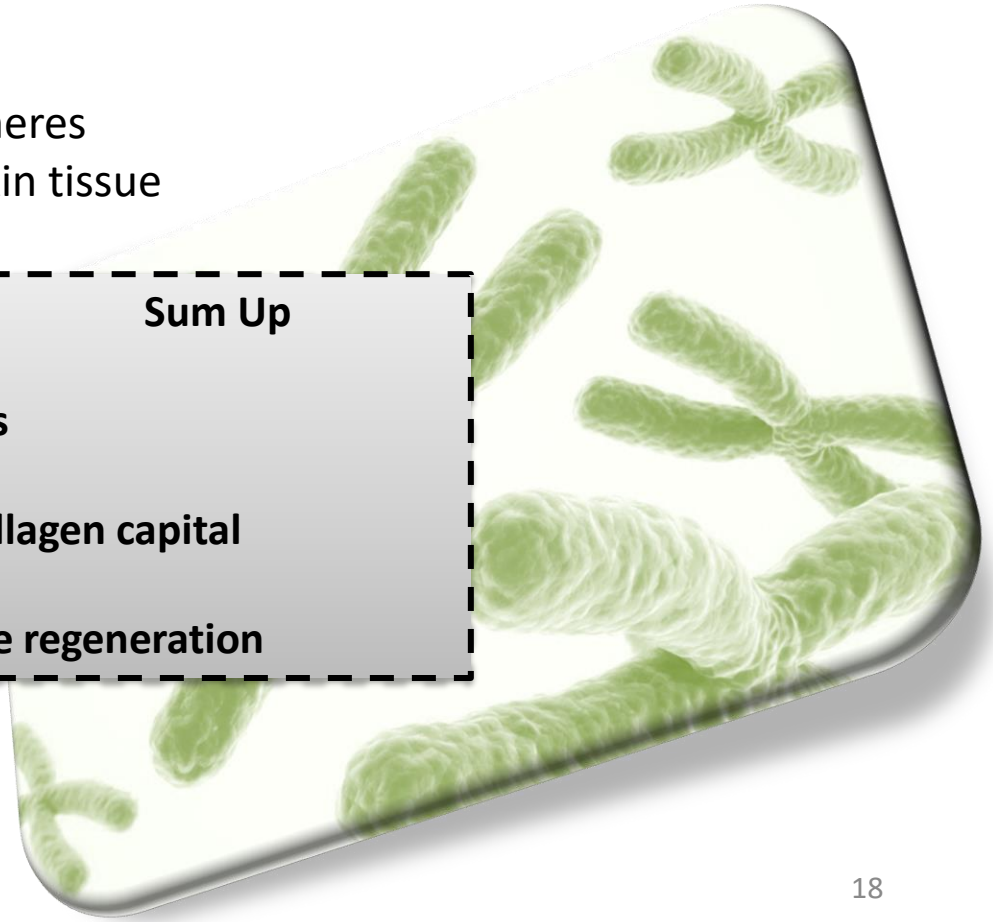
Genic 2

Sum Up

✓ **Activation of Telomerases**

✓ **Preserve and increase Collagen capital**

✓ **Potentiation of skin tissue regeneration**



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Genic 3

A Lenitive Anti-Ox

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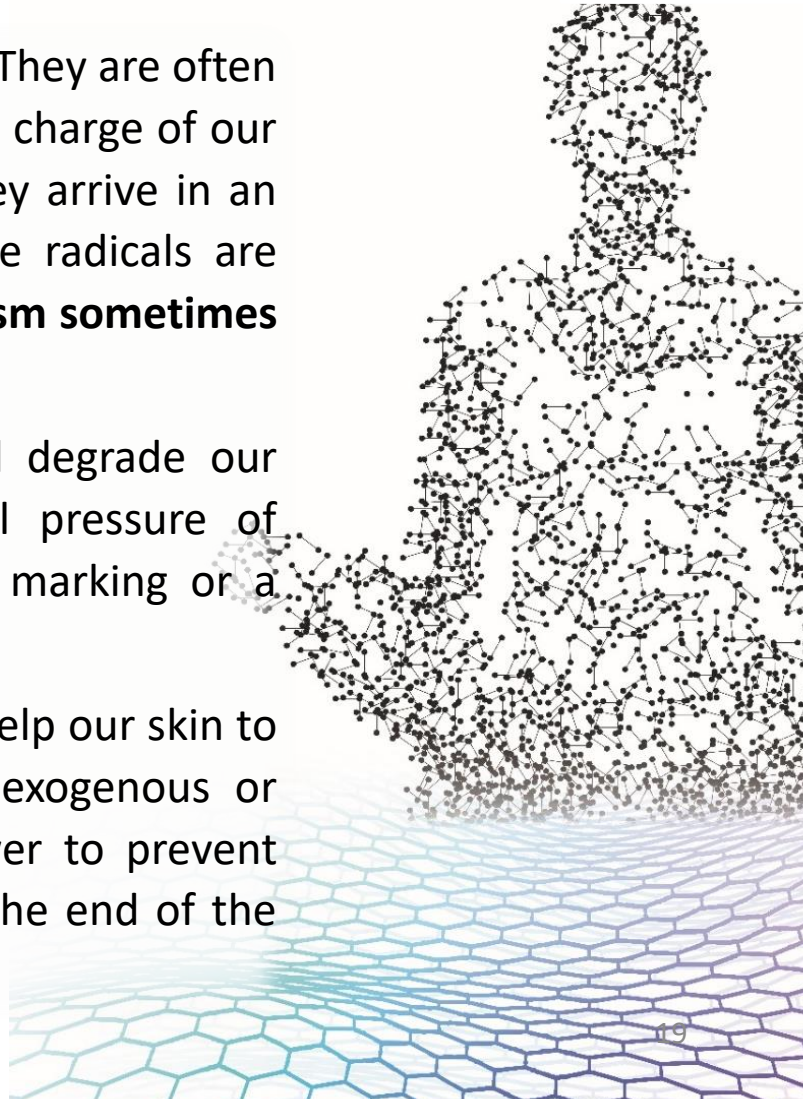
Free radicals are a constant in our urban environment. They are often linked to fine particles that are attracted to the anionic charge of our skin. These free radicals are by nature exogenous, they arrive in an imported way on the surface of our skin. Other free radicals are called endogenous. **They are the fruit of our metabolism sometimes exacerbated by the stress of our life**.

Free radicals are chemically active, they oxidize and degrade our constituents, they exert a stress or a physiological pressure of **inflammatory** type which can lead to an epigenetic marking or a genetic degradation.

To prevent this bad epigenetic influence, it is good to help our skin to fight against these free radicals, whether they are exogenous or endogenous. **EphySTEM** brings a very effective answer to prevent and treat skin stress in order **to make you ZEN** until the end of the corneocytes.



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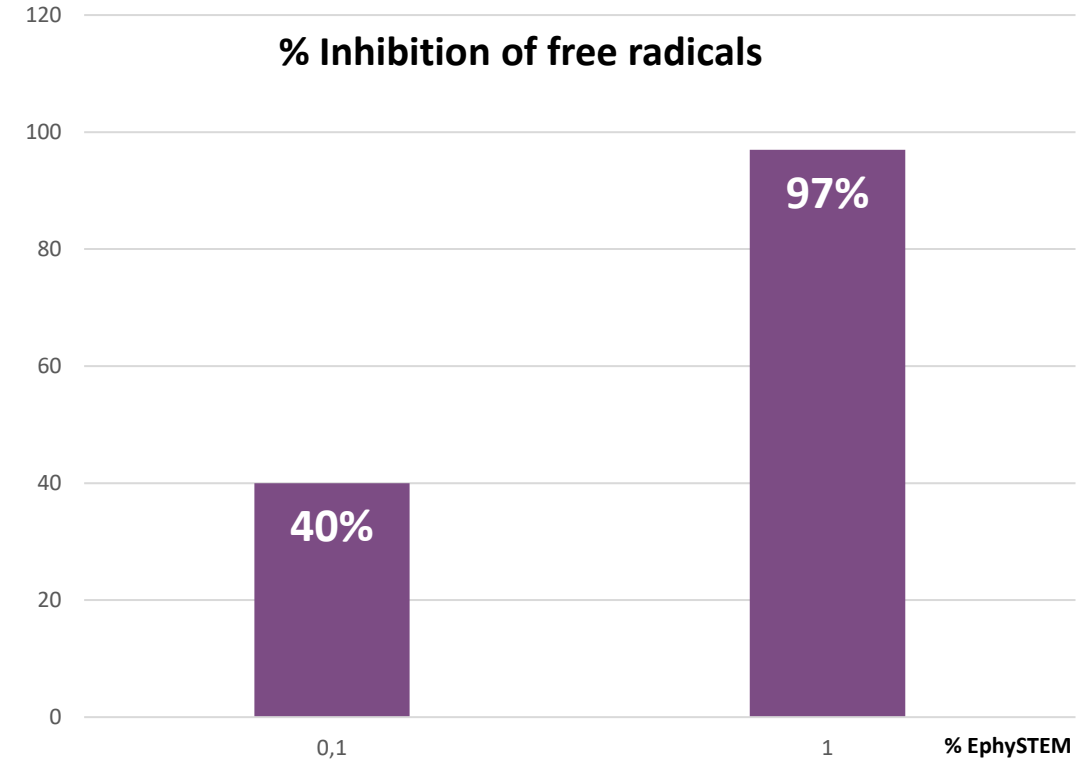
Genic 3

A Lenitive Anti-Ox

EphySTEM



Graphic 7 *:* **Biochimical Test_** *In Tubo evaluation of the inhibition of the oxidative potential according to the DPPH model. Test carried out in triplicate with controls.*

De-stress

EphySTEM provides a very effective **anti-free radical shield** effect.
The stress caused by free radicals is **avoided**;
at a dose of **1%,** a **97% inhibition** of free radicals is observed.

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Genic 3

The Lenitive Action

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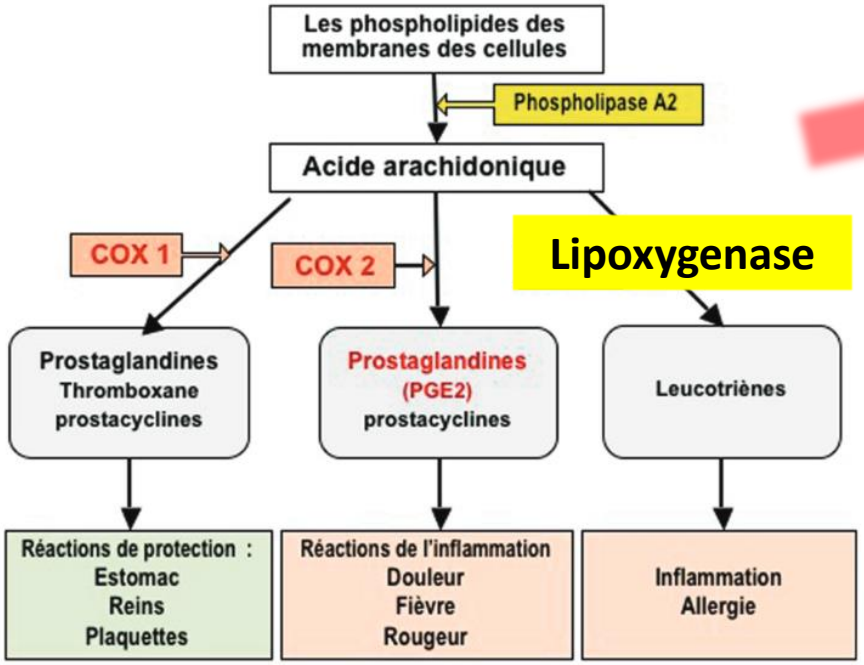
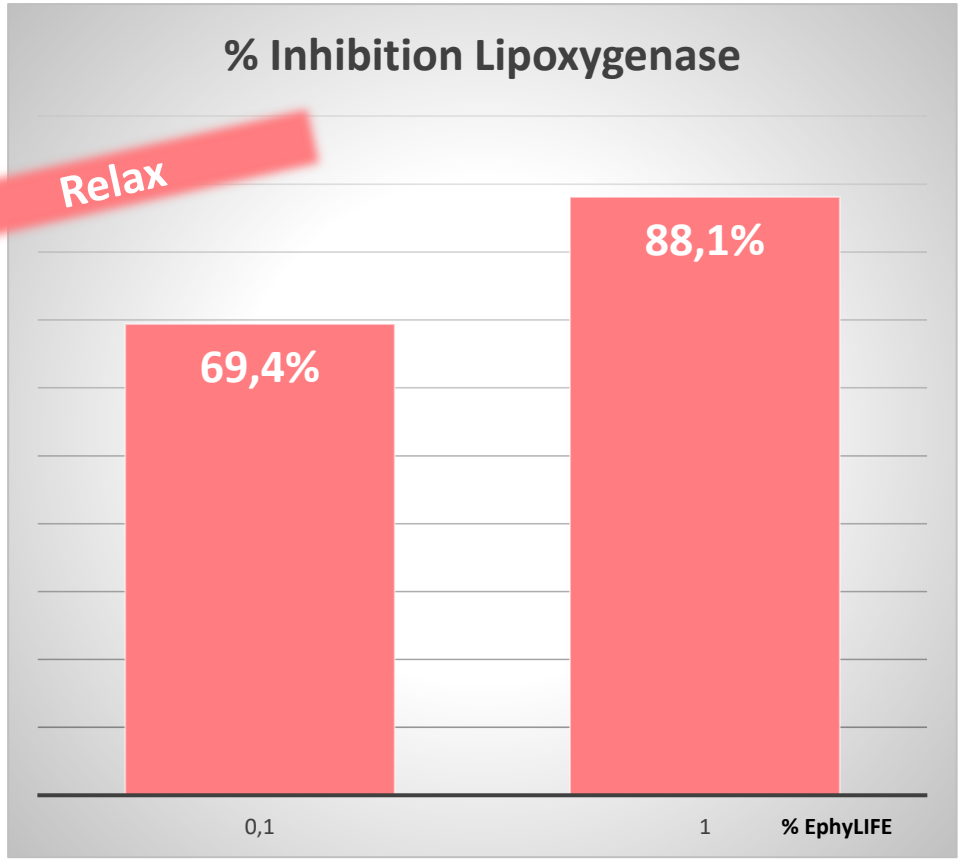
The arachidonic cascade (inflammation)





Graphique 8 : ***Enzymatic Test*** *In Tubo test evaluating the inhibition of the basal activity of the Lipoxygenase enzyme (LIPOX) of the arachidonic cascade. Test carried out in triplicate with controls.*

EphySTEM at a dose of 1% is able to inhibit by **more than 88%** the activity of **LIPOXYGENASE**

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Stay ZEN in the middle of the action

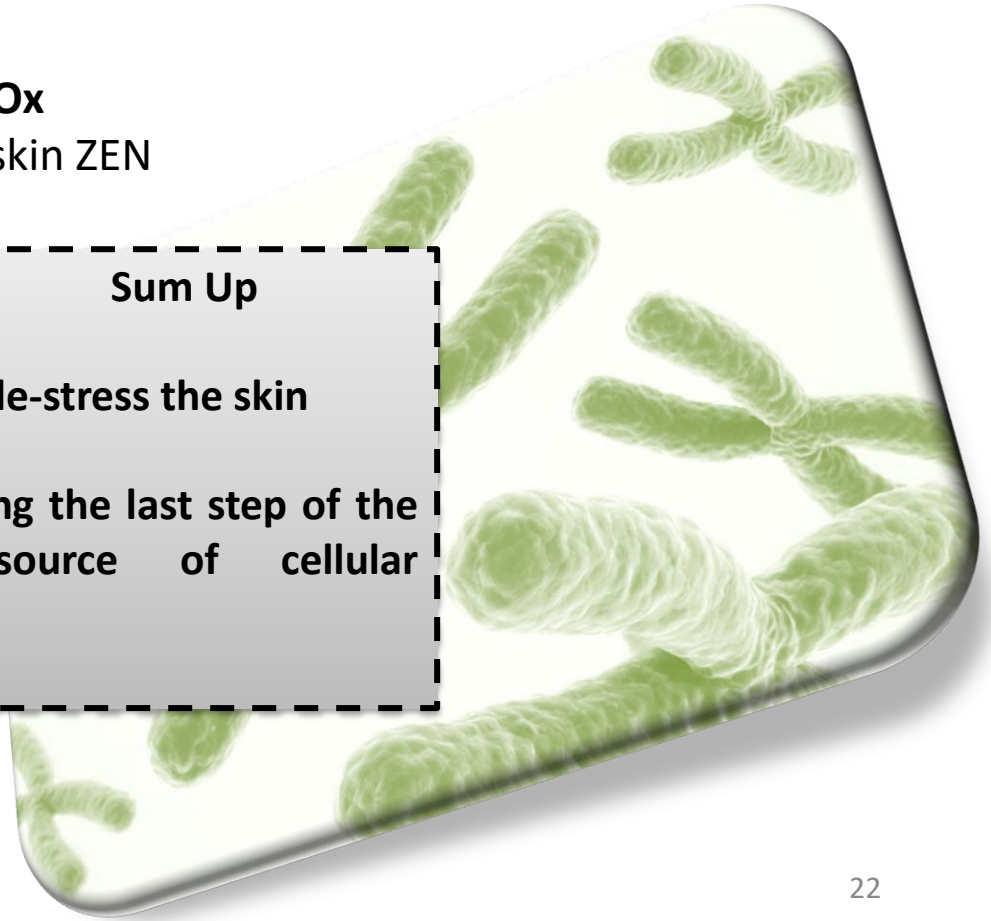
EphySTEM

❖ **A Lenitive Anti-Ox**
Keeping your skin ZEN

Genic 3

Sum Up

- ✓ **Free-radicals inhibition to de-stress the skin**
- ✓ **Soothing effect by inhibiting the last step of the arachidonic cascade (source of cellular inflammation)**



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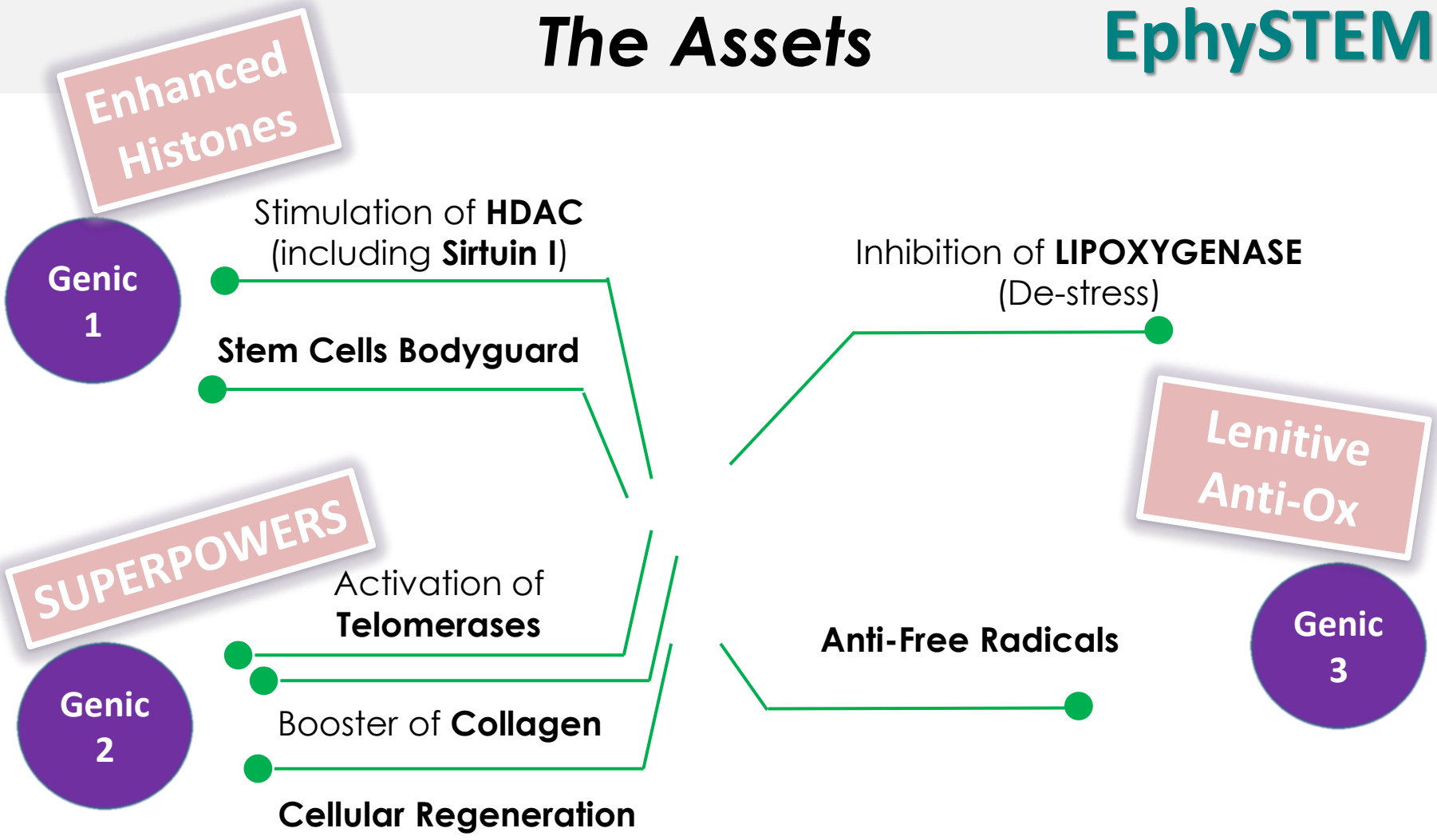
The Assets

EphySTEM



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Technical data sheet

EphySTEM

- INCI: **Propanediol, Dimethyl isosorbide, Caesalpinia sappan extract**

- CAS: 504-63-2, 5306-85-4, NA
- Einecs: 207-997-3, 226-159-8, NA
- IECIC Index N° 00006 (Propanediol), N° 06469 (Dimethyl isosorbide), N° 06469 (Caesalpinia sappan extract)

- APPEARANCE: pale yellow liquid (Room Temperature)

- FORMULATION: Water-soluble

- STORE CONDITIONS: 24 months in a ventilated area

- DOSE OF USE: 1 - 2%

- TOLERANCE:
  - Skin irritation: non-irritating
  - Eye irritation: moderate irritation
  - Phototoxicity: not phototoxic
  - Mutagenicity (AMES): not mutagenic & not pro-mutagenic
  - Sensitization (HRIPT): non-sensitizing

✓ ***No allaergen according to regulation CE 1223/2009***

References

EphySTEM

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EPHYLA
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