



ACTIVATEUR DE BRONZAGE  
TANNING BOOSTER

*THALITAN*

# THALITAN

A PRO-TANNING ACTIVE INGREDIENT

TO TAN BETTER WITH LESS SUN  
AN OPTIMIZED, ENHANCING TAN

THALITAN is an original oligosaccharide.

Magnesium and manganese were chelated with a marine-derived oligosaccharide.

This oligosaccharide was obtained through enzymatic depolymerization of a polysaccharide extracted from the brown algae *Laminaria digitata*. It is composed of gluconic and mannuronic acid.

This brown algae is called Tali in the Breton language in Brittany, France.

The body needs only a low dose of sunlight to benefit from its positive effects. The more the skin is exposed to sunlight, the more damage UV rays can cause.

THALITAN helps stimulate tanning while protecting the skin from the harmful effects of the sun.

RESULTS : REINFORCED TANNING

PROTECTION AGAINST THE DAMAGING EFFECTS OF UVA & UVB

COMBATS PREMATURE SKIN AGING

ITS MODE OF ACTION

## PRO-TANNING ACTION

- Stimulation of tyrosinase
- Stimulation of melanogenesis
- Increase of melanin synthesis
- Bond with the endothelin receptor to promote melanin synthesis

## PHOTOPROTECTION

- Anti-free radical protection
- Protection of cellular proteins against pro-free radical attack:  
UVA and UVB rays.UVA & UVB.
- DNA protection:
  - Inhibition of apoptosis caused by UVB rays
  - Inhibition of the expression of the nuclear protein p53, a specific marker of cells damaged by UV rays
  - Prevention of the formation of “sunburn” cells

## IMMUNOPROTECTION

- Protection of immunocompetent cells of the dermis and epidermis from the harmful effects of UVB and UVA rays.

### THE SUN AND ITS BENEFITS

The sun is synonymous with well-being. It is beneficial for our morale as it promotes the production of endorphins. It also helps set Vitamin D and improves the condition of the skin, notably in the case of psoriasis and eczema.

### THE SOLAR SPECTRUM:

The sun emits radiance composed of ultraviolet, visible light and infrared rays. The longer the ultraviolet wave, the more the UV rays penetrate deeply into the skin and cause damage. There are three types of ultraviolet rays:



UVC rays are the most damaging ultraviolet rays but they are absorbed as soon as they pass through the highest regions of the ozone layer.

UVB rays represent 5% of solar UV rays that reach the earth's surface. They are very energetic and stimulate pigmentation. However, they also cause sunburns and DNA damage.

UVA rays represent 95% of solar ultraviolet rays that reach the earth's surface. They penetrate deep in the skin down to the dermis, causing free radicals to form. This damages the DNA.

An epidermis exposed to UVB and UVA rays thickens and "sunburn cells" appear. The expression of the p53 gene increases. These cells also inhibit the immune functions of Langerhans cells. This reduces the skin's defense mechanisms.

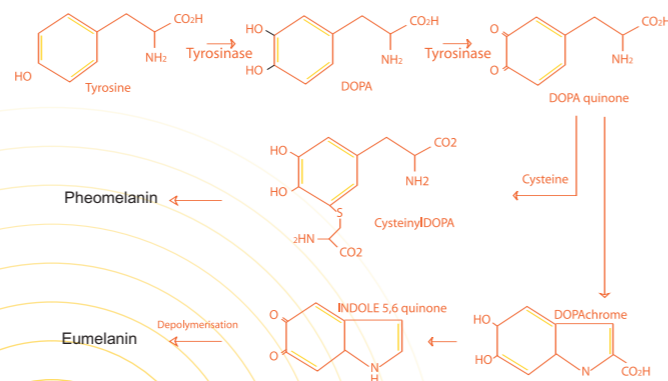
UVA rays are thus largely responsible for premature skin aging.

### TANNING

All the same, tanning is one of the skin's protective mechanisms. It is a response that adapts to photoinduced aggression.

Melanocytes, localized in the basal layer of the epidermis, produce melanin. This is a pigment that colors the skin and hair.

This synthesis is caused by an amino acid, tyrosine, under the action of an enzyme called tyrosinase. The synthesized melanin builds up in vesicles called melanosomes. There are two groups of melanin: eumelanin, which is brown and black, and pheomelanin, which is an orange-yellow color.



### THE SUN AND ITS DAMAGE

While it is wonderful to enjoy the sun, prolonged exposure can have harmful effects on the health.

The sun can also be an enemy and damage the skin.

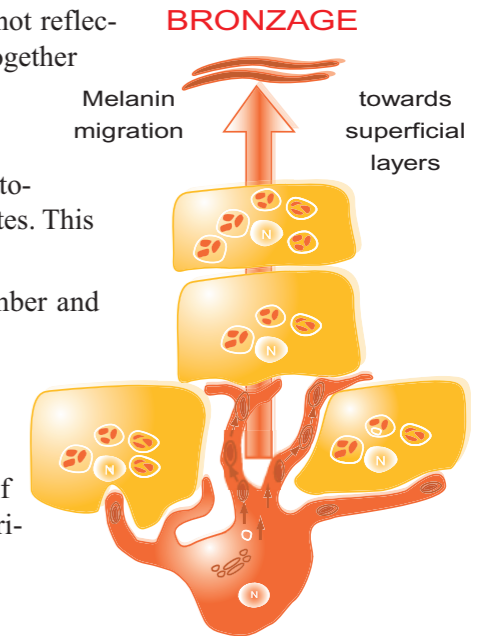
Melanin plays a photoprotective role. It absorbs rays that are not reflected by the skin and thus protects cellular DNA by grouping together around the nuclei.

There is about 1 melanocyte per 40 keratinocytes.

The transfer of melanin to the keratinocytes occurs on the cytoplasmic extensions of the melanocytes, which are called dendrites. This transfer is heightened under the effect of UVB rays.

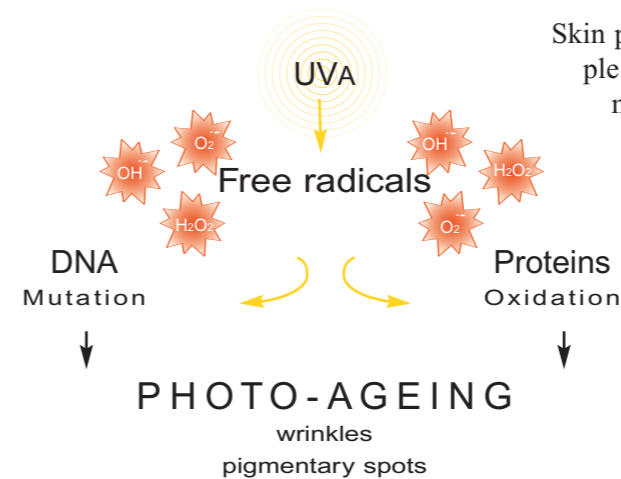
Sun exposure stimulates melanogenesis and increases the number and size of melanocytes.

UV rays also stimulate the secretion of endothelin by the keratinocytes. Endothelin acts like a messenger by attaching itself to a specific receptor type B located on the melanocytes. When attached to its receptor, endothelin stimulates the division of melanocytes and increases the number and length of the dendrites. It also stimulates the synthesis and activity of tyrosinase.



The body only needs a small dose of sunlight to benefit from its positive effects. The more exposed the skin is to sunlight, the more damage UV rays may cause.

### CAUSE OF PREMATURE AGING



Skin photoaging is characterized by skin that is less supple and radiant. Gradually, the complexion appears more uneven. The skin seems darker in certain places and dark spots may develop. In addition to natural expression lines, other fine lines may form.

These phenomena are the result of the cumulative and synergic effect of UVB and UVA rays, which promote the formation of free radicals. Free radicals then disrupt the skin's cellular mechanisms.

- DNA damage appears.

- Immunocompetent cells, called Langerhans cells, lose their immunoprotection abilities. These cells are responsible for recognizing foreign bodies. Yet, they have more difficulty identifying these foreign bodies, which are only partially eliminated by the immune system.

Tanning gradually fades away and disappears after a few weeks, but the harmful effects last and can build up over time.

THALITAN is a solution for controlled tanning.

# || activateur de bronzage

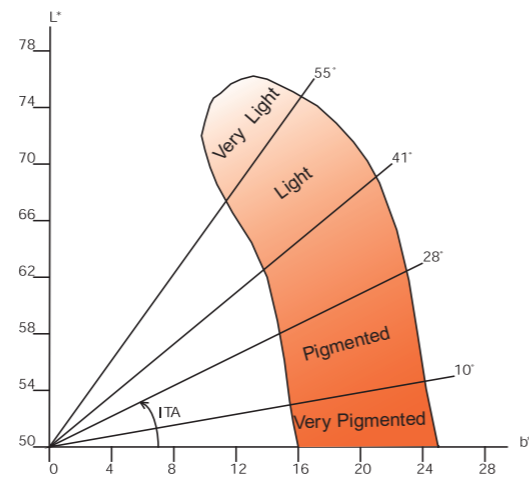
## *in-vivo test*

Skin color was measured with a Chromameter. This device defines a luminous parameter, L\*, clarity from dark to pale; and a chrominance factor: b\*, the range of blues to yellows.

These parameters have been designed to measure the Individual Typological Angle.

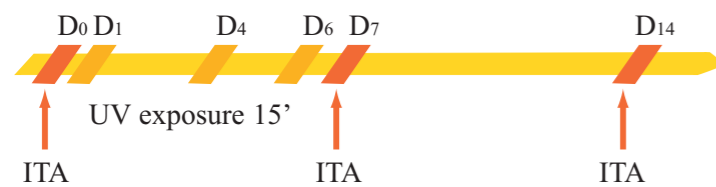
$$ITA = [\text{Arc tan}((L^*-50)/b^*)] \times 180 / \pi$$

The ITA defines the degree of an individual's skin pigmentation. The lower the ITA, the more pigmented the skin.



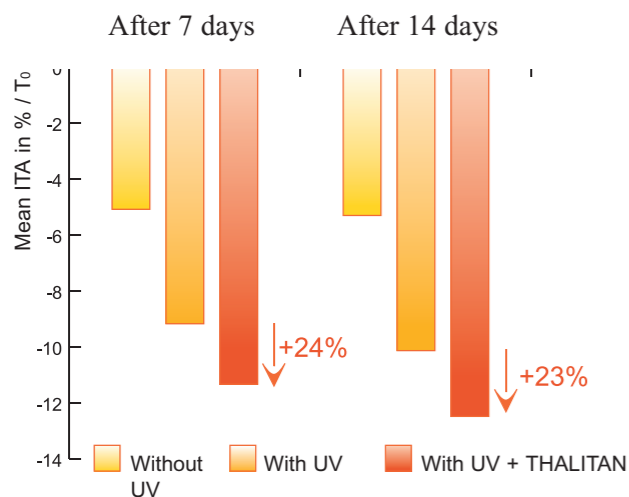
Study on 11 volunteers with phototype III. Each subject is his or her own control subject.

Twice-daily application of a cream containing 2.5% THALITAN for 14 days.



UV sessions (low doses) with a tanning bed for 15 minutes, the first, fourth and sixth days.

Measurement of skin color on the three zones on the 7th and 14th days.



After UV exposure, tanning was noticed.

After 7 and 14 days, the ITA diminishes significantly. THALITAN thus notably improves tanning.

Moreover, after the UV sessions are over, the tanning effect is long-lasting. The tan is preserved.

The THALITAN product at 2.5% helps activate tanning induced by UV exposure.

# || activateur de bronzage

## *in-vitro test*

### ● Stimulation of tyrosinase activity

#### Enzym

Tyrosinase was incubated at 37°C for 2 hours with tyrosine (0.015%, i.e. 0.8mM). The product of this reaction is analyzed by measurement of the optical density at 475 nm. Stimulation of tyrosinase activity is noted when optical density increases.



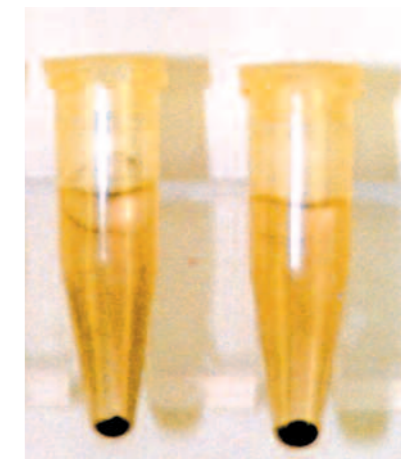
THALITAN statistically increases tyrosinase activity by 79%.

#### Explant de peau

Then, the enzymatic activity of endogenous tyrosinase was demonstrated on human skin explants through the enzymatic reaction of DOPA oxidation.

L-DOPA, the substrate of tyrosinase, was added to the explant incubation medium. This led to the formation of a black melanin pigment.

In the presence of hydroquinone [0,05M], an inhibitor of tyrosinase activity, color disappeared.



Without the substrate L-DOPA, the quantity of extracted pigment is insignificant.

In the presence of L-DOPA[0,005M], the quantity of pigment is visible.

[0.2%] [1%]  
In the presence of THALITAN[0.2%], [1%], the concentration of synthesized pigment increases with a dose-dependent effect.

#### Mélanocytes

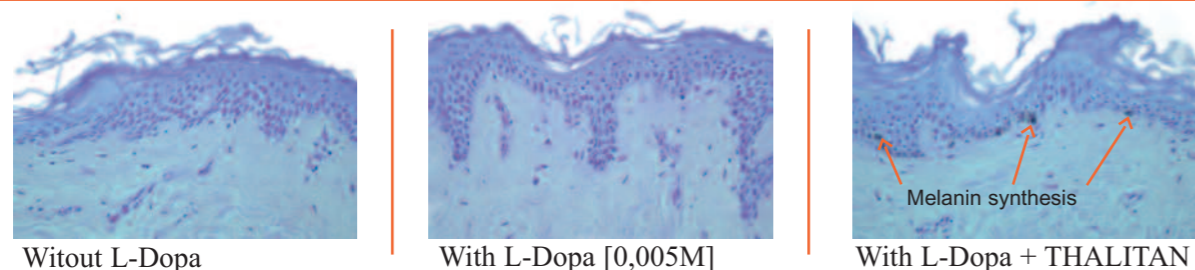
THALITAN [0,001%] was added to a culture medium of isolated human melanocytes. After 10 days, the melanin pigments produced by the melanocytes were extracted with a Soluene solution. The optical density of the solution was measured by spectrophotometry at 405 nm.

Kojic acid [250µM], used as a negative control, reduced melanin synthesis by 20%, while alpha MSH[100nM], used as a positive control, increased melanin synthesis by 13%.



THALITAN [0,001%] increases melanin synthesis in human melanocytes by 27%.

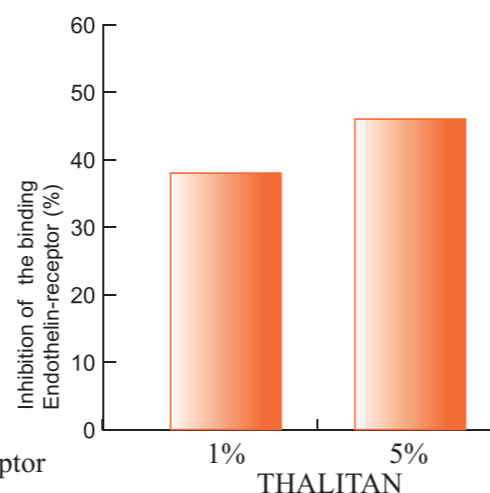
This same experiment was renewed on human skin explants with THALITAN.



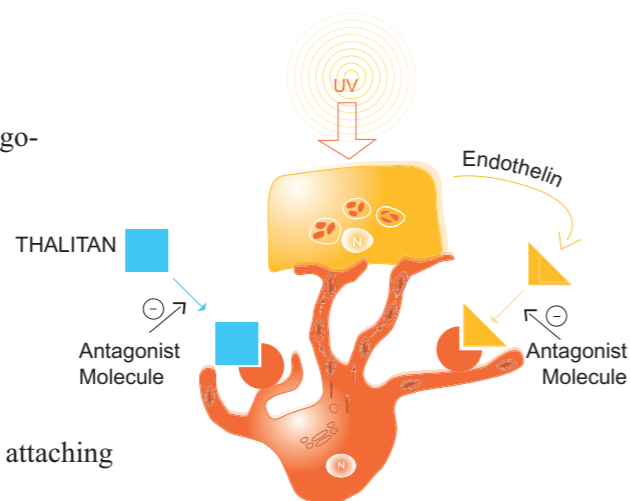
THALITAN [0,2%] increases melanin synthesis in human melanocytes by 84%.

### “Endothelin-like” effect

Radiomarked endothelin was incubated for 2 hours at 37°C in the presence of THALITAN in different concentrations, with CHO cells that express the endothelin receptor type B on their surface. The fixation of endothelin on its receptor was measured by a scintillation counter after washing. This specific link was calculated by measuring the difference between the total links and the non-specific links determined in the presence of excess cold endothelin at 0.1µM.



THALITAN acts like a ligand between the receptor and endothelin.



Moreover, THALITAN was shown to have an agonist action.

An activity test was carried out. The addition of THALITAN increases this endothelin activity.

The addition of an endothelin antagonist reduces it.

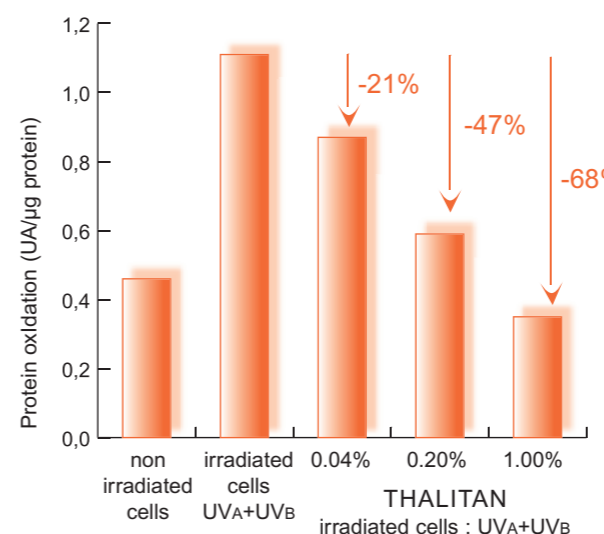
UV rays naturally stimulate the secretion of endothelin, which plays a role in tanning by attaching itself to its receptor.

THALITAN provides an activity similar to endothelin WITH or WITHOUT UV.

## photoprotection

UV rays damage the cellular structure and DNA of keratinocytes. These damaged cells trigger their own programmed cellular death, i.e. apoptosis. These non-functional cells are then eliminated.

### Protection of cellular proteins.



UV rays cause the oxidation of cellular proteins, which changes their structure.

Human fibroblasts were incubated for 24 hours with THALITAN, then exposed to UVA + UVB (325mJ/cm<sup>2</sup>).

After 4 hours of incubation, the proteins were extracted in order to measure their oxidation rate.

These oxidized proteins contained carbonyl protein derivatives that, in the presence of dinitrophenylhydrazine, could be revealed via anti-DNP antibodies.

THALITAN protects cellular proteins from oxidation caused by UVA and UVB rays.

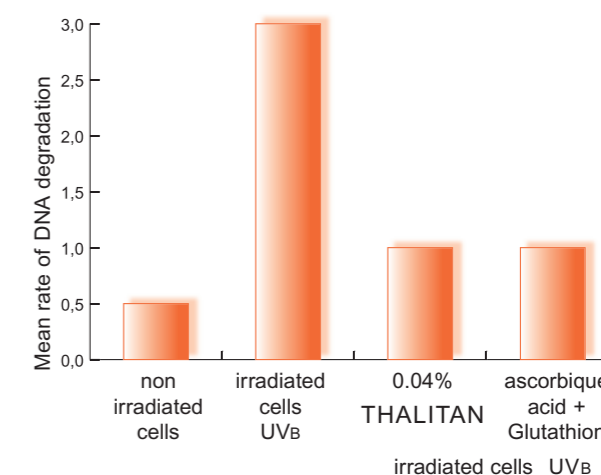
### DNA protection

#### TUNEL method

This method shows the fragmented DNA of cells undergoing apoptosis.

Human fibroblasts were incubated for 24 hours with THALITAN and then exposed to UVB (325mJ/cm<sup>2</sup>). The positive control was composed of ascorbic acid [50µg/ml] and Glutathione [50µg/ml]

The TUNEL method detects fragmented DNA in cells undergoing apoptosis. Fragmented DNA was detected by a fluorescent component of biotinyl DNA obtained with terminal deoxynucleotidyl transferase (TdT).



THALITAN protects cells from DNA fragmentation caused by UV rays.

# photoprotection

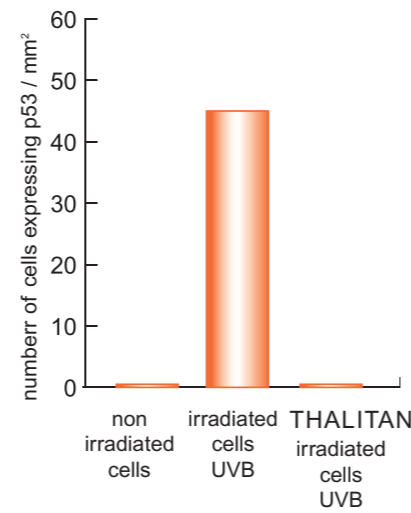
## p53 protein

P53 is a nuclear protein produced by the cells when DNA is damaged in order to protect the integral structure of the genome. Composed of 3 subunits, this protein plays 2 roles: it either stops the cellular cycle to allow for DNA repair when possible or it triggers cellular suicide (apoptosis) when the damage is irreparable.

Numerous studies show that the rate of p53 nuclear proteins increases after exposure to UVB rays (Ueda-1996/Tyrell-1996).

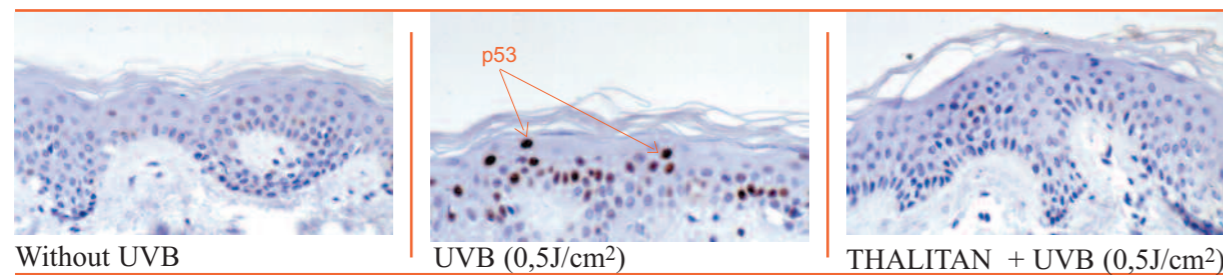
THALITAN was applied in the form of an emulsion to the surface of human skin explants exposed to UVB rays (0,5J/cm<sup>2</sup>).

After 24 hours, cells expressing p53 were detected by immunomarking with a monoclonal antibody and then observed under a microscope.

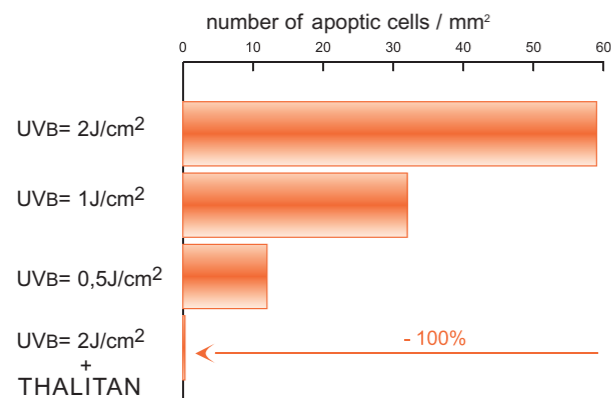


When DNA is not damaged, the p53 protein is not expressed. A reduction of p53 thus shows DNA protection from damage caused by UV rays.

THALITAN protects DNA from damage caused by UV rays.



## “sun burn cells”



We also see an overexpression of p53 associated with the formation of “sunburn cells”(Brash-1996/Griffits-1998). These are keratinocytes in apoptosis, characterized by fragmented DNA and a loss of cohesion between the keratinocytes.

THALITAN was applied in the form of an emulsion to the surface of human skin explants exposed to UVB rays (2J/cm<sup>2</sup>). After 24 hours, cells in apoptosis were identified by the coloring of their cytoplasm with eosin.

THALITAN protects the epidermis against the appearance of “sunburn cells”, the proof of cellular damage caused by exposure to UVB rays.

# immunoprotection

Langerhans cells make up 2% to 5% of the cellular population of the epidermis. They feature long dendritic extensions that stretch between the keratinocytes.

These are the “guards” of the immune system. They are able to induce and adapt the defense responses of the body.

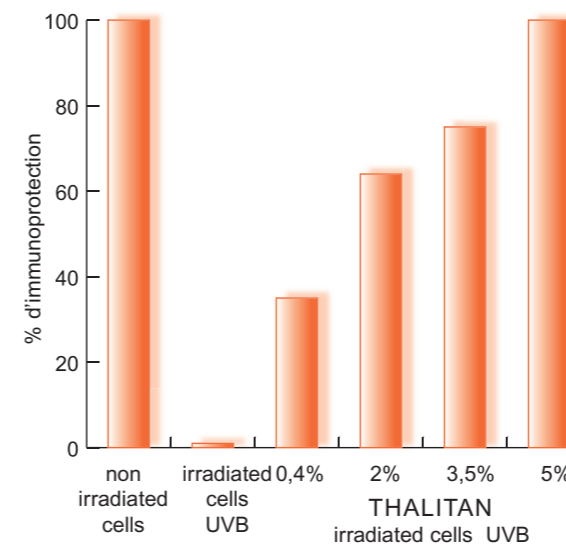
These mobile cells are responsible for immunization against the antigens present in the skin.

Their number diminishes after exposure to UVB rays (Murphy. - 1993) and to UVA rays (Iwaii. -1999). This disappearance of the skin’s immune functions is also a sign of skin aging.

## UVB and UVA

Langerhans cells express the CD1a molecule on their surface, which makes it possible to detect them via immunomarking using an anti-CD1a antibody.

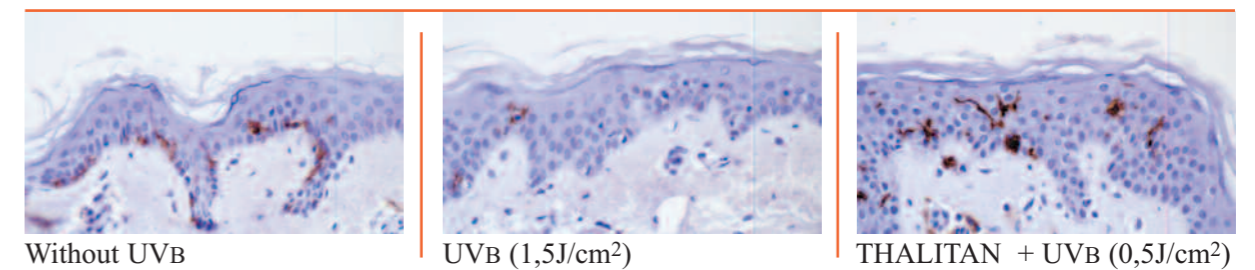
The immunoprotective properties of THALITAN were evaluated on skin explants exposed to UVA and UVB rays.

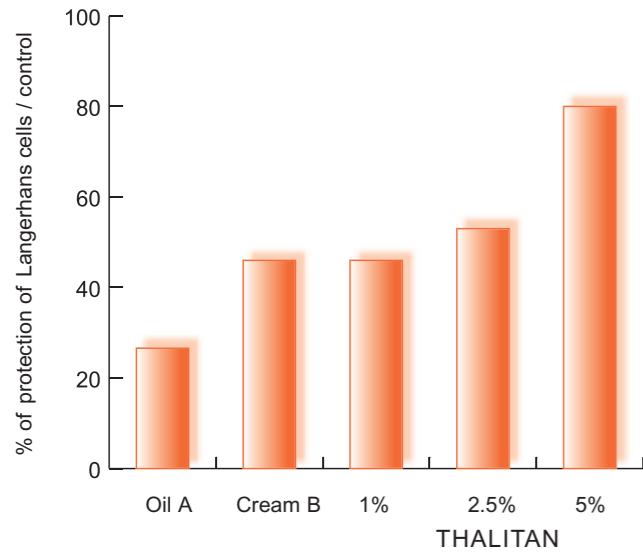


## UVB

THALITAN was added twice a day to the surface of human skin explants for 4 days, then irradiated with doses of UVB of 1.5J/cm<sup>2</sup>.

THALITAN [5%] maintains the integral structure and functions of Langerhans cells irradiated with UV rays.





### UVA

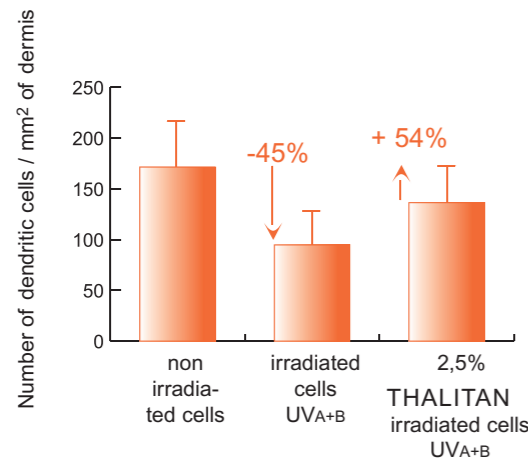
THALITAN, formulated at 5% in an emulsion, was applied to the surface of human skin explants.

The explants were irradiated with UVA doses of 6J/cm<sup>2</sup> (365nm spectrum), 30 minutes after application. The Langerhans cells were then counted after 24 hours of culture.

Two sun care products containing UVA filters (2% oxybenzone) were tested in the same conditions:

- a sun care oil: oil A
- a sun care cream: cream B

THALITAN [5%] protects 80% of Langerhans cells irradiated with UVA rays.



The dendritic cells of the dermis are the principal immunocompetent cells of the dermis. They play the same role as the Langerhans cells in the epidermis.

These cells can be detected by immunomarking using anti-DC-SIGN antibodies.

THALITAN was tested at 2.5% on the surface of human skin explants irradiated with UVA doses of 1J/cm<sup>2</sup> and UVB doses of 1J/cm<sup>2</sup>.

THALITAN protects the immunocompetent cells of the dermis from the destructive effects caused by UVB and UVA rays.

### NOMENCLATURE

INCI USA	INCI EUROPE	N° CAS	N° EINECS
Water	Aqua	7732-18-5	231-791-2
Hydrolyzed algin	Hydrolyzed algin	73049-73-7	/
Magnesium sulfate	Magnesium sulfate	7487-88-9	231-298-2
Manganese sulfate	Manganese sulfate	7785-87-7	232-089-9

### PRESERVATIVES (2 versions)

THALITAN : Propylene glycol + Chlorphenesin + Phenoxyethanol + Methylparaben.  
 THALITAN P : Phenoxyethanol.

### PHYSICO-CHEMICAL SPECIFICATIONS

Aspect : Limpid liquid to cloudy liquid with deposit  
 Color : Yellow – honey  
 Odeur : Characteristic  
 pH (20° C) : 5,00 - 6.00  
 Refractive index (20° C) : 1,334 - 1,350  
 Relative density (20 °C) : 1,050 - 1,070  
 Dry residue (2g /105°C/2 h) : 5.00 - 10.00%

### BACTERIOLOGICAL SPECIFICATIONS

Total mesophilic aerobic germ: < 100 germs/g  
 Yeast and mould: < 100 germs/g  
*Pseudomonas spp* : Absence in 1g  
*Staphylococcus aureus* : Absence in 1g  
*Candida albicans* : Absence in 1g

### TOLERANCE

- NON IRRITANT FOR EYES : Classe I - Slightly irritant (by neutral red release method)
- NON IRRITANT FOR SKIN: Slightly irritant - tested on rabbits in 1998.
- NON MUTAGENIC : Genotoxicity on sur *Salmonella typhimurium* (Ames & coll.)
- NON PHOTOTOXIC : Patch test on 10 volunteers.
- HYPOALLERGENIC : Repeated epicutaneous applications on 100 volunteers.

### FORMULATION

- Recommended concentration : 1 - 2,5%
- Incompatibility : [ethanol] > 10% may create precipitate.
- Storing : Keep closed in original packaging at moderate temperature (15 to 25°C).
- Conditions for incorporation : At the end of formulation (T<35° C).

### PRO - TANNING CREAM

	Trade name	INCI USA	%
Phase A	Eau	Water	64,80
	Glycérine	glycerin	3,00
	NaCl	Sodium Chloride	2,00
Phase B	DC 5200	Lauryl PEG/PPG - 18/18	2,00
	DC 9040	Cyclomethicone and Dimethicone crosspolymer	10,00
	DC 345	Cyclomethicone	5,00
	Arlamol HD	Isohexadecane	3,00
	Parleam	Polydecene	3,00
	Arlamol E	PPG-15 Stearyl ether	1,00
	Phenonip	Phenoxyethanol and methylparaben and ethylparaben and propylparaben and isobutylparaben and butylparaben	1,00
Phase C	Cegermil	Zea Mays and glycine soja and Helianthus Annuus	2,00
Phase C	Micropearl M100	Polymethyl methacrylate	2,00
Phase D	THALITAN	Aqua and hydrolyzed algin and magnesium sulfate and manganese sulfate	1,00
	Parfum	Fragrance	0.20

Prepare phase A while stirring (speed : low).

Prepare phase B while stirring (speed : low). Verify the homogeneity.

Emulsify :  
 Add phase A in phase B, while stirring (speed : rapid).  
 Add phase C, while stirring (speed : low), and then phase D.

*We are unable to guarantee the stability of this formula in view of a limited stability study.*

The only guaranteed analytical specifications are those appearing in the analysis data sheet sent at each delivery. The data contained in this leaflet are given for information only and do not involved any guaranties from us regarding the use of our products that are place under the sole user's responsibility.



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