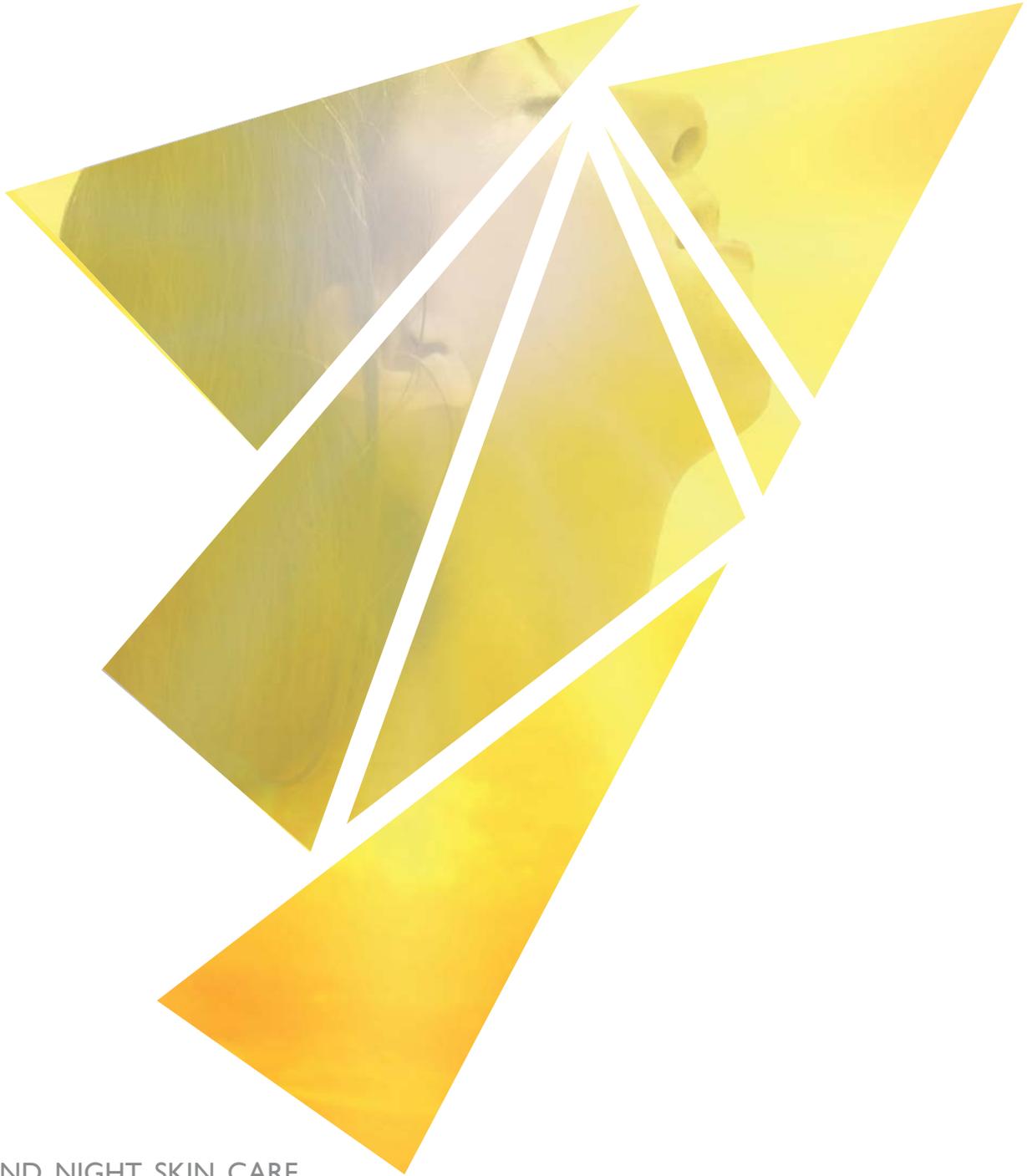


CHRONOCYCLIN[®]



DAY AND NIGHT SKIN CARE

TEMPORARY OR LONG-TERM CUTANEOUS DAMAGES:

OVERWORKED, TIRED, LACK OF SUN EXPOSURE, JET LAG

ANTI-AGING BENEFITS

SKIN AWAKENING:

STIMULATION OF CUTANEOUS NATURAL DEFENSES

VITAMIN D BIOTRANSFORMATION ACTIVATION

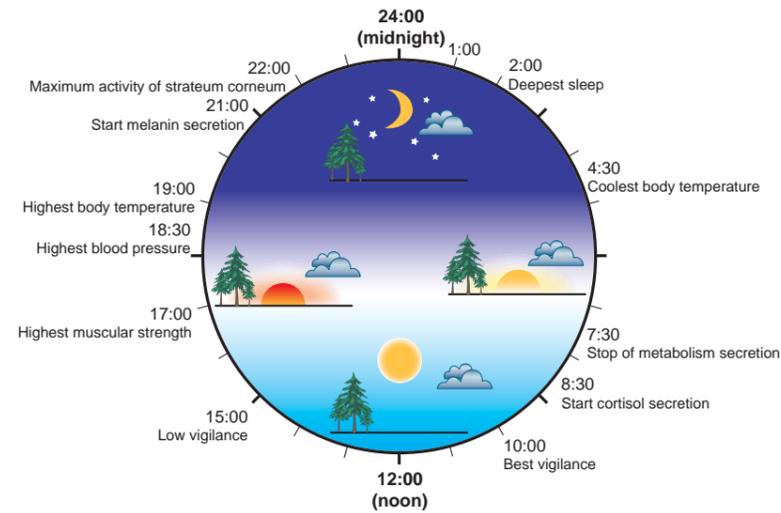
EXSYMOL
MONACO

Biorhythm circadian genes

Living organisms are regulated by an internal clock of 24 hours – the biorhythm – that controls circadian genes expression periodically.

The purpose of this rhythmic activation of the circadian genes is to initiate adapted metabolism and protein synthesis in function of the variable daily environmental constraints.

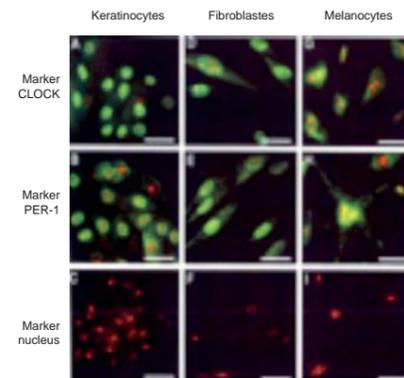
Sun exposure is one of the activator that synchronizes the biorhythm and therefore the adapted periodicity of the expression of the circadian genes towards the environment (seasons, jet lags...). The retina and the skin are the main receptors of the sun radiations.



Circadian genes and cutaneous physiology

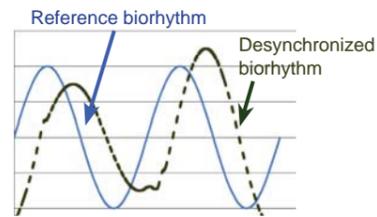
The physiological activity of the cutaneous tissue is closely controlled by the biorhythm. Cutaneous cells mainly focus on strengthening skin natural defense during daylight (resistance against U.V., pollution...), while they emphasize on regenerative metabolism at night.

Research studies have linked the activation of cutaneous circadian genes such as CLOCK and PERIOD-1 with cellular proliferative activities (keratinocytes, fibroblastes and melanocytes).



Irregular biorhythms and skin premature aging

Numerous factors can alter biological rhythms periodicity. Aging, seasons, variable sun exposure, fatigue, stress, insomnia and jet lag are responsible for small variations of the biorhythm that can accumulate. This irregularity of biorhythm is at the origin of variations of the activation cycles of circadian genes and therefore of the variations of the cutaneous physiological metabolisms.

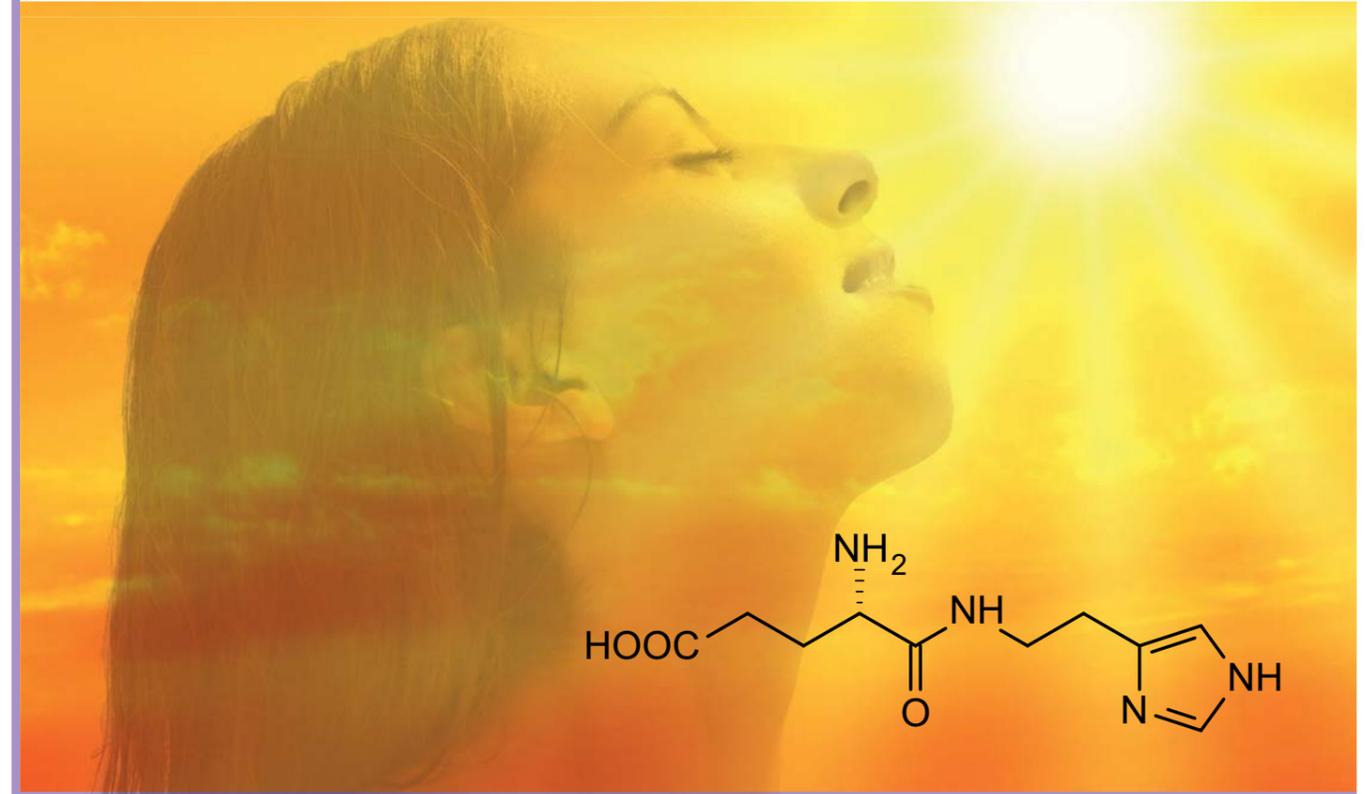


=> Variation of phases and amplitude of biorhythm

Consequences of the circadian genes activation fluctuation

The disorderliness of biorhythm is among the factors that can induce skin's premature aging. Indeed cutaneous cells physiological activity offering less adapted response to environmental conditions and can be responsible for:

- weakening of skin natural defenses,
- slowdown of night cell regeneration process,
- less efficient vitamin D bio-transformation (vit D participates to calcium incorporation and therefore could improve hydration via calcic channels).



INCI name: GLUTAMYLAMIDOETHYL IMIDAZOLE

CHRONOCYCLIN is an anti-aging chronopeptide that mimics sun exposure activation of the circadian genes.
CHRONOCYCLIN is an anti-aging active ingredient that optimizes skin physiological activities of defense and cells regeneration.

Skin benefits

- Optimized Vitamin D activity
- Resynchronized circadian rhythms
- Stimulated circadian genes



Cosmetic uses

- Day and night skin care
- Temporary or long-term cutaneous damages:
Anti-aging: Anti tiredness, anti-stress, lack of sun exposure, jet lag
- Skin awakening: Stimulation of cutaneous natural defenses
Vitamin D biotransformation activation

CHRONOCYCLIN

Applied research: *in vitro* results

CHRONOCYCLIN

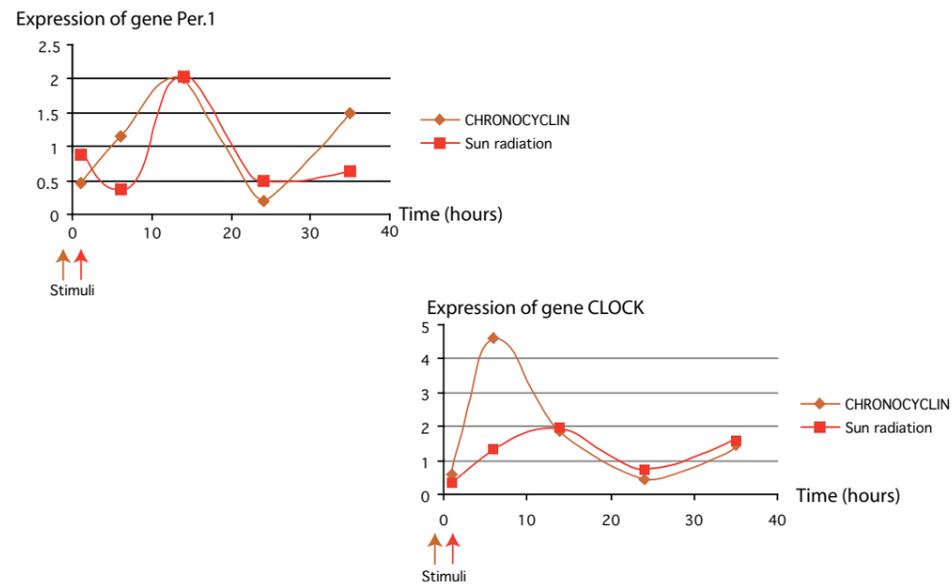
Applied research: *in vitro* results

Mechanism

CHRONOCYCLIN mimics the effects of sun exposure on circadian genes expression.

Synchronizing activity CHRONOCYCLIN

Our studies on reconstructed epidermis show that circadian genes such as CLOCK and PERIOD-1 are activated periodically following the biorhythm after initiation by UV radiation. The use of CHRONOCYCLIN on reconstructed epidermis in dark environment demonstrated that our product is able to imitate the UV signal and to induce circadian genes expression.



=> Effect of CHRONOCYCLIN on expression of genes Per I and CLOCK.

Skin benefits

CHRONOCYCLIN stimulates the natural periodicity of expression of the circadian genes in order to have the best correlation between cutaneous cells physiological activities and the environmental constraints.

Daytime benefits:

- Optimized natural cells defenses (keratinocytes and fibroblastes)
- Optimized enzymatic expression for Vitamin D bio-transformation.

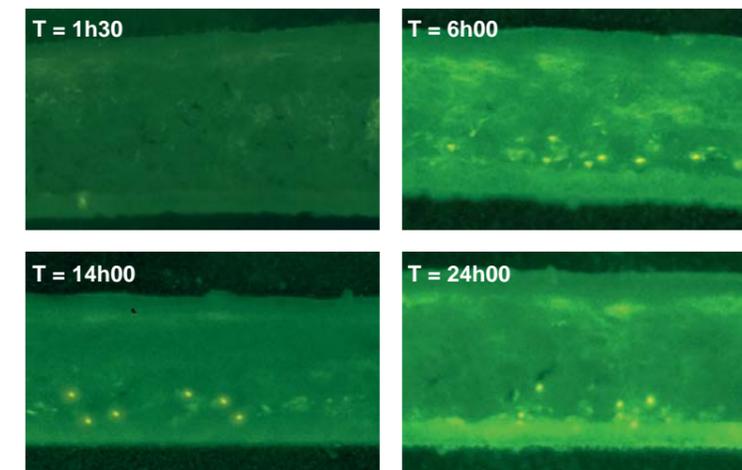
Nighttime benefits:

- Optimized cells renewal and regeneration (corneocytes and keratinocytes)
- Optimized microcirculation (detoxification and nutrient supply).

CHRONOCYCLIN anti-aging activity by circadian genes induction

Cellular proliferation and regeneration

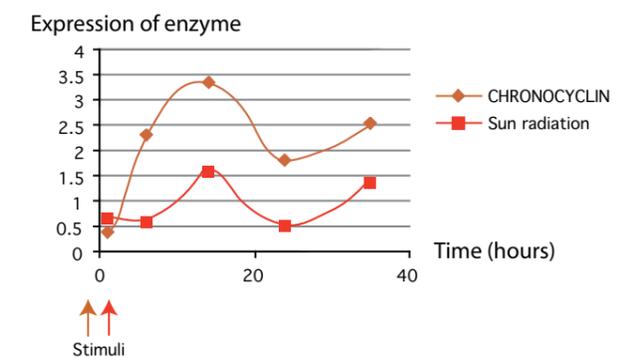
Our studies on reconstructed epidermis, placed in a dark environment demonstrated that CHRONOCYCLIN induces an equivalent periodic keratinocytes renewal to the one that can be observed when placed under sun exposure.



=> CHRONOCYCLIN periodic induction of keratinocytes proliferation.

Vitamin D photo-transformation activation

Circadian genes express the enzyme involved in Vitamin D photo-transformation CHRONOCYCLIN is able to reproduce the sun exposure periodic enzyme expression on a reconstructed epidermis placed in a dark environment.



=> Effects of CHRONOCYCLIN on Vitamin D enzyme expression.

CHRONOCYCLIN

Applied research on volunteers

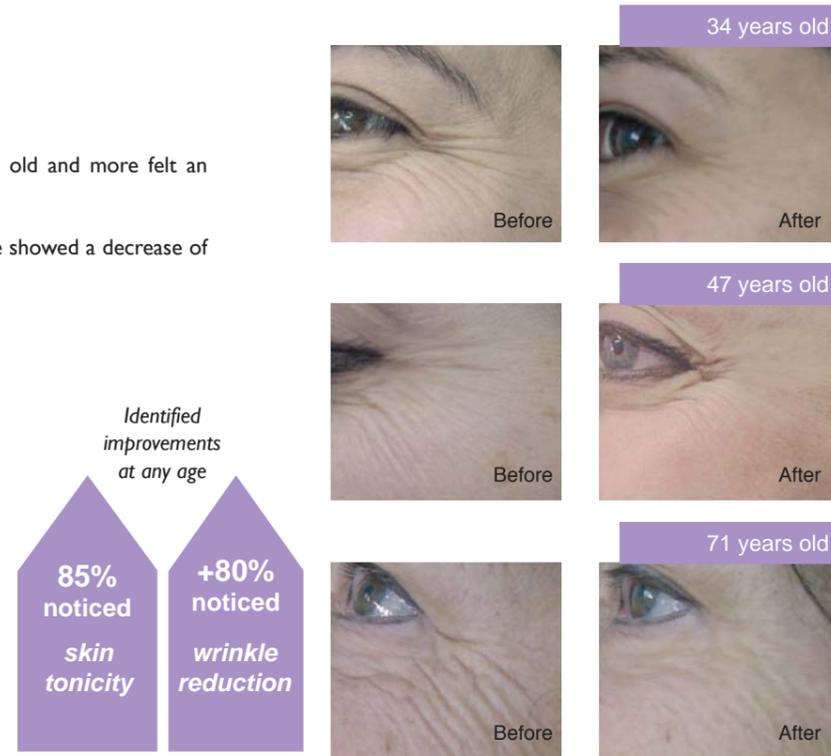
ANTI-AGING EFFICACY – IN VIVO TESTING

The clinical evaluation is undertaken on 54 women for a period of 4 weeks. The applied gel cream contains 0.2% CHRONOCYCLIN and 0.3% MS HC.
Scientific publication_1052

Wrinkles reduction

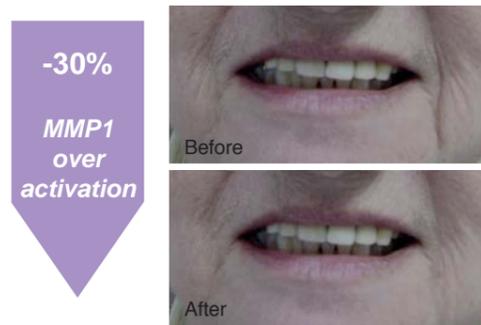
More than 85% of the volunteers, aged 40 years old and more felt an increase of their skin tonicity

80% of the volunteers aged 40 years old and more showed a decrease of their wrinkles.



MMP1 over activation inhibition

After 4 weeks treatment, an average 30% decrease of the MMP-1 over activation was observed.



ANALYTICAL COMPOSITION

L-Glutamyl-amidoethylimidazole 1%
Preservative 0.4%
Water (sqf) 100%

TECHNICAL CHARACTERISTICS

Colorless liquid.
pH: approx 5.
Density at 20°C: approx 1.0.
Soluble in water, alcohol and glycols.

PRESERVATIVE

Different preservative systems are available in order to fit with your requirements. Among these versions, we try to develop as often as possible preservative free ingredients. Please contact us for details about the available versions.

TOLERANCE STUDY

CHRONOCYCLIN does not show any toxicity. Tolerance studies were undertaken by *in vitro* alternative methods (cell culture and reconstructed epidermis) and on volunteers. Details on the tolerance studies can be found on the product MSDS.

FORMULATION

CHRONOCYCLIN is a stable solution.
Use level: 0.2 to 1%
Incompatibilities: no particular incompatibilities.

AVAILABILITY

CHRONOCYCLIN is available in 1, 5 and 30 kg drums.

EXSYMOL
MONACO

4 avenue Albert II - MC 98000 MONACO
Tel. : +377 92 05 66 77 - Fax : +377 92 05 25 02
www.exsymol.com



P8_1268GB1609E