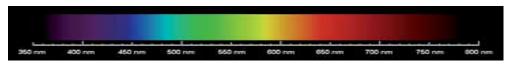


Human skin is the primary target organ for sunlight.

Solar radiations, especially UV and IR, are the major responsible factors for premature skin aging. UV (main focus of research in terms of photo-aging) only account for 7% of the total amount of solar energy reaching the human skin, while IR count for more than 50%.

However, it needs to be taken in consideration that UV energy level is much higher than IR's and therefore more noxious.



The ray wavelength, (UV=290-400nm, IR=760-4000nm) determines which skin compartment (epidermis, dermal-epidermic junction or dermis) will be principally targeted by "toxic energies" that might, in turn, generate various free radicals.

The accumulation of cellular and/or metabolic alterations can lead to the emergence of skin clinical damage such as dehydration, wrinkles and/or aging spots.

### IR-induced skin damages

IR-A	IR-B and -C
Affect dermal collagen balance (by targetting the mitochondria)	Affect the upper skin layers (mainly epidermis)
Up-regulate MMP-1 expression (responsible for collagen degradation)	Slow down keratinocyte proliferation rate (epidermal renewal)
Induce cell death (apoptosis)	

### **UV-induced skin damages**

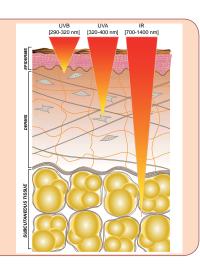
UV-A	UV-B
Affect the dermis and the epidermis	Affect mainly the epidermis
Generate structural proteins cross-linkage and/or degradation	Generate DNA alterations in keratinocytes (Sunburn Cells)
Alterate cell metabolism (DNA mutation)	Slowly participate to structural protein's alterations of the dermis

Active photoprotection against sun radiations-induced alterations requires an active ingredient able to complement sunscreen passive photoprotection.

Indeed, as efficient as sunscreens can be, toxic species still can generate damages in any compartment of the skin (location is determined by rays wavelengths).

Generated toxic species can be found in any skin compartment. They can be of the following types:

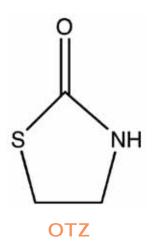
- ROS, Reactive Oxygen Species
- Q RNS, Reactive Nitrogen Species
- RCS, Reactive Carbonyl Species (toxic aldehydes)





#### Designed for performance:

- P Bio-availability
- P Broad spectrum anti-oxidant activity
- P Photoconversion into an active compound: taurine
- P Safe byproducts release after scavenging



#### **INCI** name: **OXOTHIAZOLIDINE**

OTZ 10 (PRO-TAURINE) is a 10% dilution of an optimized (predictive molecular design) photo-protective compound (OTZ).

OTZ 10 (PRO-TAURINE) displays antioxidant and electrophilic scavenging properties. It has demonstrated its ability to detoxify any skin layer, hence limiting UV and IR-induced cutaneous damages.

#### Skin benefits

#### Protection from IR and UV-induced alterations

Large scope of scavenging activity: ROS, RNS, RCS

DNA protection (epidermal and dermal cells)

#### Control of the premature skin aging process

Limits the risk of apoptotic cells (such as Sunburn Cells)

Down-regulates MMPI expression (responsible for collagen degradation)

#### Preservation of the skin compartments quality

**Epidermis** 

Dermal-epidermic junction (DEI)

**Dermis** 

#### High bio-availability through the cutaneous tissue

Skin penetration (epidermal and dermal compartments)

Cell penetration

#### Control of the inflammatory response

Benefits of its detoxification efficacy

### **Cosmetic Applications**

#### **Anti-photoaging**

Prevention of skin structural collapse: anti-wrinkles

Sun care: tissue detoxification, epidermal reinforcement

Compatible with sensitive skin: global control of skin inflammation +

intracellular production of taurine for osmotic balance

#### **CUTANEOUS BIO-AVAILABILITY**

(IFSCC MAGAZINE, VOL. 11, N°2/2008)

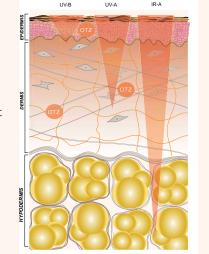
Requirements: Access to epidermis (UV-B, -A and IR)
Access to dermis (UV-A and IR-A)

### Skin penetration (extracellular scavenging)

Primary objective for a global photo protective compound => fast absorption

- OTZ permeability constant: 5 times higher than caffeine.
- OTZ remarkable diffusion: global protection of the different skin compartments.

OTZ  $Kp = 6.1 \mu m/h$ Caffeine  $Kp = 1.2 \mu m/h^{1}$ 



### Cell penetration

(intracellular scavenging)

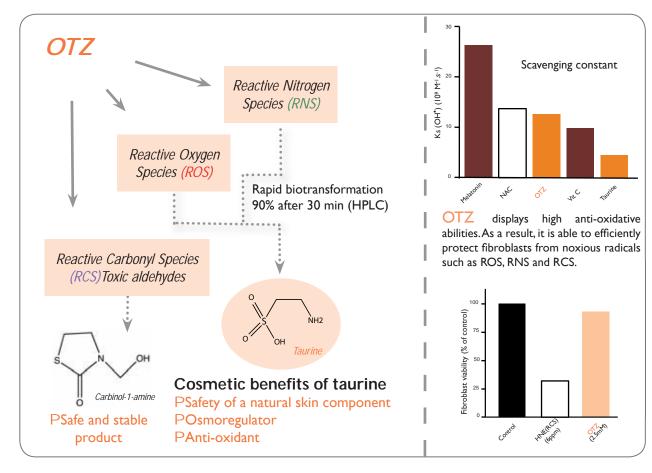
Mostly important as free radicals are also produced inside the cells

• By monitoring intracellular ROS formation after UV exposure, flow cytometry study showed that OTZ was able to reach the intracellular compartment, hence providing a 4 fold increased UV protection.

#### **MULTI-LEVEL SUPER SCAVENGER**

(IFSCC MAGAZINE, VOL. 11, N°2/2008)

Requirements: Broad antioxidant activity spectrum
Safe byproducts after scavenging



#### IR (INFRA-RED)

#### -INDUCED DAMAGES PROTECTION

(IFSCC MAGAZINE, VOL. 13 (2010), 105-112)

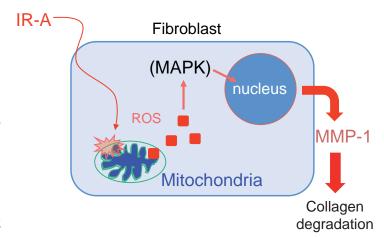
#### IR and skin architecture collapse

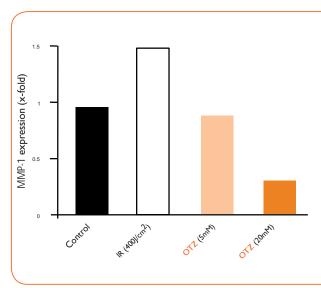
The UV and IR impact on the dermal compartment (essentially structural protein degradation) leads to premature skin aging. Unlike UV-A, once IR reach the dermis, they do not have a direct impact on the extra cellular matrix.

IR mainly target fibroblast's mitochondria, inducing the expression of proteins kinase (MAPKs) that can lead to MMP-I production and collagen degradation.

This mechanism was identified by in vitro studies where a MMP-I over-expression was observed after exposure to IR stress (P. Schroeder et al, IID, 2008).

Requirements: Preserving cell metabolism Preserving collagen biosynthesis





#### Intracellular scavenging of IR-induced ROS

=> Protects from collagen degradation

Pre-incubation of human dermal fibroblasts with OTZ showed that OTZ has strong detoxifying abilities (scavenging of mitochondrial ROS). This protective effect is reflected by the decrease in MMP-1 expression in response to IR exposure.

Furthermore, OTZ has no effect on TIMP-1 expression (an endogenous inhibitor of MMP-1). This suggests that OTZ leads to a direct inhibition of MMP-1 expression

#### Global skin protection against IR-induced damages

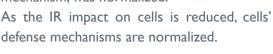
In response to IR exposure, several genes expression are altered. Treatment with OTZ normalized the expression of these genes.

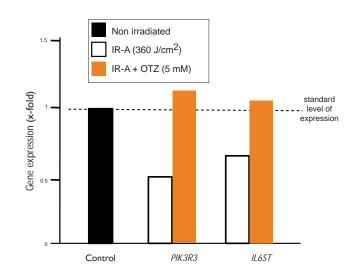
PIK3R3 expression, involved in tissue quality, was normalized.

These results demonstrate OTZ abilities to reduce the IR impact on the skin metabolism.

IL6ST expression, involved in stress defensive mechanism, was normalized.

defense mechanisms are normalized.





**UV-A (ULTRA-VIOLET)** 

-INDUCED DAMAGES PROTECTION (IFSCC MAGAZINE, VOL. 13 (2010), 105-112)

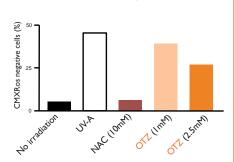
Requirements: Preserving fibroblast metabolism Preserving skin architecture

Fibroblasts mitochondrial protection

#### Fibroblasts DNA protection

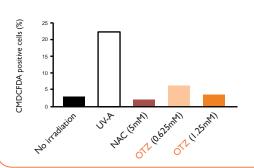
# Nbr of apoptotic fibroblats (% of control) FAC (10nm) OT LOSIMA

Cytometry studies demonstrated OTZ abilities prevent mitochondrial and DNA damages. Used in a preventive mode, OTZ almost counteracts any cell's effects of UV exposure.



#### Optimized fibroblasts survival

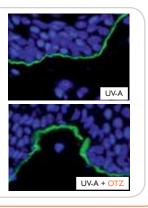
Preventive treatment



#### Skin protection

Irradiated (UV-A 15]/cm<sup>2</sup>) real human skin treated with OTZ

- + 150% Epidermal cell proliferation
- + 50% DEI resistance
- + 75% Dermal metabolism
- 80% Tissue inflammation
- 75% MMP-I expression



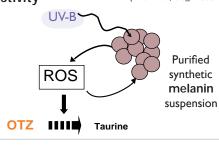
#### **UV-B (ULTRA-VIOLET)**

-INDUCED DAMAGES PROTECTION

(IFSCC MAGAZINE, VOL. 13 (2010), 105-112)

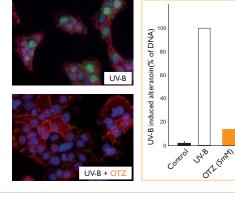
Requirements: Preserving epidermal natural defense Supporting skin first protective layer

#### Supporting melanin natural defense activity (EXSYMOL, CO\_1280GB)



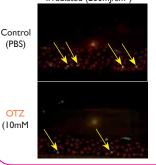
OTZ has the ability to cooperate with melanin (a natural solar radiation absorber) in order to keratinocytes' DNA and therefore, to prevent UV-induced apoptosis.

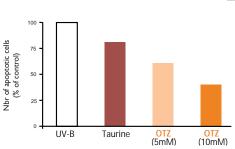
#### Model for keratinocytes DNA protection



### Prevention against apoptotic cells

Protect skin first defense compartment Irradiated (200mJ/cm<sup>2</sup>)





Treatment with OTZ reduces the UV-induced DNA damages and therefore the resulting apoptotic cells as observed on human reconstructed epidermis measured using the TUNEL assay (an apoptosis specific assay that dyes in yellow (->) any apoptotic

## **ANALYTICAL COMPOSITION**

Oxothiazolidine 10% (w/w)
Butylene glycol 8.18%
Sodium benzoate 0.6%
Water (sq)100%

### TECHNICAL CHARACTERISTICS

Limpid to slightly opalescent liquid Colorless to slightly yellow  $pH\approx 5.5$  Density at 20°C  $\approx$  1.0

#### **PRESERVATIVES**

Different preservative systems are available in order to fit with your requirements. Please contact us for additional details about the available versions.

## TOLERANCE & TOXICITY STUDIES

OTZ-10® is perfectly tolerated. Tolerance and toxicity studies were performed using both in vitro (cell culture and reconstructed epidermis) and in vivo (human volunteers) methods.

#### **FORMULATION**

Advised doses: min 0.2%. pH for formulation: between 3 and 9. Incompatibilities: No particular formulation restriction.

#### **AVAILABILITIES**

OTZ 10 is available in 1, 5, 30 and 60 kg drums.



