

South Beach  
Symposium  
medical + aesthetic dermatology

CELEBRATING 20 YEARS  
OF PREMIER MEDICAL & AESTHETIC  
DERMATOLOGY EDUCATION

REIMAGINING  
MEDICAL AND  
AESTHETIC  
DERMATOLOGY



# Spotlight on Sunscreens

LivDerm

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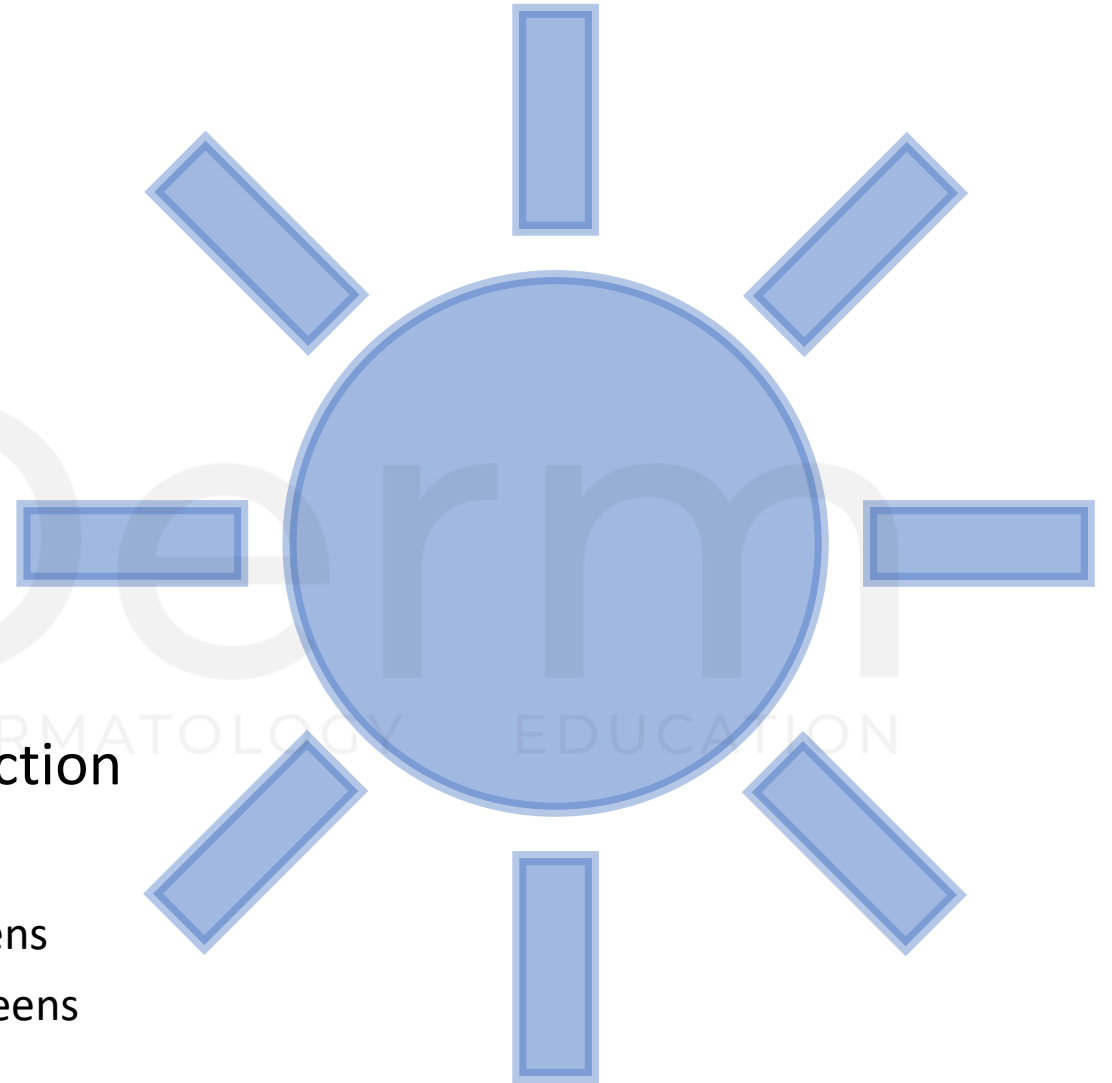
# Outline

## UV light and its effects

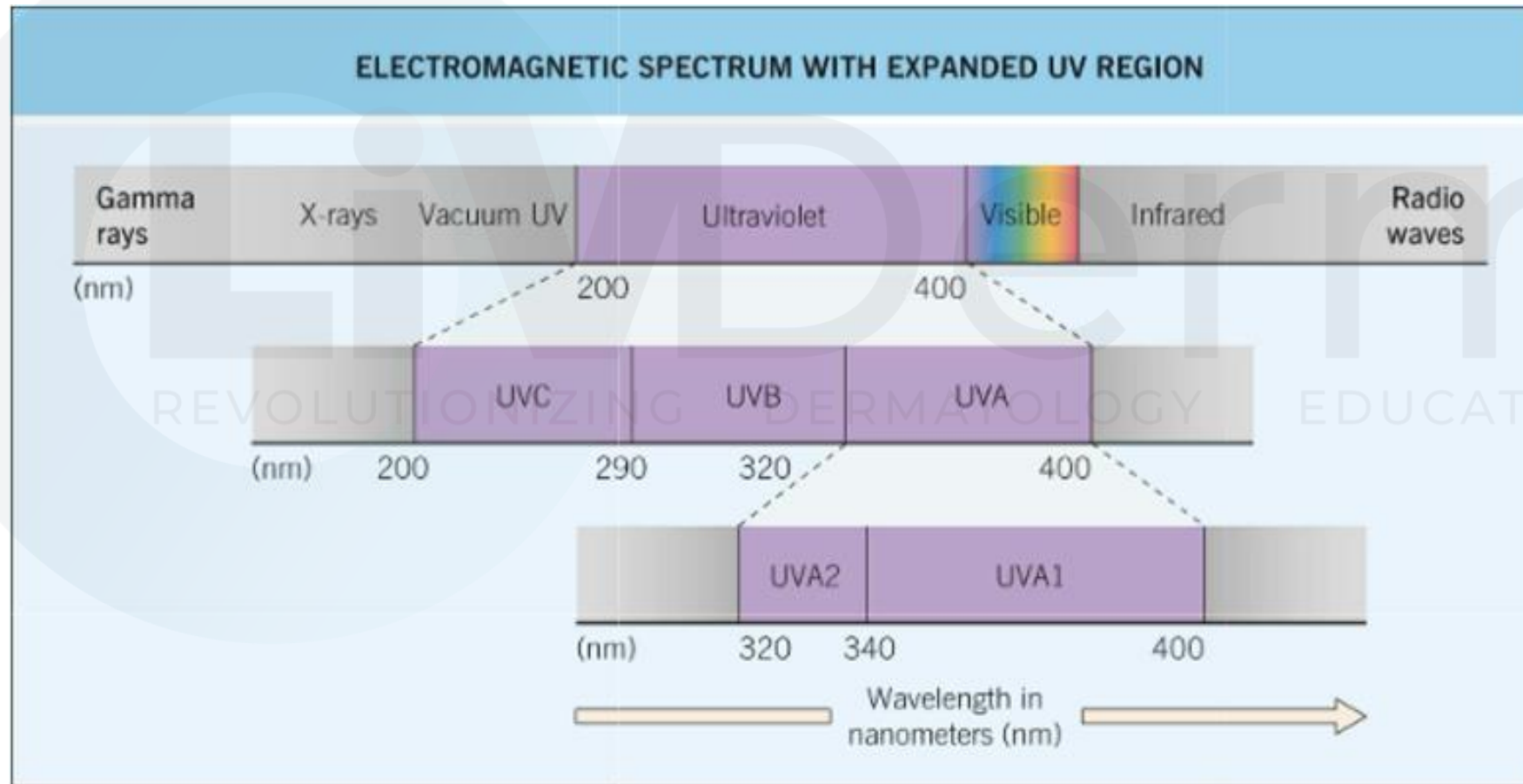
- The action spectrum
  - Sunburn
  - Tanning
  - Photoaging
  - Carcinogenesis
- UV effect at the molecular level
  - Chromophores
  - DNA damage

## Sunscreens

- History
- Regulation
- Properties
  - SPF
  - Substantivity
  - UVA protection
- Labeling in US
- Mechanism of action
- Categories
  - Organic sunscreens
  - Inorganic sunscreens
- Efficacy
- Safety



# Spectrum of UV light



# UV light

**UVC**  
**(200-290 nm)**

**Almost all** absorbed by  
earth's atmosphere

**UVB**  
**(290-315 nm)**

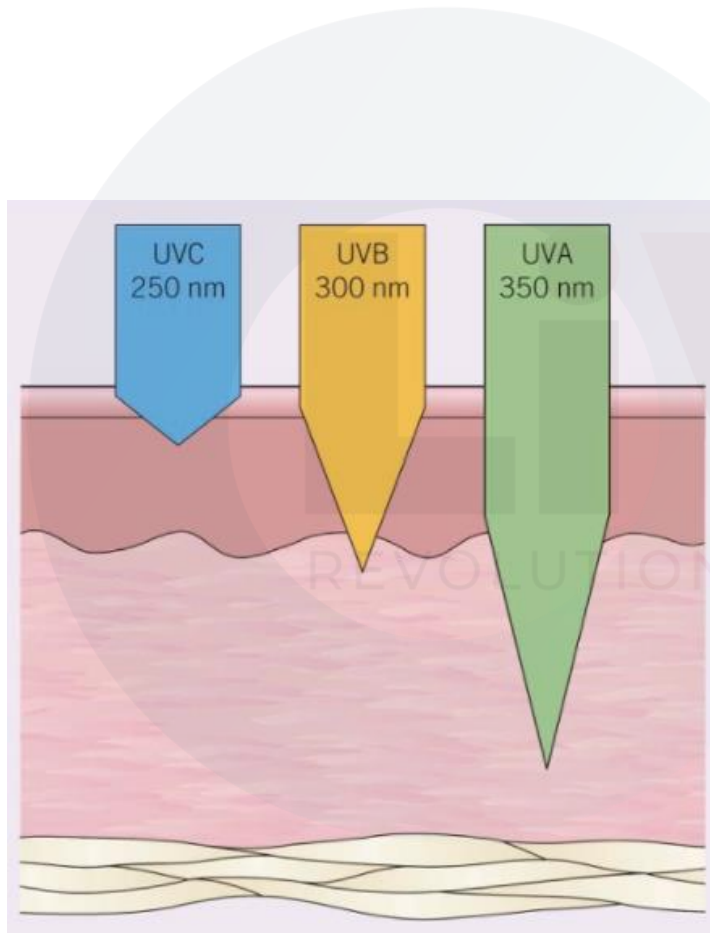
**Most** absorbed by  
earth's atmosphere

**UVA**  
**(315-400 nm)**

Composes **95%** of what  
reaches earth

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# UV light



## UVC (200-290 nm)

Almost all absorbed by earth's atmosphere

Penetrates **stratum corneum** and **superficial epidermis**

## UVB (290-315 nm)

Most absorbed by earth's atmosphere

Penetrates only **superficial dermis**

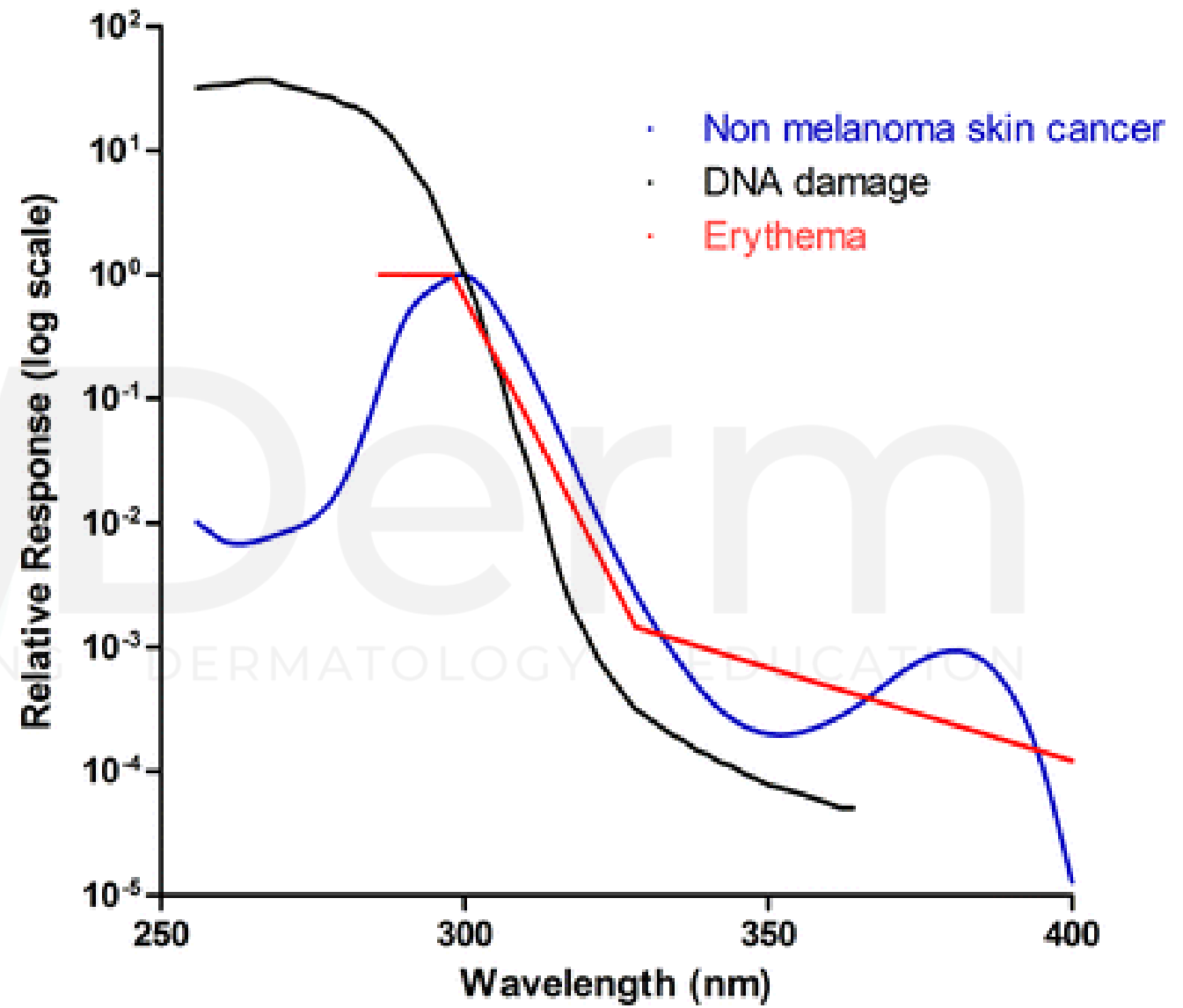
## UVA (315-400 nm)

Composes **95%** of what reaches earth

Penetrates to **deep dermis**

# The Action Spectrum

PLOT OF WAVELENGTH VERSUS  
RECIPROCAL OF THE DOSE  
REQUIRED FOR A GIVEN  
OUTCOME:



# UVR induced disease

Effect	Spectrum of light			Type of evidence
	UVB	UVA	Visible	
Sunburn	++++	+		1
Photoaging	++++	++	?	3,4
Squamous cell carcinoma	++++	+		2,3,4
Basal cell carcinoma	+++	?		2,4
Cutaneous melanoma	++	+		3,4
Photoimmune suppression	++++	++		1,3,4
Photosensitivity	+	+++	+	1 (varies with disease)

# Solar radiation summary

Radiation TypeD	Characteristic Wavelength	Effects on Human Skin	Visible to Human Eye?	Penetration in Human Skin
UVC	200-290 nm	DNA Damage	No	Superficial Epidermis
UVB	290-320 nm	Sunburn DNA Damage Skin Cancer	No	Superficial Dermis
UVA	320-400 nm	Tanning Skin Aging DNA Damage Skin Cancer	No	Deep Dermis
Visible	400-800	None Known	Yes	Stratum Corneum (polarized to superficial epidermis)
Infrared	800-120,000 nm	Heat Sensation	No	Deep Dermis



# Sunburn

**The ability to induce sunburn rapidly declines with increasing wavelengths**

- **UVB (290-315 nm)**
  - Little if any immediate erythema reaction
  - Sunburn peaks 6-24 hours after exposure
- **UVA (315-400 nm)**
  - Doses present in sunlight rarely enough to induce a sunburn
  - **Immediate** erythema reaction
  - Distinct **delayed** erythema reaction 6-24 hours later

# Personal UVR sensitivity

- Correlates with Fitzpatrick Skin type
- Can be measured by minimal erythema dose (MED)
  - Amount of UVR needed to induce just perceptible erythema 24 hours after exposure
  - Used to calculate SPF (more on this later)



# The Fitzpatrick Scale



Skin Type	Tanning Ability	Typical Features
I	Always Burns Never Tans	Pale white skin Red Hair with Freckles Blond Hair, light eyes
II	Burns Easily Tans minimally	Fair Haired Caucasians Northern Asians
III	Sometimes Burns Slowly tans to light brown	Darker Caucasians Some Asians
IV	Burns Minimally Always Tans to Moderate Brown	Mediterranean & Middle-Eastern Caucasians Southern Asians
V	Rarely Burns Tans Well	Some Hispanics Some African & African Descendants
VI	Never Burns Always Tans	Darker Africans Indigenous Australians

# Tanning

- **UVA (315-400 nm) – “tanning bed tan”**
  - **Immediate** pigment darkening
  - Oxidation and redistribution of existing melanin
  - UVA-induced tan provides **5-10x less protection** against sunburn from subsequent UV exposure
- **UVB (290-315 nm)**
  - **Delayed** reaction: Tanning peaks 3 days after exposure
  - Increased melanocytes, increased melanin synthesis, increased arborization of melanocytes, and transfer of melanosomes to keratinocytes

## Photoaging

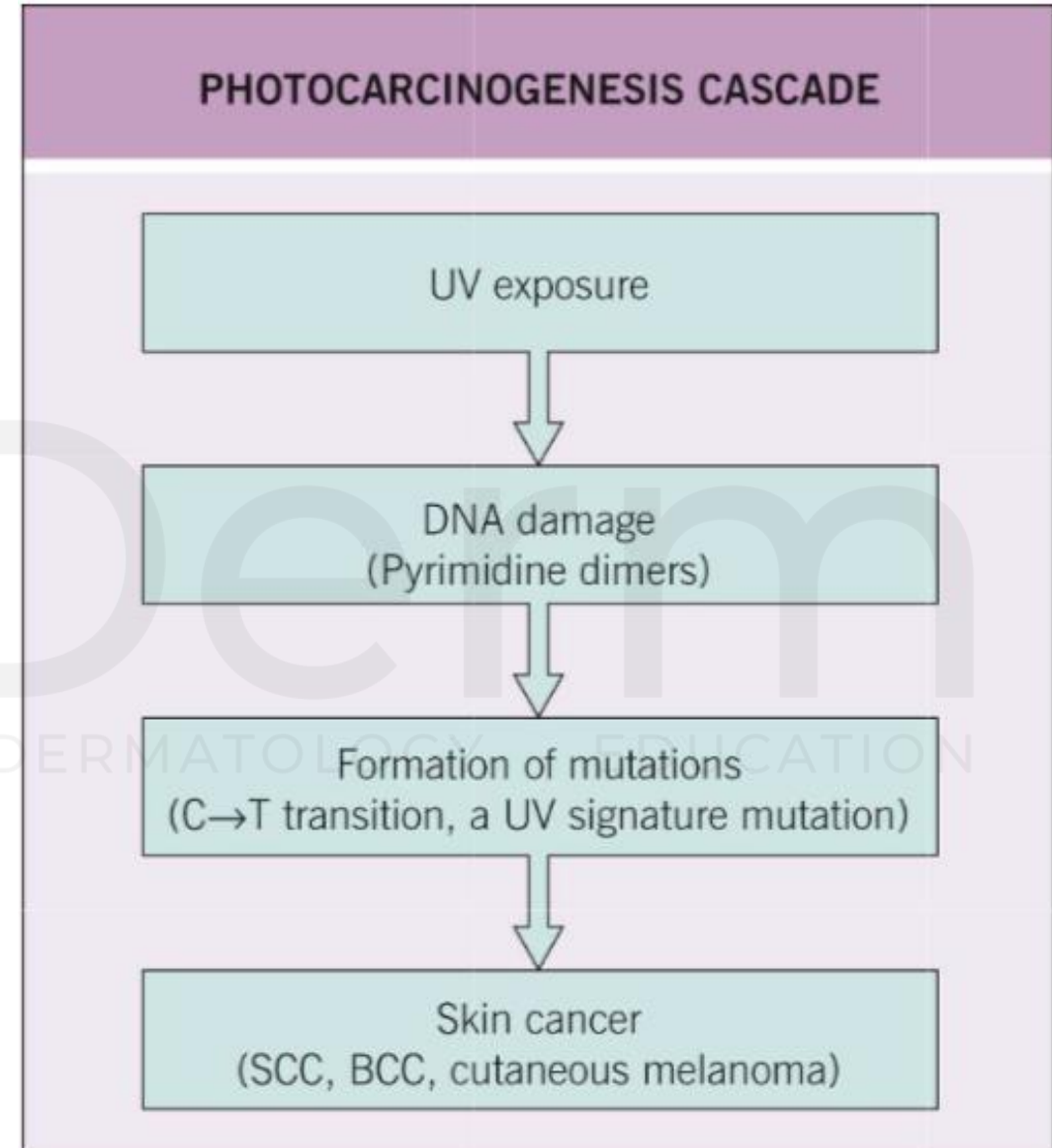
- **UVA (315-400 nm)**
  - Thought to play main role in **dermal** changes of photoaging
  - Less important in photocarcinogenesis



Only UVA penetrates through window glass

## Photocarcinogenesis

- All else equal, UVB > UVA in inducing cutaneous malignancy
- **However, UVA is**
  - More abundant in natural sunlight
  - Penetrates glass and clothing
  - Penetrates more to basal layer

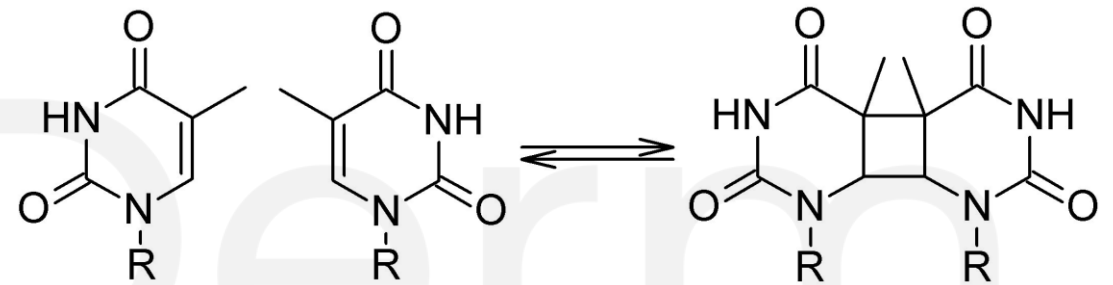


# Chromophores

- Epidermal and dermal chromophores absorb UV light as energy, become unstable
  - Direct effect: structural change, binding to other molecules
  - Indirect effect: generation of ROS, damage to adjacent molecules like DNA or proteins
- Chromophores include:
  - Endogenous: DNA, melanins, urocanic acid, aromatic amino acids, flavins, and porphyrins
  - Exogenous: photosensitizing drugs (psoralen, fluoroquinolones, SUNSCREENS)

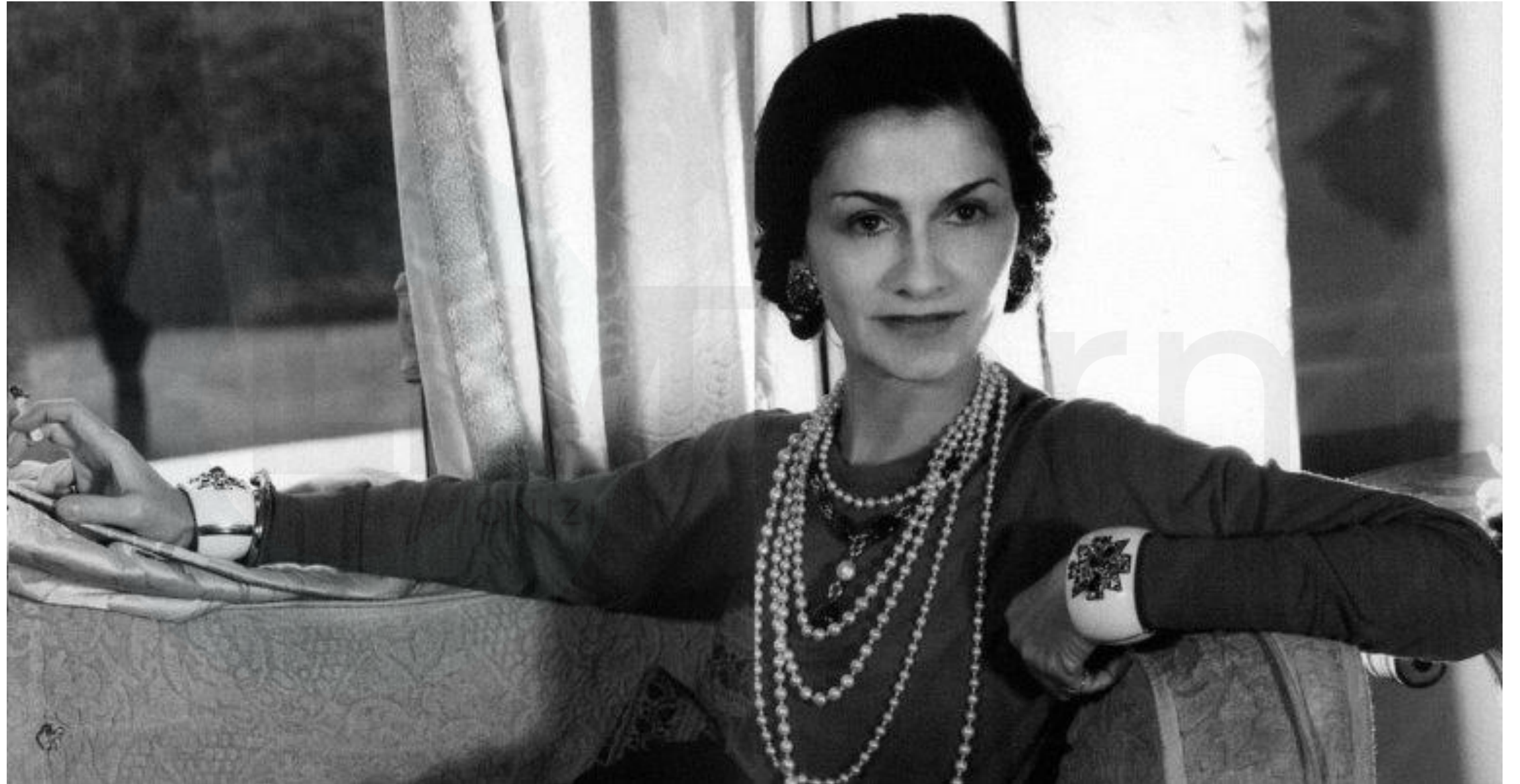
# DNA damage

- Cyclobutane pyrimidine dimers (CPDs)
  - Caused by low (even suberythemal) doses of UVB
  - Lead to transition mutations: C→T, CC→TT, implicated in NMSC
  - ?Melanoma. UVR exposure a/w 65% of melanoma cases, 90% of NMSC
  - Leads to expression of MMP-1, which degrades collagen → photoaging
- Pyrimidine (6-4) pyrimidones
  - 1/3<sup>rd</sup> frequency of CPD, but more mutagenic
- CPD and PPs removed by nucleotide excision repair, which is defective in XP
  - 10,000x risk of NMSC
  - 2000x risk of melanoma



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# Sunscreen history

- 1928: First modern sunscreen introduced (benzyl salicylate and benzyl cinnamate)
- 1930s: Red petrolatum used as sunscreen in WWII
- 1943: Para-aminobenzoic acid (PABA) patented
- 1970s: Sunscreen use started to become mainstream

**TAN... don't burn... use  
COPPERTONE**

Get a faster, deeper tan plus **GUARANTEED** sunburn protection!



*Sunbanned Screening* does it! With Coppertone, you get a faster, smoother, deeper tan, with maximum sunburn protection—than with any other leading product! That's because Coppertone's special screening agent, homomethyl salicylate, lets in the ultraviolet tanning rays that activate coloring matter deep within your skin... as it shuts out rays that burn and coarsen your skin.

*Conditions Skin, too!* The extra lanolin and other protectives in Coppertone keep it on the skin longer, protect you even after swimming. Coppertone prevents oily drying and peeling, too.

*America's Favorite!* Originated in sunny Florida, Coppertone now far outsells all other suntan products. Use it whenever you're out in the sun—at beach, pool, fishing, or right in your own backyard. Available in Lotion, Oil, Cream, Spray, and now Coppertone Shade for children and those with sensitive skin. Also Nookote. Get a rich, long-lasting Coppertone tan! Get Coppertone in large size to save most.

Also available in Canada. Another quality product of Health Inc.

Don't be a paleface!

# Sunscreen Regulation

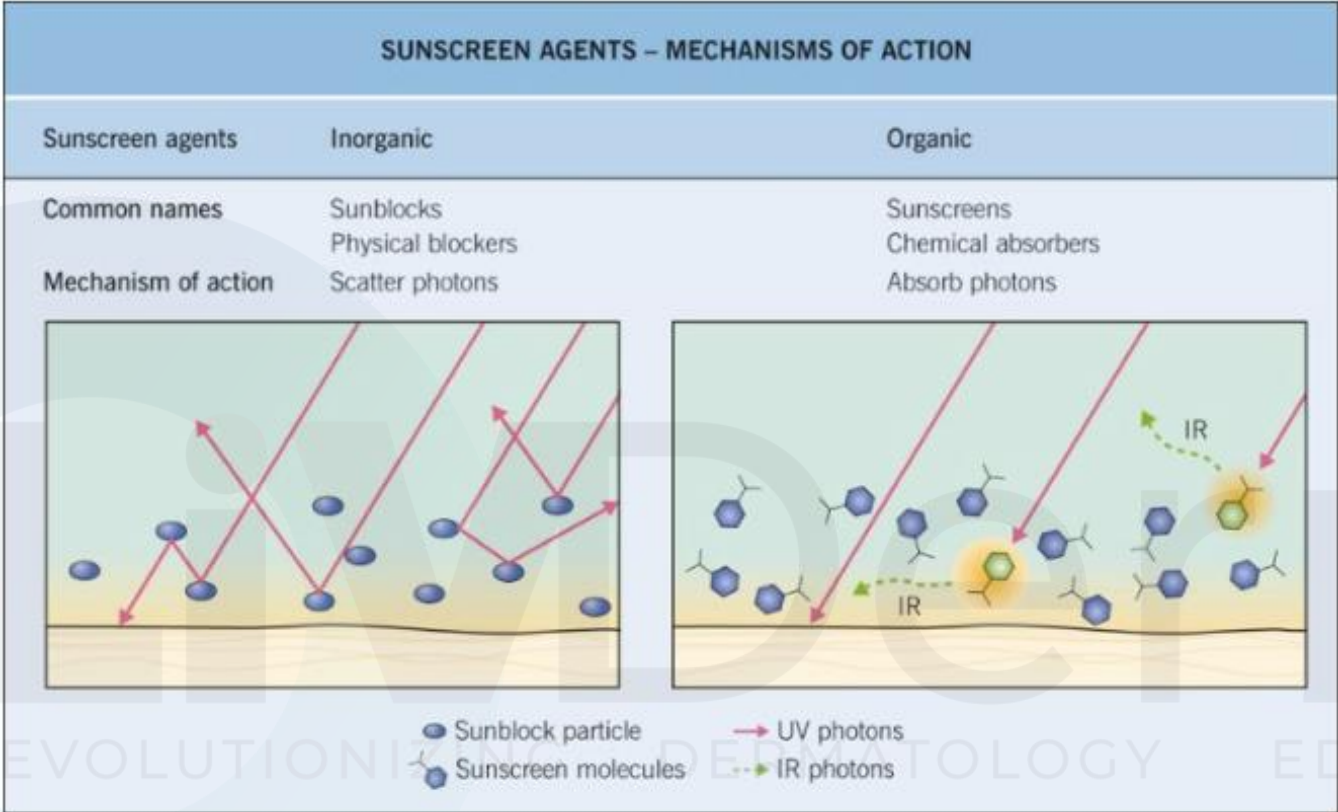


- In US, considered an over-the-counter drug, subject to FDA regulation
- In Canada, considered drug unless contain only titanium dioxide, zinc oxide, or PABA (then are “natural health products”)
- Australia: “therapeutic goods”
- Areas in Europe, Asia, South America: “cosmetics”

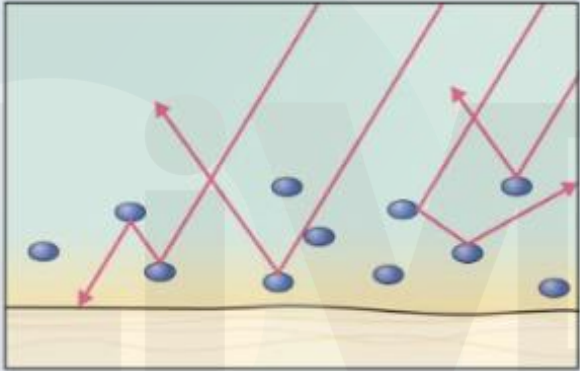
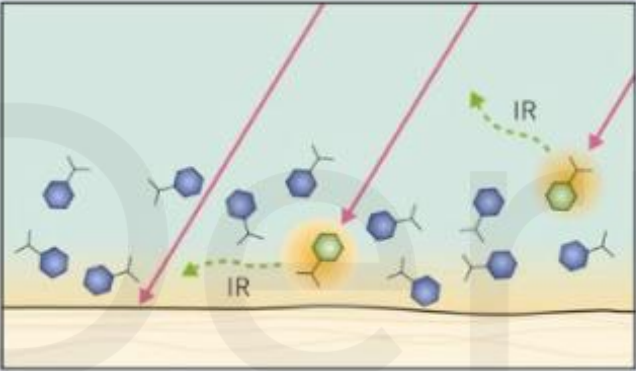

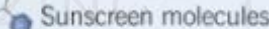
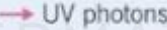
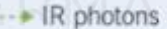
# Principle of sunscreen Effectiveness

- Protective layer of sunscreen effectively prevents sun from reaching the skin by one of two mechanisms
  - Absorption
  - Reflection

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Sunscreen MOA

SUNSCREEN AGENTS – MECHANISMS OF ACTION		
Sunscreen agents	Inorganic	Organic
Common names	Sunblocks Physical blockers	Sunscreens Chemical absorbers
Mechanism of action	Scatter photons	Absorb photons
		
	 	 

Physical sunscreens **scatter**  
 Based on particle size  
 Radiation reflected  
 away from the skin

Chemical sunscreens **absorb**  
 Based on chemical  
 structure  
 Radiation absorbed is  
 converted to energy in  
 form of heat

S u n s c r e e n M O A

# Organic “chemical” sunscreens

Category	Examples	Absorption spectrum	
PABA derivatives	<ul style="list-style-type: none"> <li>• PABA (para-aminobenzoic acid)</li> <li>• Padimate O (octyl dimethyl PABA)</li> </ul>	UVB only	<ul style="list-style-type: none"> <li>• PABA stains clothing (rarely used now)</li> </ul>
Cinnamates	<ul style="list-style-type: none"> <li>• Octyl methoxycinnamate (octinoxate, Parsol MCX)</li> <li>• Cinoxate</li> </ul>	UVB only	<ul style="list-style-type: none"> <li>• Octyl methoxycinnamate is MC ingredient used in US</li> <li>• Not as potent as PABA derivatives</li> </ul>
Salicylates	<ul style="list-style-type: none"> <li>• Octisalate</li> <li>• Homosalate</li> <li>• Trolamine salicylate</li> </ul>	UVB only	Weak absorbers, but stabilize other agents. Used in combination
Benzophenones	<ul style="list-style-type: none"> <li>• Oxybenzone</li> <li>• Sulisobenzene</li> <li>• Dioxybenzone</li> </ul>	UVB, UVA2 UVA2>UVA1 UVB>UVA2	Oxybenzone used MC

# Other organic sunscreens

Examples	Absorption spectrum	
Octocrylene	UVB	Stabilizes photolabile agents
Ensulizole	UVB	Stabilizes photolabile agents
Enzacamene	UVB	
Ethylhexyl triazone	UVB	
Avobenzene	UVA2, UVA1	Photolabile
Menthyl anthranilate	UVA 2	Weak efficacy
Ecamsule	UVA 2, UVA1	
Drometrizole trisiloxane	UVB UVA2, UVA1	
Bisotrizole	UVB UVA2, UVA1	
Bemotrizinol	UVA 2, UVA1	
Diethylamino hydroxybenzoyl hexyl benzoate	UVA 2, UVA1	
Bisdisulizole	UVA 2, UVA1	
Iscotrizinol	UVB, UVA2	



# Inorganic “physical” sunscreens

Examples	Absorption spectrum	
Titanium dioxide	UVB, UVA2, UVA1, some visible light	Large particle size have broad spectrum protection Micronized formulations lose UVA1 and visible light protection
Zinc oxide	UVB, UVA2, UVA1, some visible light	



# Newer Formulations

- Non-greasy
- Lightweight
- Not opaque



# Physical Blockers



- Other Physical Blockers:

- Tinted sunscreens (pigment particles act as physical blockers)

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# Chemical Blockers

- Formulations containing one or more of the following:
  - PABA, PABA Esters
  - Benzophenones
  - Cinnamates
  - Salicylates
  - Digalloyl trioleate
  - Anthranilates
- Mechanism: Absorb UV Radiation

PABA

- Very effective UVB chemical sunscreen
- Most effective at 5% in 70% Alcohol
- Maximum benefit when applied 60 minutes prior to exposure for stratum corneum binding
- Contact dermatitis
- May stain clothing

## PABA Esters (Padimate a, o, Glyceryl Paba)

- Very effective UVB sunscreen
- Most effective in 2.5-8% concentration in 65% alcohol
- Penetrates less effectively than PABA
- Similar application and adverse effect
- Less likely to stain

Benzophenones  
(oxybenzone,  
dioxibenzone,  
sulisobenzone)

- Slightly less effective than PABA
- Effective in both UVA and UVB ranges
- Synergistic with PABA and PABA esters (enhances effect of either and is enhanced by combination with either)
- Can prevent photosensitivity reactions
- Rare contact dermatitis

Cinnamates,  
Salicylates

- Minimally effective
- UVB range
- Not generally used alone

Revividerm  
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Anthranilates

- Minimally Effective
- UVA absorption
- Usually combined with UVB absorbers to broaden spectrum

## Ideal Sunscreen Characteristics

Absorb/Reflect UVR in the 280-320 nm range

Water resistant

Stable to heat, light, perspiration

Odorless, mild odor usually acceptable

Non-toxic, non-irritant, non-sensitizing

Capable of maintaining sunscreen properties for several hours

Non-staining

Not rapidly absorbed

Rapidly soluble in appropriate vehicles

# Sun Protection Factor

## Requirements for testing of SPF

- 10 human subjects with skin type I or II
- Light source mimicking solar spectrum
- Determine MED in protected and unprotected skin



# Sun Protection Factor

- Ratio of doses of solar-simulated radiation causing erythema with sunscreen applied to that without sunscreen
- $SPF = \text{MED with sunscreen} / \text{MED without sunscreen}$
- SPF 15 allows 15 times as much time in the sun with the same resultant erythema as without the product in a given individual



## RELATIONSHIP OF THE SUN PROTECTION FACTOR (SPF) TO BLOCKAGE OF ERYTHEMAL RADIATION

Blockage of erythemal radiation (%)
90
92.5
95
97.5

# Substantivity

- To test “water resistance,” subjects immersed in whirlpool bath after application and before MED testing
  - 40 minutes: 2 x 20 min immersions
  - 80 minutes: 4 x 20 min immersions

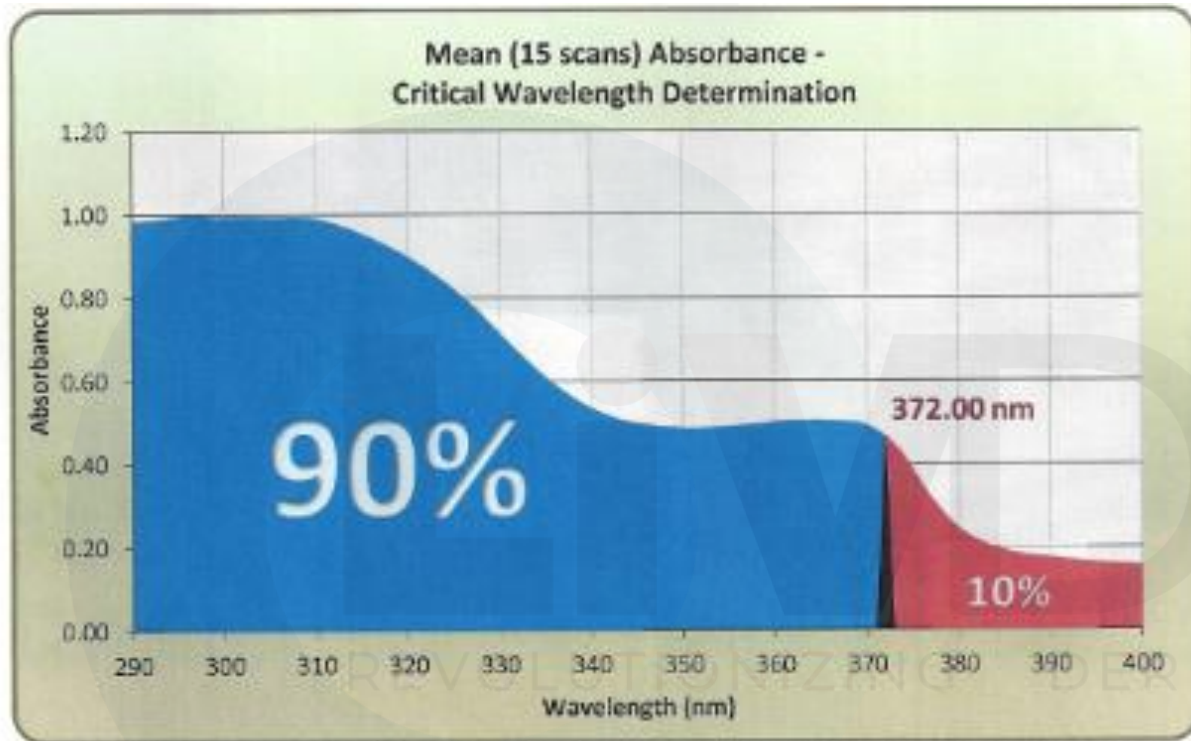


# UVA protection

- Sunburn is a good indicator of UVB exposure
- UVA exposure does not have a similar endpoint that can be easily measured



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The Critical Wavelength of the above test material (AMA Lab No.: N-9078; Client No.: Sunscreen Lotion SPF 45 Lot # 44606 Sunscreen-Comp EM 001 Active: ZnO 9%, Octinoxate 7.5%) is 372.00 nm, and satisfies the criteria for "Broad Spectrum" labeling (minimum of 370 nm required).

## UVA protection

- **In vivo method:** measures either immediate or delayed pigment darkening
- **In vitro method:** absorption spectrum of sunscreen is determined by a spectrophotometer
  - **Critical wavelength:** wavelength below which 90% of solar-simulated radiation is absorbed
  - Higher critical wavelength = more UVA coverage

# Labeling of sunscreens

## **FDA published “The Final Rule” on labeling in 2011**

- Sun protection factor (SPF): up to 50+ (will consider higher ratings if data supportive)
- UVA protection
  - “Broad spectrum” only if critical wavelength above 370 nm (must do in vitro testing)
  - Otherwise this label is not included
- Substantivity
  - Water resistant (40 minutes) or water resistant (80 minutes)



# Labeling of sunscreens



-  Waterproof
-  Sunblock
-  All day protection
-  Sweat proof

# Labeling of sunscreens

- SPF  $\geq$  15 **AND** broad spectrum:
  - “This product can help to reduce the risk of skin cancer and the risk of early skin aging, when used regularly and as directed in combination with other sun protection measures”
- SPF  $<$  15 **OR** not broad spectrum
  - “Spending time in the sun increases your risk of skin cancer and early skin aging. This product has been shown only to help prevent sunburn, not skin cancer or early skin aging”



## Drug Facts

### Active Ingredients

Avobenzone 3%  
Homosalate 10%  
Octyl methoxycinnamate 7.5%

### Purpose

Sunscreen

### 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 sun

### Warnings

For external use only

Do not use on damaged or broken skin

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

Stop use and ask a doctor if rash occurs

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

### Directions

- apply liberally 15 minutes before sun exposure
- reapply:
  - after 40 minutes of swimming or sweating
  - immediately after towel drying
  - at least every 2 hours

**Sun Protection Measures**—Depending on 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 of 15 or higher and other sun protection measures including:

- limit time in the sun, especially from 10 a.m. – 2 p.m.
- wear long-sleeve shirts, pants, hats, and sunglasses
- children under 6 months: Ask a doctor

### Inactive ingredients

aloe extract, barium sulfate, benzyl alcohol, carbomer, dimethicone, disodium EDTA, jojoba oil, methylparaben, octadecene/MA copolymer, polyglyceryl-3 distearate, phenethyl alcohol, propylparaben, sorbitan isostearate, sorbitol, stearic acid, tocopherol (vitamin E), triethanolamine, water

### Other information

- protect this product from excessive heat and direct sun

### Questions or comments?

Call toll free 1-800-XXX-XXXX

# Sunscreen effectiveness - sunburn

- Pre-marketing studies show ability to prevent sunburn
  - 2 mg/cm<sup>2</sup> (for average adult: 2 tablespoons per application)
- In real world, not so much
  - Studies show sunscreens users apply on 25-75% of that
  - SPF reduced proportionally: SPF 20 has a practical SPF of 5 to 15
  - Reapplication?



# Sunscreen effectiveness - photoaging

- In animal studies, prevents clinical and histologic changes of photoaging
  - May reduce damage that already occurred
- In human studies, reduction in dermal elastosis, prevention of biochemical measures of sun damage



# Sunscreen effectiveness - photocarcinogenesis

- The wavelengths of light most responsible for photocarcinogenesis is debated
- **SCC and BCC** are thought to be caused mostly by UVB, although UVA may play a role
- **Melanoma** very controversial. Most likely UVB
- **Remember, 10-20x as much UVA as UVB in sunlight. Someone wearing UVB protective sunscreen may stay in sun longer, getting UVA radiation**

# Sunscreen effectiveness - photocarcinogenesis

- NMSC
  - AKs studied because earlier endpoint
  - Significantly fewer when wearing SPF 29 over 2 years
  - In Australian prospective study:
    - Active intervention group: Sunscreen supplied and use encouraged vs. background rate of sunscreen use in general population
    - Sunscreen group had less SCCs, no difference in BCCs
    - Matches with clinical distribution of SCC vs. BCC

# Sunscreen effectiveness - photocarcinogenesis

- Melanoma risk using nevi as marker
  - Sun exposure in children linked to more nevi AND higher risk melanoma
  - Retrospective studies: children using sunscreens have **increased** number of nevi
  - Prospective controlled study: sunscreens suppress development of nevi in children
- Melanoma
  - Retrospective studies of melanoma patients: some show decreased risk with sunscreen usage, others show increased risk
  - Meta-analysis: sunscreen doesn't increase risk, but can't confirm that it prevents melanoma
  - Randomized trial of daily vs. discretionary sunscreen use.  
11 melanomas in daily, 22 in discretionary group (p=0.05)



# Sunscreen effectiveness – photoimmune suppression

- UVB > UVA
- Sunscreen protects against it, but not as well as it protects against sunburn
- Some investigators want to put “immune protection factor” (IPL) on the label

# Sunscreen effectiveness – photosensitive disorders



UVA, VISIBLE LIGHT > UVB



AVOBENZONE AND ECAMSULE  
PRODUCTS MOST EFFECTIVE

# Polymorphous light eruption (PMLE)

- UVA > UVB



# Hydroa Vacciniforme

- UVA > UVB



# Solar urticaria

- UVA, Visible > UVBB



# Chronic Actinic Dermatitis

- UVB > UVA > Visible



# Actinic Prurigo

- UVA = UVB



Photoallergic,  
Photoirritant,  
Phototoxic drug  
reactions

- UVA >> UVB, Visible





# Porphyria

- Visible



# Cutaneous lupus erythematosus

- UVB > UVA



# Sunscreen effectiveness – photosensitive disorders

CLASSIFICATION AND ACTION SPECTRA OF PHOTOSENSITIVE SKIN DISEASES			
Disease	Spectrum of light		
	UVB	UVA	Visible
Polymorphic light eruption	+	++	
Hydroa vacciniforme	+	++	
Solar urticaria	+	++	++
Chronic actinic dermatitis	+++	++	+
Actinic prurigo	++	++	
Photoallergic contact dermatitis		+++	
Photoirritant contact dermatitis		+++	
Photodrug reactions	+	+++	+
Porphyria			+++
Cutaneous lupus erythematosus	+++	++	

# Sunscreen safety

- No human studies suggest carcinogenic or mutagenic
- Sunscreen ACD/ICD usually due to additive, not sunscreen itself
  - However, allergy to oxybenzone, padimate O, avobenzone described
- Lack of Vitamin D: confirmed in studies (though still in normal range)