## Sunscreens

#### WHY WORRY ABOUT TOO MUCH SUN ? ? ?

#### THE EFFECTS OF UV EXPOSURE:

#### SUNBURN

Involves skin redness, tenderness, swelling and blistering.



(Atlas of Skin Cancer Pg: 155, 1991)

Saja Hamed, Ph.D



#### PREMATURE SKIN AGING

Too much exposure to sun can change the skin texture giving it a leathery appearance and causing discoloration.



(Atlas of Skin Cancer Pg: 158, 1991)





#### SKIN CANCER

Exposure to the sun and severe sunburns can lead to skin cancer.



**Basal Cell Carcinoma.** A large cystic basal cell carcinoma is present in an area of chronic sun damage.

(Atlas of Skin Cancer Pg:158, 1991)



The CDC states that: 'A majority of skin cancers are caused by exposure to ultraviolet(UV) radiation from the sun or from indoor tanning devices, and are, therefore, preventable. Evidence clearly links exposure to UV radiation and a history of sunburn (indicating both intensity of UV exposure and skin sensitivity to radiation) to an increased risk of skin cancer'.

Osterwalder, U., Sohn, M. and Herzog, B. (2014), Global state of sunscreens. Photodermatol. Photoimmunol. Photomed., 30: 62-

80. <a href="https://doi.org/10.1111/phpp.12112">https://doi.org/10.1111/phpp.12112</a>



## EFFECTS OF UV EXPOSURE (CONTD...)

#### SUN SENSITIVITY

Development of hives, blisters or blotchy areas as an allergic reaction to sun exposure.

#### IMMUNE SYSTEM SUPPRESSION

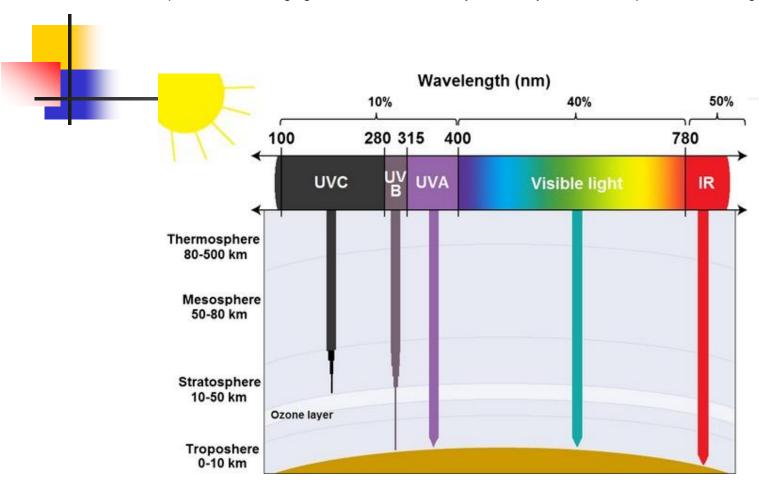
Damages the immune system making the body vulnerable to infections and cancer.



#### Simple tips for sun safety from the American Cancer Society (ACS) include:

- Do not use tanning booths, beds or lamps. These devices do not provide a 'safer way' to tan.
- When outdoors, stay in the shade whenever possible particularly between the hours of 10:00 am 4:00 p.m. when the sun's rays are most intense.
- Wear sun protective clothing such as a long-sleeved shirt, a wide-brimmed hat and UV protective sunglas ses.
- Use a broad spectrum sunscreen with an SPF of 30 or higher on all skin that is not covered every day, even on a cloudy day.
- Reapply sunscreen every two hours or immediately after swimming or sweating.
- Visit your healthcare professional every year for a skin exam.

http://www.cosmeticsinfo.org/products/sun screens-how-read-label-expert-tips-etc Saja Hamed, Ph.D Photoprotection in changing times – UV filter efficacy and safety, sensitization processes and regulatory aspects



#### **PHOTOBIOLOGY**



INFRARED RAYS

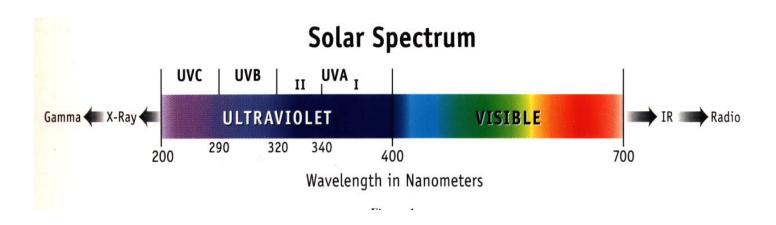
700nm - 1000nm

VISIBLE RAYS

400nm - 700nm

ULTRAVIOLET RAYS

200nm - 400nm



## Energy

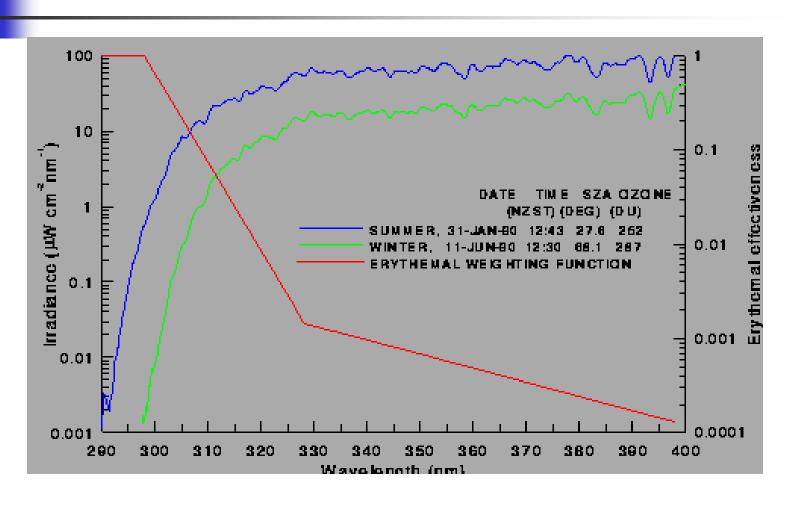
- Einstein's equation
  - $E = hv = hC/\lambda$ 
    - h is Plank's constant =  $6.625 \times 10^{-34} \text{ J-s}$
    - $\upsilon$  = frequency
    - $\lambda$  = wavelength
    - C = speed of light =  $3 \times 10^8$  m/s
- Energy is inversely proportional to λ
- Longer wavelengths are lower energy

## Energy of radiation at various wavelengths

Table 31-1 The Energy Associated with Quanta of Visible and Invisible Wavelengths

	"Color"	Wavelength (nm)	Energy in kcal/mol	Approximate Energy per Photon in eV
	X-ray	.001	>28 × 10 <sup>6</sup>	>12 × 10 <sup>5</sup>
	UVC	200	143	6.2
Y 1 1	UVC	250	114	5.0
Invisible	UVB	280	102	4.4
	UVB	300	95	4.1
	UVA	360	79	3.4
	UVA/violet	400	72	3.1
	Violet	420	68	2.9
	Blue	470	60	2.6
Visible	Green	530	54	2.3
	Yellow	600	47	2.0
	Orange	630	45	1.9
	Red	700	41	1.8
Lauricible	Near infrared	1000	29	1.2
Invisible	Far infrared	105	.29	.012

## Solar irradiance and the erythema action spectrum (red line)



## Light that encounters the skin surface is reflected, refracted and scattered.

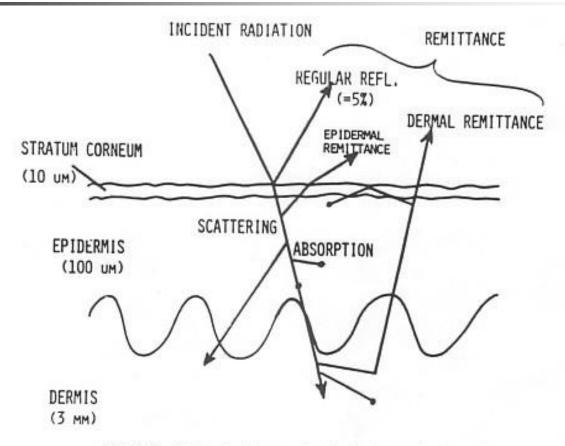
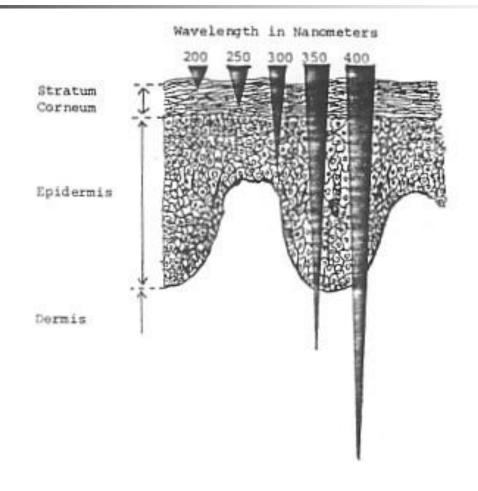


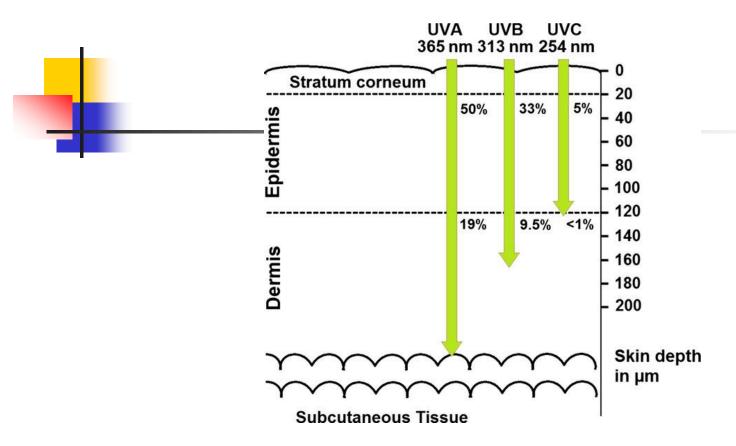
Fig. 31-3 Schematic diagram of optical pathways in skin.

# Scattering is inversely proportional to the $4^{th}$ power of $\lambda$ so longer wavelength penetrate deeper



- humans sense IR radiation as heat and VIS radiation optically, UV radiation is not directly perceivable.
- Depending on the wavelength, UV radiation can be divided into UVC (200–280 nm), UVB (280–315 nm) and UVA radiation (315–400 nm).
- Only part of UV radiation reaches the surface and depends on the location, the season, the clouds, the air pollution and the humidity
- The majority of UVC and UVB radiation is absorbed by oxygen and ozone in the atmosphere. On average, approximately 20 times more UVA rays than UVB rays reach the earth's surface

- Due to their different wavelengths, UV rays can penetrate the skin to different depths and can cause cellular changes.
- UVB mainly penetrates the epidermis
- UVA penetrates deeper into the skin down to the dermis



- In addition to natural sources, artificial sources must also be mentioned.
- Except for occupational exposure, sun lamps and tanning beds are the most common source of artificial UV light in everyday life.
- Commercial tanning beds emit high UVA levels and variable amounts of UVB (1–5%).
- Some EU countries, including Germany, the United Kingdom and Austria, have adopted legal provisions that prohibit adolescents under 18 years from indoor tanning

 balanced exposure to sunlight is essential to make optimal use of positive health effects without unnecessarily burdening the skin.

#### Sunscreen testing and classification

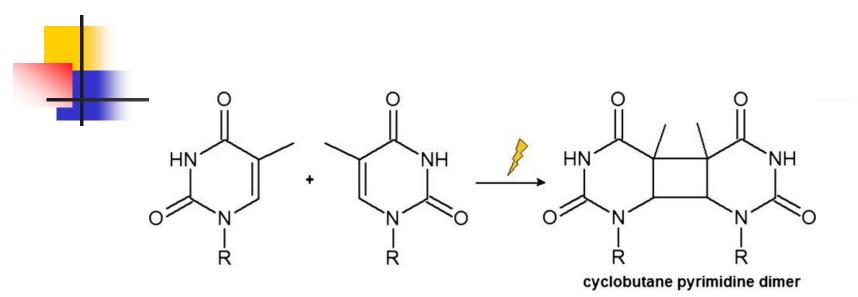
UVB	UVA
<ul> <li>Wavelength 290–320nm</li> <li>Most are intercepted by the ozone layer but with the depletion of the ozone layer more UVB rays are now reaching the earth's surface</li> <li>Its intensity varies by season, location, and time of day but in the summer months it is most intense between 10 am and 4 pm</li> <li>At high altitudes and surfaces such as snow and ice, up to 80% of UVB rays are reflected so they hit the skin twice</li> <li>The main cause of skin reddening and sunburn and damages the upper epidermal layers of skin</li> <li>20-30 minutes of UVB exposure a day helps the skin to produce bone-building vitamin D3</li> <li>Suppresses skin immune function</li> </ul>	<ul> <li>Wavelength 320–400nm</li> <li>UVA I 340–400nm</li> <li>UVA II 320-340nm</li> <li>Accounts for up to 95% of UVL reaching the earth's surface</li> <li>Present with relatively equal intensity throughout the year</li> <li>Can penetrate clouds and glass</li> <li>Penetrates the skin more deeply than UVB rays and damages skin cells in the basal layer of the epidermis</li> <li>Responsible for causing a deep tan which is an injury to the skin's DNA</li> <li>Contributes to and may even start the development of skin cancers</li> <li>Suppresses skin immune function</li> </ul>

https://dermnetnz.org/topics/sunscreen-testing-and-classification

#### **UVB** radiation

#### 280-320 nm

- Mainly penetrates the superficial skin layers (epidermis)
- Major cause of sunburn
- Leading factors of skin cancer
- Immediate result on skin is skin redness and thickening of SC (defense reaction)
- Responsible for the synthesis of vitamin D in the skin
- Do not significantly penetrate glass



UVB radiation has a strong carcinogenic effect. It causes direct damage to the DNA and RNA and leads to the generation of thymine—thymine cyclobutane pyrimidine dimers (TT-CPDs) and pyrimidine—pyrimidine (6-4) adducts (6-4 PPs)

#### **UVA** radiations

- 320-400 nm
- Penetrate deeper into the skin, down to the dermis. Penetrate window glass
- Short term effect: skin tanning
- Tanning cause cumulative damage leading to photo aging
- UVA radiation leads to a balance shift towards the collagen-degrading matrix metalloproteinases (MMPs)
- UV radiation leads to a decrease in antioxidant enzymatic activity in cultured fibroblasts, and repeated UV exposure before enzyme activity fully returns can lead to additional damage to the skin tissue
- UVA damages keratinocytes in the basal layer → may cause skin cancer
- Weaken the immune system
- Photosensitivity reactions are also mediated by UVA
- Indoor tanning (can emit doses up to 12 times that of sun)associated with increased risk of skin cancer and the risk is higher with use in early life

# Natural photoprotection of the skin

- The most important protection is the pigmentation of the skin by formation of melanin which acts as radical scavenger and ensures light absorption up to the visible range.
- UVA radiation is mainly responsible for the immediate and persistent pigment darkening (IPD and PPD) by photooxidation of melanin precursors, which are already present in the skin
- UVB radiation results in delayed tanning reaction (DTR).
   Pigment formation takes place in the basal layer and is based on the proliferation of specific enzymes, especially tyrosinase.

Saja Hamed, Ph.D

# Natural photoprotection of the skin

A further protection mechanism is the formation of the UV-induced hyperkeratosis. Under UV radiation (especially UVB light), the basal cells are stimulated to proliferate what causes a thickening of the horny layer. Without further exposure to UV radiation, the hyperkeratosis disappears

## Natural photoprotection of the skin

- There are also repair enzymes that are able to identify, cut and replace faulty DNA sequences. For strongly damaged cells - so-called sunburn cells - apoptosis can be initiated as a protection mechanism.
- And there are endogenous redox systems, such as ubiquinone, glutathione and a-lipoic acids, which have an antioxidative effect and react with free radicals before they can damage other cell constituents, such as lipid membranes, proteins and nucleic acid. However, the quantities of these substances produced by the body itself are rapidly depleted under UV radiation by the formed ROS. Saja Hamed, Ph.D.



- As natural skin protection becomes ineffective after a short time (depending on the skin type, between 10 and 40 min) other protection measures are needed:
- avoidance of direct midday sun,
- wearing protective clothes and sunglasses,
- and usage of appropriate sun protection products

# Natural photoprotection of the skin

- Tanning is not healthy. It is a sign of skin damage
- DNA damage and cellular damage that can lead to photocarcinogenesis

### Sunscreen Definitions

- Erythema: Redness that appears within a few minutes of sun exposure.
- **Sunburn:** Erythema that appears after sun exposure and then fades after several days. Skin may peel or in extreme cases blister.
- •MED The minimum dose of UV required to produce visual erythema on a given individual.
- **SPF**: Sun Protection Factor: The ratio of the MED after the application of sunscreen to the MED before application.
- •**IPD**: Immediate Pigment Darkening: a clinically visible brown pigmentation within the boundaries of a square produced immediately after irradiation
- **PPD:** a clear pigmentation 3 h after irradiation
- **•DT**: Delayed Tanning, occurs a few days after exposure.

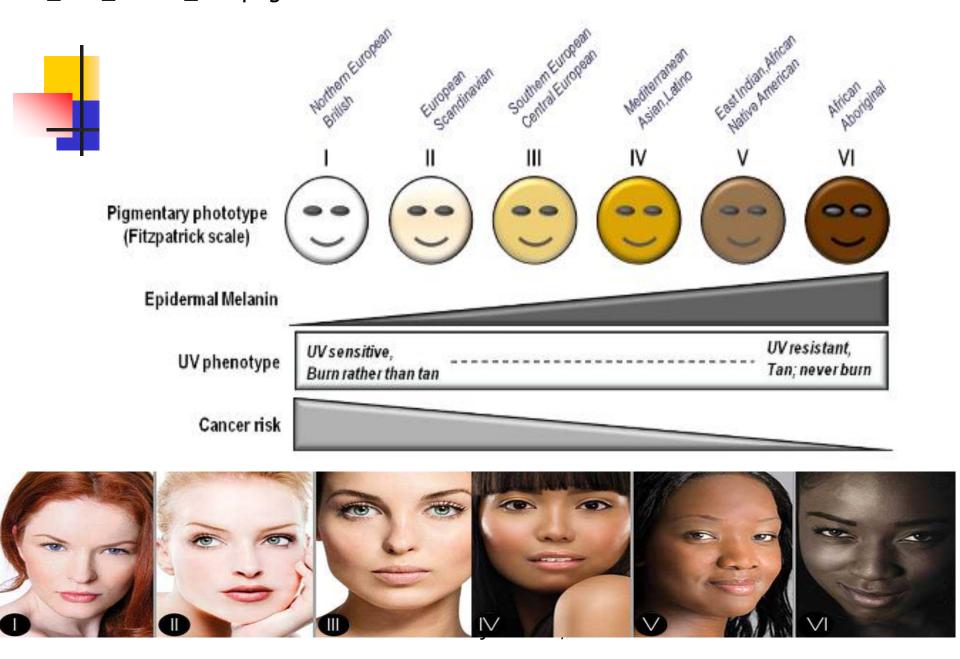
Skin type	Unexposed buttock skin	Sun sensitivity and pigment response*	UVB MED (MJ/cm <sup>2</sup> )
I	White	Always burn easily, tan little or none	20-30
II	White	Always burn easily, tan minimally with difficulty	25-35
III	White	Always burn moderately, tan average (light brown)	30-50
IV	Light brown	Burn minimally, exhibit IPD, tan easily (moderate brown)	50-75
V	Moderate Burn with difficulty and minimally exhibit intense IPD and tan profusely		60-90
VI	Dark brown, black	Insensitive, never burn, tan profusely	100-200

<sup>•</sup>Based on first 30 to 45 minutes of sun exposure after winter season or without previous sun exposure

Saja Hamed, Ph.D

•IPD: Immediate pigment darkening

https://en.wikipedia.org/wiki/Fitzpatrick\_scale#/media/File:Influence\_of\_pigmentation\_on\_skin\_cancer\_risk.png



### Sunscreens

- The purpose of a sunscreen is to absorb light in the correct wavelength range to protect the skin. Modern sunscreens protect from both UVB and UVA
- In order to achieve this goal the molecular structure of the sunscreen molecule must allow it to absorb light at the required wavelengths.

# Sun protection factor (SPF) value

- Represents the ability of a sunscreen to delay sun-induced erythema
- •The UV energy required to produce an MED on protected skin divided by the UV energy required to produce an MED on unprotected skin
- •SPF value = MED (protected skin (PS))/MED (unprotected skin (US)), where MED (PS) is the minimal erythema dose for protected skin after application of 2 milligrams per square centimeter of the final formulation of the **sunscreen** product, and MED (US) is the minimal erythema dose for unprotected skin, i.e., skin to which no **sunscreen** product has been applied

## Sun Protection Factor (SPF):

- There is a popular misconception that SPF relates to time of solar exposure. For example, many consumers believe that, if they normally get sunburn in one hour, then an SPF 15 sunscreen allows them to stay in the sun 15 hours (i.e., 15 times longer) without getting sunburn
- Rather, SPF is a relative measure of the amount of sunburn protection provided by sunscreens. It allows consumers to compare the level of sunburn protection provided by different sunscreens. For example, consumers know that SPF 30 sunscreens provide more sunburn protection than SPF 8 sunscreens.

## Sun Protection Factor (SPF):

- SPF is not directly related to time of solar exposure but to amount of solar exposure
- Although solar energy amount is related to solar exposure time, there are other factors that impact the amount of solar energy
- More UVB reach the earth's at higher altitude than at sea level
- For example, the intensity of the solar energy impacts the amount. The following exposures may result in the same amount of solar energy:

one hour at 9:00 a.m.

15 minutes at 1:00 p.m.



- Generally, it takes less time to be exposed to the same amount of solar energy at midday compared to early morning or late evening because the sun is more intense at midday relative to the other times.
- Because clouds absorb solar energy, solar intensity is generally greater on clear days than cloudy days.



- The internationally agreed upon standard quantity of sunscreen per unit of skin surface required to measure SPF in humans is 2mg/cm<sup>2</sup> of skin
- For an adult to apply this amount of sunscreen to the entire body, 30 ml of sunscreen is required

## Measurement of SPF

- Determine the MED on at least 20 but not more than 25 qualified subjects
- The MED is that amount of UV radiation required to produce the first perceptible redness reaction with clearly defined borders at 22 to 24 hours after irradiation
- To determine the MED, a series of 5 exposures of increasing energy is administered to the subject's unprotected skin
- Each exposure is 25% greater than the previous exposure
- At 22 to 24 hours after exposure, a trained grader other than the person who conducted the irradiation or who applied the sunscreen evaluates the redness of each exposure site
- The MED on unprotected skin is used to calculate the radiation exposure for the sunscreen-protected site



- To determine the water resistance of a sunscreen formulation you must first subject the skin with sunscreen test material to repeated exposures to fresh water maintained at 23 to 32 C.
- The sunscreen is applied to the skin and allowed to dry
- The subject enters the water and engages in moderate activity for 20 minutes, the subject exits the water to rest for 20 min, being careful to avoid rubbing off the sunscreen



## Measurement of SPF

- For a water-resistant claim, the 20 minutes in the fresh water is repeated once more (total 40 minutes in water)
- For a very water resistant claim the 20 minutes in fresh water is repeated three more times (total of 80 minutes in water)



- For the water-resistant sunscreen:
- The lipophilic base allows the products to adhere well to the skin
- Greasy feel
- The higher SPF formulations tend to be oilier or more opaque
- " waterproof": Not allowed in the labeling



## Sun Protection Factor (SPF):

- Points to note:
- It is a system based mainly on ultraviolet B exposure
- UVA exposure and dose are not accounted for in the current methods of measuring SPF
- Most people do not apply the sunscreen as thickly as it is applied in the testing



 A study demonstrated that most users probably achieve a mean SPF of between 20 and 50% of that expected from the product label because they do not apply the sunscreen as thickly as is done in laboratory conditions

(Stokes & Diffey: How well are sunscreen users protected? Photodermatol Photoimmunol Photomed, 13: 186, 1997)



- A useful-rule-of-thumb is that the protection most people get from a sunscreen is equal to about one-third of the SPF
- SPF 15 sunscreen at a typical application thickness to the face provide about fivefold protection



**1.Physical** sunscreen ingredients (more correctly known as **inorganic** (mineral) sunscreen ingredients): zinc oxide and titanium dioxide.

**2. Chemical** sunscreen ingredients (more correctly known as **organic** sunscreen ingredients).

# Sunscreen Ingredients Classification:

- At present, all organic UV absorbers used in sunscreens possess aromatic moieties.
- The substitutions at the aromatic ring are of great importance for the UV spectroscopic properties. An increase in the number of resonance structures stabilizes the excited state



 You can have sunscreens containing only organic filters, only inorganic filters, or a combination of both.

# Sunscreen Ingredients Classification:

- The basic requirements for all UV filters that are used in sunscreens are:
- 1) efficacy,
- 2) safety
- 3) registration, and
- freedom-to-operate with respect to the status of intellectual property

# Sunscreen Ingredients Classification:

- Both ingredients absorb UV at certain wavelength range
- Inorganic sunscreens also scatter and reflect about 5-10% of the incoming UV,
- Some particulate organic sunscreens like
   Tinosorb M also scatter and reflect UV light
- better to be classified as both chemical and physical.

# Sunscreen Classification: A. Physical sunscreens

- For these UV filters, the term 'physical UV filters' was initially used, attributed to their first known mechanism of sun blocking through the physical manner of reflection and scattering. However, small inorganic UV filter particles also absorb part of the incident light
- Are rarely associated with allergic reactions. They remain on the skin's surface and are not systemically absorbed
- People with sensitive skin are more likely to tolerate this type of sunscreen than the chemical type
- Are recommended when intense sun exposure is expected



- Titanium dioxide (TiO<sub>2</sub>)
- Zinc oxide (ZnO)
- Cosmetically acceptable translucent or colloidal suspension that consist of micronized preparations of ZnO and TiO<sub>2</sub> have been developed



- Titanium dioxide and zinc oxide impart high SPF values, provide broad spectrum protection, and relatively inexpensive
- The difficulty in formulating with them is creating a product with acceptable consumer qualities

# Sunscreen Classification: A. Physical sunscreens

- Metal oxides may produce oxygen free radicals at their surface when irradiated
- However to affect skin, the particles would have to traverse the SC
- They are too large to enter the skin
- Most companies minimize the photoreactivity of these agents by coating the surface with dimethicone or silicone
- They're processed to get rid of toxic contaminants, and often need to be coated in synthetic chemicals to stop them from being photocatalytic, and prevent them from clumping up and causing patchy protection → that's why the natural claim is questionable.

Saja Hamed, Ph.D



## **Drug Facts**

## Active ingredients

Purpo:

Titanium dioxide 11%. Sunscre

### Uses

- helps prevent sunburn
- if used as directed with other sun protection measures (see Directions), decreases the risk of skin cancer and early skin aging caused by the s

## Warnings

For external use only

Do not use on damaged or broken skin

When using this product keep out of eyes. Rins with water to remove.

Ston use and ack a doctor if rach occurs



## ANTHELIOS 50

MINERAL

### **ULTRA LIGHT SUNSCREEN FLUID**

100% mineral UV filter system Matte finish. Universal tint

Advanced Protection

with CELL-OX SHIELD TH

UVA/UVB + ANTIOXIDANT

WATER RESISTANT (40 MINUTES) Fragrance-free, Paraben-free Tested on sensitive skin

1.7 FL OZ - 50 ml

## Drug Facts

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Purpose Summerment

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#### Warnings For external use only

Do not use on damaged or broken skin

When using this product keep out of eyes. Firese with water to remove.

Stop use and ask a doctor if rash occurs

Keep out of reach of children If swellowed, get medical help or contact a Poison Control Center right away.

#### Directions

- · shake well before use
- · apply generously 15 minutes before sun exposure
- · after 40 minutes of swimming or sweating
- · immediately after towel drying
- · at least every 2 hours
- Sun protections Measures. Spending time in the sun increases your risk of skin cancer and early skin. aging. To decrease this risk, regularly use a sunscreen with a Broad Spectrum SPF value of 15 or higher and other sun protection measures including:
- . limit time in the sun, especially from 10 a.m. 2 p.m.
- · wear lang-sleeved shirts, pants, hats and sunglasses children under 6 months of age: Ask a doctor

#### Other information

· protect the product in this container from excessive heat and direct our

#### Inactive ingredients

water, isodotecare, C12-15 ally/ benzone, directricone, undecane, trieffy/hisonoin, isotexadecane, styrene/acy/lates copolymer, nylon-12, caprylyl methicone, butyloctyl salicylate, phonethyl benzsata, silica, tridecano, dicaprylyl carbonate. dicaps/yl other, talc, dimethicane / PEG-10/15 crosspelymer, aluminum steasste, pentylene plycol, CS-15 fluoroaloshol phosphate, tocopherol, phenoxyethanol, stearic acid, diethytherol. syringuli denemalorate, PEG 3 polydimethyl slovyethyl dimethicone, magnesium sultate, PEG-8 laurate, PEG-9, polyhydrosysteeric acid, maltodoctrin, benzoic acid, iron oxides, propylene glycol, propylene carbonate, caprylyl glycol, distoardimenium hectorite, cassia alata lesf extract, alumina, aluminum hydroxide

#### a Questions or comments? 1-888-LRP-LABO

Monday - Friday (9 a.m. - 5 p.m. EST)

8582023 US Pat Pending Code F.I.L.: D50867/1

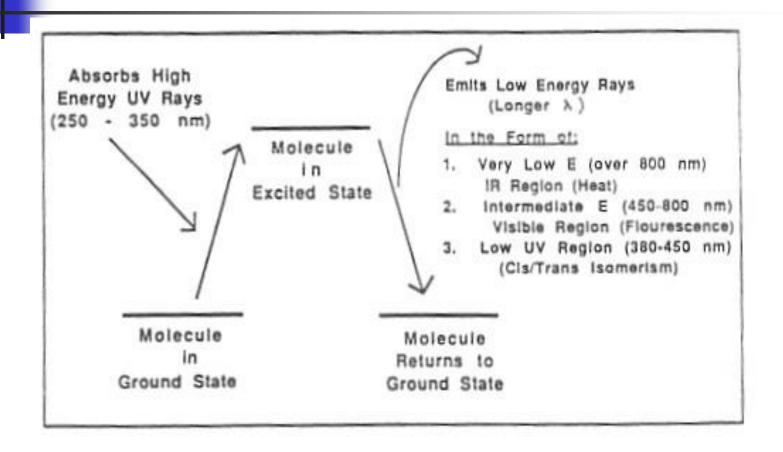


- They are usually combined with physical sunscreens or with each other to form high-SPF products
- Chemical sunscreens absorb ultraviolet radiation
- The absorbed radiation must then be dissipated as either heat or light.
- In most cases, the radiation simply is emitted again at a longer wavelength and does not lead to free radical formation

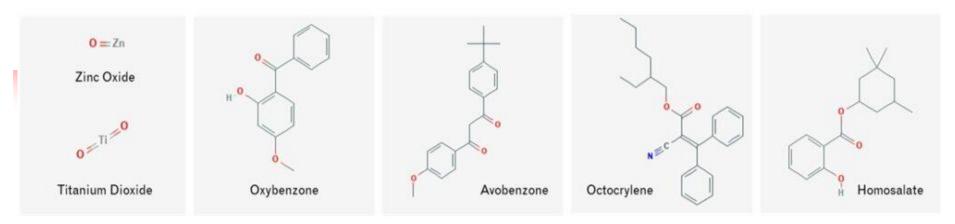


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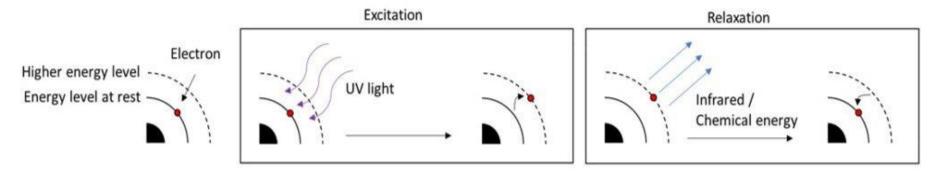
# Sunscreen Classification: B. Chemical sunscreens



### Chemical structures of common UV filters



### Electron transitions in UV filters



Sunscreens contain UV filters that absorb UV light and convert it into different forms of energy that are less harmful to the skin. (Chemical structures from PubChem)



- They are synthetically prepared organic chemicals that can be labeled as UVB or UVA absorbing substances or both
- Colorless and often odorless agents that prevent UV radiation from penetrating the epidermis by acting as filters as they absorb and reflect UV radiation

# Sunscreen Classification: B. Chemical sunscreens

- Drawbacks:
- Many chemical sunscreens have been reported to cause allergic or photoallergic reactions in susceptible people
- In addition, some of them are unstable when exposed to ultraviolet radiation. E.g. 15 minutes of solar-simulated light destroys 36% of avobenzone
- Some are systemically absorbed and levels have been demonstrated in the urine of humans using the product (Hayden et al.: Systemic absorption of sunscreen after topical application. Lancet, 350: 863, 1997) → chemical sunscreens should not be used in children under 2 years of age

## THE CHEMISTRY OF SUNSCREEN

Summer sun brings with it the risk of sunburn, so we'll all be slapping on the sunscreen to guard against it. But what are the chemicals that keep you from turning as red as a lobster? This graphic looks at them and how they work.



### **TYPES OF UV RADIATION**

## UVA 320-400nm

Accounts for 95% of solar UV radiation reaching Earth's surface. Penetrates deepest into skin, and contributes to skin cancer via indirect DNA damage.

## UVB 290-320nm

Accounts for 5% of solar UV radiation reaching Earth's surface. Causes direct DNA damage, and is one of the main contributors to skin cancer.

## UVC 290-100nm

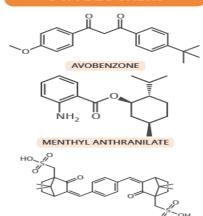
Filtered out by ozone in the Earth's atmosphere, and as a result does not reach the surface of the Earth, and doesn't cause skin damage.

SUNSCREEN ACTIVE INGREDIENTS APPROVED IN THE USA

28
SUNSCREEN ACTIVE INGREDIENTS
APPROVED IN THE EU

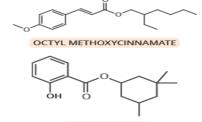
Inorganic chemicals in sunscreen, such as zinc oxide and titanium oxide, both absorb and scatter UV light. Organic chemicals are also used – the chemical bonds in these absorb UV radiation, with the chemical structure affecting whether they absorb UVA, UVB, or both. Several different chemicals are used in sunscreen to ensure full protection.

#### **UVA BLOCKERS**



ECAMSULE

#### UVB BLOCKERS



#### HOMOSALATE

### OTHER UVB BLOCKERS (Italicised = not approved in USA)

PABA Octylocrylene
Padimate O Ensulizole
Cinoxate Octyl riazone
Octyl salicylate Enzacamene
Trolamine salicylate Amiloxate

#### **UVA & UVB BLOCKERS**

#### SULISOBENZONE

#### OTHER UVA & UVB BLOCKERS (Italicised = not approved in USA)

Dioxybenzone Neo Heliopan AP
Mexoryl XL Uvinul A Plus
Tinosorb S UVAsorb HEB
Tinosorb M

All currently approved in EU, Canada & Australia



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# B. Chemical sunscreens: UVB-Absorbers p-Aminobenzoate derivatives

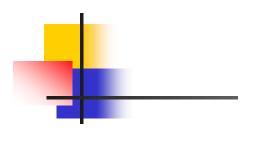
- The UVB filter 4-aminobenzoic acid (PABA) was one of the first commercially available and one of the most popular UV filters worldwide. However, it soon became apparent that both PABA and its derivatives were known triggers of photoallergic reactions.
- In 2008, PABA was banned as a cosmetic UV filter in the EU. The usage of ethylhexyl p-aminobenzoic acid (OD-PABA) has also significantly decreased in the past 20 years, and nowadays, it has been almost completely replaced by other UV filters.

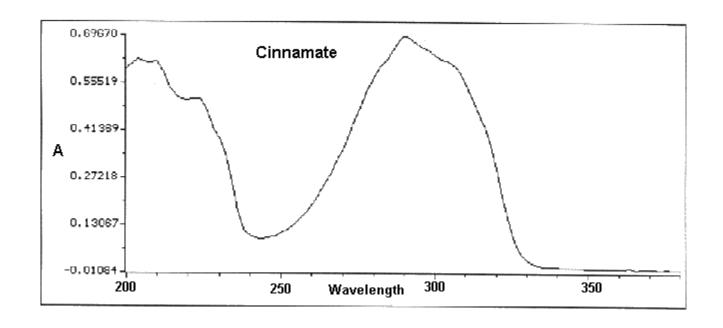


- Ethylhexyl methoxycinnamate (EHMC,Octyl methoxycinnamate, OMC, octinoxate) is one of the most common UV filters worldwide and is often used in combination with other UVB filters to achieve high SPF values.
- Cinnamates are poorly soluble in water → often included in water-resistant and very-water-resistant sunscreens
- Photoallergic reactions have been reported (rare)
- People allergic to this compound may also be allergic to fragrances and flavorings that contain cinnamic aldehyde and cinnamon oil

# B. Chemical sunscreens: UVB-Absorbers Cinnamate derivatives

 Octocrylene: The UVB filter OCR also belongs to the group of cinnamates. there is more and more evidence that OCR has developed into one of the most common photoallergens



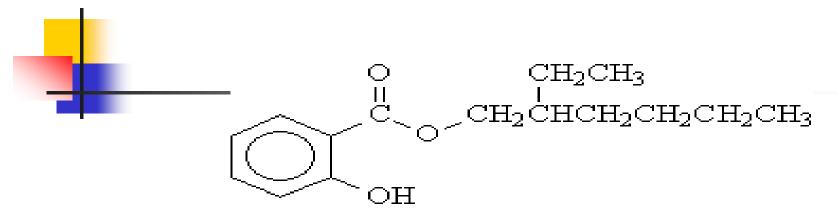


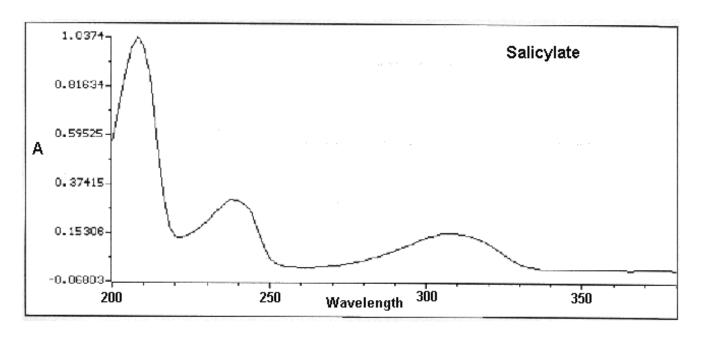


- The UVB filters ethylhexyl salicylate (EHS) and homosalate are typical representatives of this group.
- Salicylate derivatives are rather weak UVB absorbers but are often used to augment other UVB filters.
- Due to their insolubility in water, they show good water resistance.

# B. Chemical sunscreens: UVB-Absorbers Salicylate derivatives

- Cosmetically used salicylates are rarely associated with allergic or photoallergic reactions, and do not have notable oestrogenic activity.
- In addition, EHS shows only a slight tendency to penetrate the skin .
- Therefore, especially EHS with its good photostability and solubility is a common ingredient in sunscreens
- The UV absorber triethanolamine salicylate is water-soluble and is a typical photoprotective agent in hair care products.



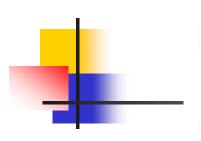




- UVA1 (> 340 nm)
- UVA2 (320-340 nm)
- Very few approved sunscreen agents are able to block in the UVA1 range
- A sunscreen's SPF gives no information about the product ability to block UVA

## B. Chemical sunscreens: Camphor derivatives

- Due to their excellent photostability, the camphor derivatives 3benzylidene camphor (3-BC) and 4-methylbenzylidene camphor (4-MBC) were popular **UVB** filters for a long time.
- In the past several years, the camphor derivatives have been under more and more criticism due to their possible endocrine potential. The increasing pressure of the public and different non-governmental organizations resulted in the near cessation of use of 3-BC and 4-MBC in sun protection products in Germany
- Terephthalylidene dicamphor sulphonic acid (TDSA, Mexoryl SX), a further camphor derivative, is an effective UVA filter, which was developed and patented by L'Oréal (Paris, France) in 1982 and was approved in 1991 as cosmetic ingredient in Europe.
- In 2006, Mexoryl SX was also approved by the FDA as part of the sunscreen 'Anthelios SX'. This was the first approval of a product with a new UV filter since 1988. TDSA shows good protection ability against the negative effects of UVA radiation. In addition, TDSA is photostable and shows no tendency for percutaneous absorption.





## LA ROCHE-POSAY LABORATOIRE DERMATOLOGIQUE

BROAD SPECTRUM SPF15

## **ANTHELIOS SX**

DAILY MOISTURIZING CREAM with SUNSCREEN

### **UVA PROTECTION**

with MEXORYLTM SX

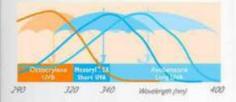
DAILY USE MOISTURIZER UVA/UVB protection 24 hr long-lasting hydration

> Fragrance-free PABA-free Light, non-greasy Suitable for sensitive skin

### ANTHELIOS SX helps provide protection from UVA rays.

How does Mexory!" SX (ecamsule) protect skin from UVA rays?

Parsol® 1789 (avobenzone) is very effective at the midpoint of the UVA spectrum, but provides less protection against short UVA wavelengths. Mexoryl™ SX (ecamsule) provides peak efficacy against these short UVA rays.



The combination of Parsol® 1789 (avobenzone) and Mexoryl™ SX (ecamsule) helps provide UVA protection.

Sun alert: Limiting sun exposure, wearing protective clothing, and using sunscreens may reduce the risks of skin aging, skin cancer, and other harmful effects of the sun.

Even if you do not burn, repeated exposure of unprotected skin while tanning may increase the risk of skin aging, skin cancer, and other harmful effects to the skin.

### UVA rays, a daily skin concern:

UVA rays have been shown to penetrate deeper into the skin, damaging its elasticity and contributing to premature skin aging.

#### UVB rays, also a skin concern:

UVB rays cause sunburn and also contribute to premature skin aging.

SPF, or "Sun Protection Factor," is the degree of protection a sunscreen offers against UVB rays.

## KEY DERMATOLOGICAL INGREDIENTS



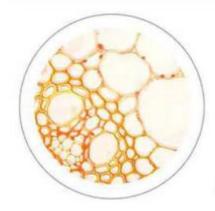
### MEXORYL™ SX

## EXCLUSIVE ULTRAVIOLET A ABSORBER

Photostable UVA/UVB filters and powerful antioxidant protection







## **BROAD SPECTRUM SPF 15**

## OXYBENZONE-FREE & OCTINOXATE-FREE

Avobenzone 2% Ecamsule (Mexoryl™ SX) 2% Octocrylene 10%



### HUMECTANT

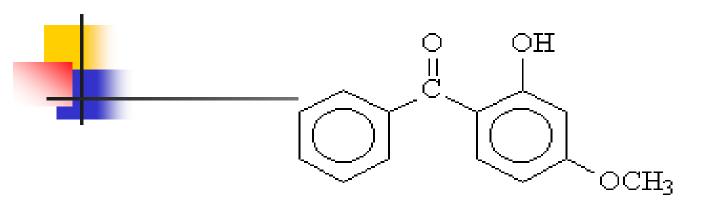
Known for its hydrating properties

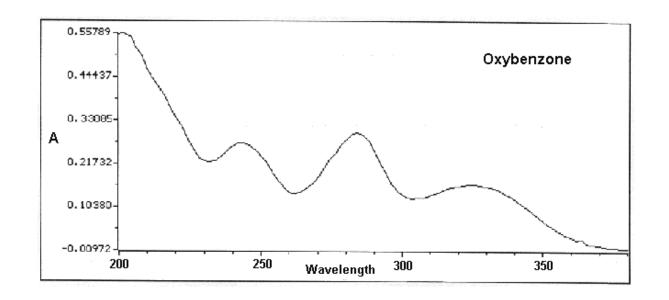


## B. Chemical sunscreens: UVA-Absorbers

### Benzophenones:

- Absorption range is in the range of 320-350 nm (absorption peak at 326 nm)
- Benzophenone-3 (Oxybenzone) is an absorber of UVA2
- The most common sunscreen agent to cause photoallergic contact dermatitis





# Benzophenone derivatives UVA/UVB Absorber

- The two UV filters benzophenone-3 (BP-3) and benzophenone-4 (BP-4), both approved in the EU, show very good photostability and broad-spectrum protection over the UVB and UVA ranges
- If used alone they do not provide complete UVA protection.
- Several studies have demonstrated that BP-3 shows a clear tendency to penetrate the human skin and was found in urine and even mother's milk. This is particularly critical because BP-3 is considered a substance with endocrine potential.
- In addition, BP-3 and BP-4 are seen as the most common photoallergens among the UV filters. Therefore, the usage of BP-3 and BP-4 in sun protection products in Germany decreased to a minimum.

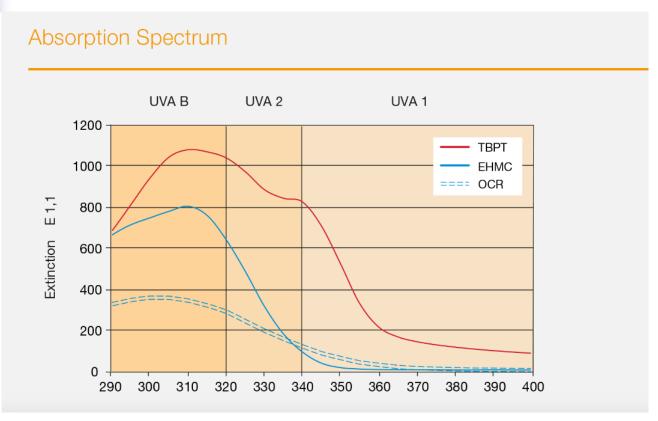
# B. Chemical sunscreensUVA-AbsorbersDibenzoylmethane derivatives

- Butyl methoxydibenzoylmethane (BMDBM) is the most common UVA filter in cosmetic products and is included in approximately 80% of the sun protection products in Germany
- BMDBM is also a known contact allergen among the UV filters
- Another critical point is the photoinstability of BMDBM, especially when it is used in combination with ethylhexyl methoxycinnamate (EHMC)
- The resulting photodegradation products also have a specific reaction potential and may be seen as further triggers for contact allergies. However, with an appropriate UV filter combination, for example with octocrylene (OCR) or by encapsulation, photodegradation can be decreased to a minimum.

# B. Chemical sunscreens UVA/UVB-Absorbers Triazones

- Recently, the development of new UV filters is based on the socalled 500 Da rule. With an increased molecular weight of more than 500 Da, skin penetration is reduced.
- This reduction is associated with increased safety and efficiency of such substances.
- The UVB filter ethylhexyl triazone (EHT), the UVB filter diethylhexyl butamido triazone (DEBT, iscotrizinol, Uvasorb HEB) and the broad-spectrum UV filter bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT, bemotrizinol, Tinosorb S) have a molecular weight well above 500 Da. These UV filters show comparatively high absorption coefficients, significant anti-inflammatory effects and are highly efficient and very photostable

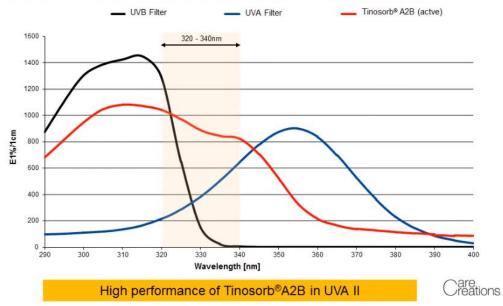
## Tris-Biphenyl Triazine Efficient UVB and UVA2 filter



https://www.carecreations.basf.com/products-formulation/products/products-detail/TINOSORB-A2B/30478125

### Why a New UV Filter?





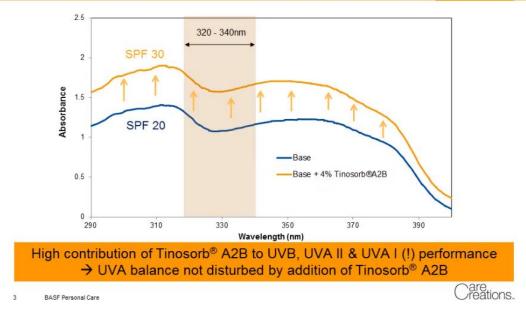
Tinosorb® A2B: An innovative broad-spectrum UV filter

https://www.youtube.com/watch?v=enBw1VQkUio



### Tinosorb® A2B Performance in a Sunscreen Formulation



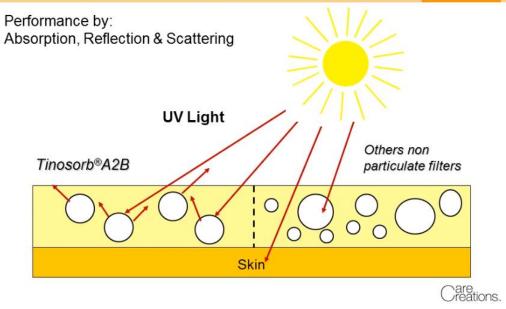


Tinosorb® A2B: An innovative broad-spectrum UV filter



#### Tinosorb®A2B – Boosting effect with soluble UV filters





Tinosorb® A2B: An innovative broad-spectrum UV filter



Tinosorb A2B protects the skin against UV wavelengths ranging from 290 to 340 nanometers, thereby being the first of a new generation of finely-ground (microrace) UV filters; It complements conventional oil-soluble UV filters by Josing the current gap between UVA and UVB absorbers, thus enabling a balanced protection.

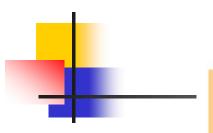
Thanks to Tinosorb A2B, the SPF performance of cosmetics such as sunscreens can be increased. As a result, a lower UV filter concentration is necessary than with conventional ingredients. "The absorption spectrum of a micronized UV filter depends on its native size by the native sizes of about 100 pagmeters."

A new generation of micronized UV filters

across the entire spectrum of solar UV radiation.

The most efficient filter to protect from UV radiation

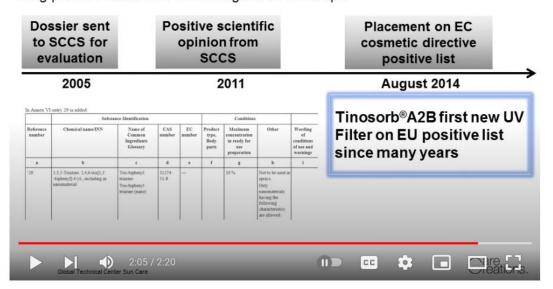
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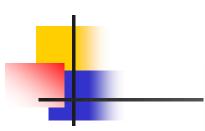
## Tinosorb® A2B Registration process EU



Long process until a new filter is registered in Europe



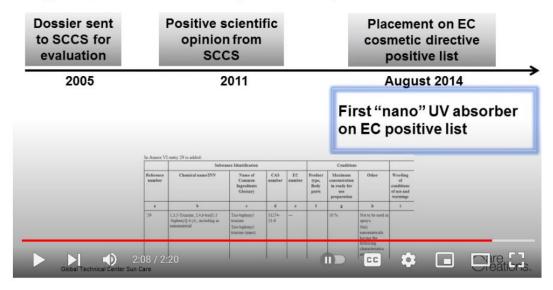
Tinosorb® A2B: An innovative broad-spectrum UV filter



## Tinosorb® A2B Registration process EU



Long process until a new filter is registered in Europe



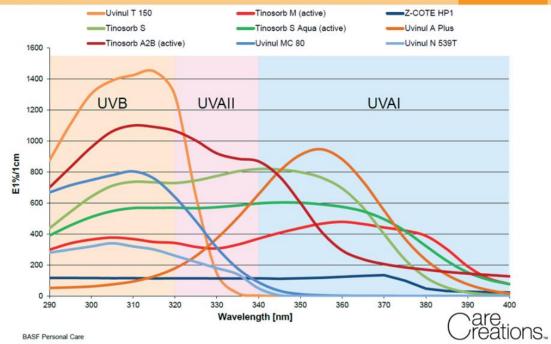
Tinosorb® A2B: An innovative broad-spectrum UV filter



### **UV Filter Performance**

#### Overview







- Many sunscreen formulations contain combination of sunscreen agents to enhance protection
- Combinations are used to achieve a higher SPF by using a lower concentration of sunscreen ingredients
- The FDA regulates which sunscreen can be combined with others
- This is because certain sunscreen ingredients are incompatible and can lower the SPF rating of a product when combined

- UV filters for sunscreens are regulated globally as either, over-the-counter (OTC) drugs, quasi-drugs, or cosmetics
- All countries have a positive list of UV filters, including maximum concentration allowed in sunscreens.
- In most countries, including Europe and Japan,
   UV absorbers are regulated as cosmetics;
- in the United States and Canada as OTC drugs;
- and in Australia as therapeutic drugs.
- The worldwide regulatory status of the UV filters is given in Table1, containing all relevant UV filters. The number of available UV filters differs from region to region.

Table 1. Common UV filters approved in Australia (AUS), Europe (EU), Japan (JP), and United States (USA)

	INCI (International Nomenclature of Cosmetic ingredients)	COLIPA (Cosmetics Europe)	USAN (United States Adopted Names)	Trademark	INCI abbreviation	Form	Concentration limits in sunscreen (%)			
							AUS	EU	JP	USA
Broad-Spectrum and UVAI	Bis-ethylhexyloxyphenol methoxyphenyl triazine	S 81	Bemotrizinol	Tinosorb® S	BEMT	р	10	10	3	*
(340–400 nm)	Butyl methoxydibenzoylmethane	S 66	Avobenzone	Parsol® 1789	BMBM	р	5	5	10	3
	Diethylamino hydroxybenzoyl hexyl benzoate	S 83	-	Uvinul® A Plus	DHHB	р	10	10	10	-
	Disodium phenyl dibenzimidazole tetrasulfonate	S 80	Bisdisulizole Disodium	Neo Heliopan® AP	DPDT	р	10	10	-	-
	Drometrizole trisiloxane	S 73	Drometrizole Trisiloxane	Mexoryl <sup>®</sup> XL	DTS	р	15	15	-	-
	Menthyl anthranilate	-	Meradimate	-	MA	р	5	-	-	5
	Methylene bis-benzotriazolyl tetramethylbutylphenol	S 79	Bisoctrizole	Tinosorb® M (active)	MBBT	d	10	10	10	*
	Terephthalylidene dicamphor sulfonic acid	S 71	Ecamsule	Mexoryl® SX	TDSA	р	10	10	10	*,†
	Zinc oxide	S 76	Zinc Oxide	Z-Cote® HP1	ZnO	p, d	no limit	#	no limit	25
UVB (290-320 nm)	4-Methylbenzylidene camphor	S 60	Enzacamene	Eusolex® 6300	MBC	р	4	4	_	*
and UVAII (320–340 nm)	Benzophenone-3	S 38	Oxybenzone	-	BP3	р	10	10	5	6
	Benzophenone-4	S 40	Sulisobenzone	Uvinul® MS40	BP4	p	10	5	10	10
	Polysilicone-15	S 74	_	Parsol® SLX	PS15	İ	10	10	10	-
	Diethylhexyl butamido triazone	S 78	Iscotrizinol	Uvasorb® HEB	DBT	р	_	10	_	*
	Ethylhexyl dimethyl PABA	S 08	Padimate O	Eusolex® 6007	EHDP	i	8	8§	10	8
	Ethylhexyl methoxycinnamate	S 28	Octinoxate	Uvinul® MC 80	EHMC	1	10	10	20	7.5
	Ethylhexyl salicylate	S 13	Octisalate	Neo Heliopan® OS	EHS	1	5	5	10	5
	Ethylhexyl triazone	S 69	Octyltriazone	Uvinul® T150	EHT	р	5	5	3	*
	Homomenthyl salicylate	S 12	Homosalate	Eusolex® HMS	HMS	İ	15	10	10	15
	Isoamyl p-methoxycinnamate	S 27	Amiloxate	Neo Heliopan® E1000	IMC	1	10	10	_	*
	Octocrylene	S 32	Octocrylene	Uvinul® N539 T	OCR	1	10	10	10	10
	Phenylbenzimidazole sulfonic acid	S 45	Ensulizole	Eusolex® 232	PBSA	р	4	8	3	4
	Titanium dioxide	S 75	Titanium Dioxide	Eusolex® T2000	TiO <sub>2</sub>	p, d	25	25	no limit	25
	Tris biphenyl triazine	5 84	_	Tinosorb® A2B	TBPT	d	1	1	1	¶

<sup>\*</sup>Time and Extent Application (TEA), Proposed Rule on FDA approval expected not before 2014.

<sup>†</sup>Approved in certain formulations up to 3% via New Drug Application (NDA) Route.

<sup>\*</sup>Not yet approved in EU, positive opinion by Scientific Committee on Consumer Safety (SCCS).

<sup>§</sup>Not being supported in the EU and may be delisted.

<sup>¶</sup>Not yet approved in EU or anywhere else (but positive Safety Opinion on 1,3,5-Triazine, 2,4,6-tris[1,1'-biphenyl]-4-yl-, SCCS Sept/Dec. 2011).

Cosmetics Europe (formerly COLIPA): http://www.cosmeticseurope.eu/, order number shows chronology of UV filter development.

Trademarks: Tinosorb®, trademark of BASF SE, Ludwigshafen Germany; Parsol®, trademark of DSM, Kaiseraugst, Switzerland; Uvasorb®, trademark of 3V Sigma, Bergamo, Italy; Uvinul®, trademark of BASF SE, Ludwigshafen Germany; Neo Heliopan®, trademark of Symrise AG, Holzminden Germany; Mexoryl®, trademark of L'Oréal, Paris France; Z-Cote®, trademark of BASF SE, Ludwigshafen Germany; Eusolex®, trademark of Merck, Darmstadt Germany.

p, powder; I, liquid; d, dispersion.



- Zinc Oxide
- Avobenzone
- Mexoryl SX







Ingredients: Aqua, Caprylic/Capric Triglyceride, Pentylene Glycol, Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (Nano), Titanium Dioxide (Nano), Ethylhexyl Salicylate, Glycerin, Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine, C12-15 Alkyl Benzoate, Diethylamino Hydroxybenzoyl Hexyl Benzoate, Ethylhexyl Triazone, C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer, Polyacrylate Crosspolymer-6, Squalane, Ectoin, Cocoglycerides, Hydrogenated Phosphatidylcholine, Vitis Vinifera Seed Extract, Decyl Glucoside, Silica, Propyl Alcohol, Alcohol, Cetyl Phosphate, Xanthan Gum, Propylene Glycol, T-Butyl Alcohol, Lecithin, Tocopheryl Acetate, Ascorbyl Tetraisopalmitate, Tocopherol, Diisopropyl Adipate, Ubiquinone.

## Sensitive Skin:

- If you're in the US, avobenzone is in almost all broad spectrum organic sunscreens (except for the ones containing L'Oreal's patented Mexoryl SX). Avobenzone is a common irritant and allergen, so it tends to be unsuitable for sensitive skin, and you're left with inorganic sunscreens only.
- If you're elsewhere in the world, the newer UVA1 filters aren't particularly irritating or allergenic.
- A few other organic sunscreens also tend to cause allergic and irritant reactions: octocrylene, oxybenzone, avobenzone, PABA, Padimate O and enzacamene.



- Sunscreen actives cause irritation to the eyes. When a water-resistant sunscreen enters the eye, the water-resistant agents adhere to the mucus membrane of the eye
- This holds the sunscreen actives in place causing sever and prolonged irritation

# Vehicle for delivery of sunscreen ingredients

- Lotion and creams:
- Lotion:

Normal to oily skin Have lower viscosity Spread more easily Less greasy

#### Cream:

Dry skin

#### Gels:

Male patients Oily skin

Water-based gels are more appropriate than alcohol based gels

#### Sticks:

Lipid-soluble sunscreen ingredients are contained in sticks

Waxes and petrolatum are added to thicken the formulations

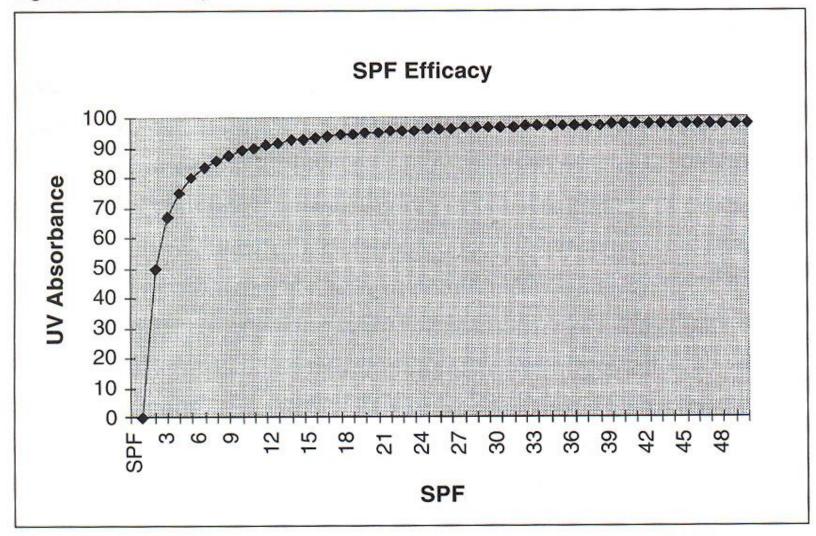
Effective for narrow and prominent areas such as the lips, ears, nose and around the eyes

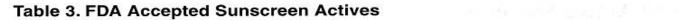
Superior for use during exercise and water activities (i.e. last longer and do not have the tendency to melt which can irritate the eyes).

## FDA Sunscreen Monograph

- 50+ → maximum SPF allowed on sunscreen package
- A sunscreen with SPF 15 blocks about 93% of UVB radiation
- A sunscreen with SPF 30 blocks 97% of UVB radiation
- An SPF 25 blocks 96% of the sunburn response
- An SPF 50 only blocks 2% more (98%)
- Very high SPF products are more expensive, may be more irritating to skin & eyes, and offer little extra protection for the average consumer

Figure 1. SPF Efficacy Versus % UV Absorbance







INCI Name	Max. Conc.	Protection Range	Trade Name(s)	Selected Supplier(s)
PABA	15%	UVB	PABA	Rona
Avobenzone	3%	UVA	Parsol 1789	Roche
Cinoxate	3%		None	None
Dioxybenzone	3%	UVA	Benzophenone-8	American Cyanamid
Homosalate	15%	UVB	HMS	Rona
Menthyl anthranilate	5%	UVA	Neo Heliopan MA	Haarman & Reimer
Octocrylene	10%	UVB/UVA	Excalol 597	ISP Van Dyke
Octyl methoxycinnamate	7.50%	UVB	Parsol MCX Escalol 557	Roche ISP Van Dyk
Octyl salicylate	5%	UVB	Escalol 587	ISP Van Dyk
Oxybenzone	6%	UVA	Neo Heliopan BB	Haarman & Reimer
Padimate O	8%	UVB	Escalol 507	ISP Van Dyk
Phenylbenzimidazole sulfonic acid	4%	UVB	Eusolex 232 Parsol HS	Rona Roche
Sulisobenzone	10%		UMS 40	BASF
Titanium dioxide	25%	UVB/UVA		Kobo
Trolamine salicylate	12%	UVB	None	None
Zinc oxide	25%	UVB/UVA		Kobo Sunsmart



- Expiration dates are not required on sunscreen labels if the products are stable for three years
- The term "sunblock" is not allowed on labels

- Assessment of UVA protection should be related to the SPF as the major claim on sunscreens, as recommended by the European commission, stating that UVA-PF/SPF≥1/3.
- Other UVA categories such as the Boots 5-star rating with a UVA/UVB ratio>0.9 go beyond the EU recommendation.

## How will consumers know how much UVA protection a sunscreen provides?

### the proposed UVA rating system:

- One star will represent low UVA protection
- Two stars, medium protection
- Three stars, high protection
- Four stars, the highest UVA protection available in an over-the-counter (OTC) sunscreen product.
- If a sunscreen product does not rate at least one star, FDA is proposing that its labeling bear a "no UVA protection" marking on the front label, near the SPF value.





- In USA, sunscreens are considered an OTC drug
- Required by law to prove efficacy
- Sunscreen formulation is both an art and a science
- It is not simply an emulsion system with sunscreen actives included in the formulation
- Formulation greatly influences the efficacy of the sunscreen actives



- The SPF is influenced by the type of sunscreen actives, the emulsion's oil phase, the emulsion water phase, the emulsification process.
- A chemical sunscreen active protect the skin by absorbing the UV radiation and transforming it into less damaging radiation such as heat and light
- They might also generate free radicals in response to UV radiation
- For both to occur the sunscreen active must maintain a high concentration in the SC for several hours



 The goal of the formulator is to develop the highest SPF possible using the least amount of sunscreen actives, because sunscreen actives are expensive and may be irritating

Formula 1. Sunscreen Lotion (SPF 30), from ISP Van Dyk

Ing	gredient Type	Wt %	
A.	Water (aqua)	50.40	
	Xanthan gum	1.00	
В.	Glyceryl stearate (and) laureth-23	6.00	
	PEG-20 stearate	3.00	
	Cetyl lactate	3.00	
	C12-15 alkyl lactate	1.00	
	Myristyl myristate	4.00	
	Octyl methoxycinnamate	7.50	
	Benzophenone-3	3.00	
	Octyl salicylate	3.00	
	Propylene glycol	6.00	
C.	Titanium dioxide, ultra fine	5.00	
	Isocetyl stearoyl stearate	3.00	
	Maleated soybean oil	3.00	
D.	Preservative	1.00	
E.	Fragrance (parfum)	0.10	
	2002	100.00	

#### **Procedure**

Mix C with a roller mill. Disperse A with high speed mixing. Heat to 75°C. Heat B to 80°C and add C. Add BC to A. Mix with homogenizer for 15 minutes. Mix while cooling to 40°C with a sweep blade. Add D and then E. Mix while cooling to 25°C.

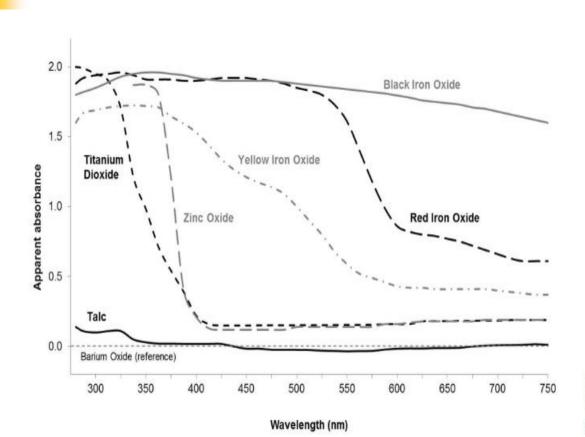


■ Terms such as sunblock, waterproof and sunproof are not allowed → misleading

## PROTECTION LEVEL

- SPF 50+ is common with both types of sunscreen
- Organic sunscreens give higher, photostable protection from UVA if you use newer filters like Tinosorbs S and M.
- Avobenzone also gives high UVA protection, but it breaks down in UV so you have to reapply every 2-4 hours (although some formulas stabilize avobenzone so it breaks down slower).

## broad spectrum protection (includes protection against longer UVA wavelength)



**Fig. 4.** Absorption of inorganic UV filters (reference barium oxide, dashed line).

Photodermatol Photoimmunol Photomed 2014; 30: 62–80 © 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd



## PHYSICAL VS CHEMICAL SUNSCREENS WHITE CAST

- Organic sunscreens leave less white cast
- inorganic sunscreens tend to leave white cast.



## Why you need to reapply

- The sunscreen is being removed by daily activities
- The film thins out
- Photodegredation (for some sunscreen ingredients)

<u>Sunscreen regulations in the world from European Union, USA, Canada to China (cosmeticsdesign-europe.com)</u>

- Sunscreen regulations in the world from European Union, USA, Canada to China (cosmeticsdesign-europe.com)
- <u>EU SPF Regulations: What's required for product claims and labels?</u>
   (ulprospector.com)