Photoprotection and Skincare

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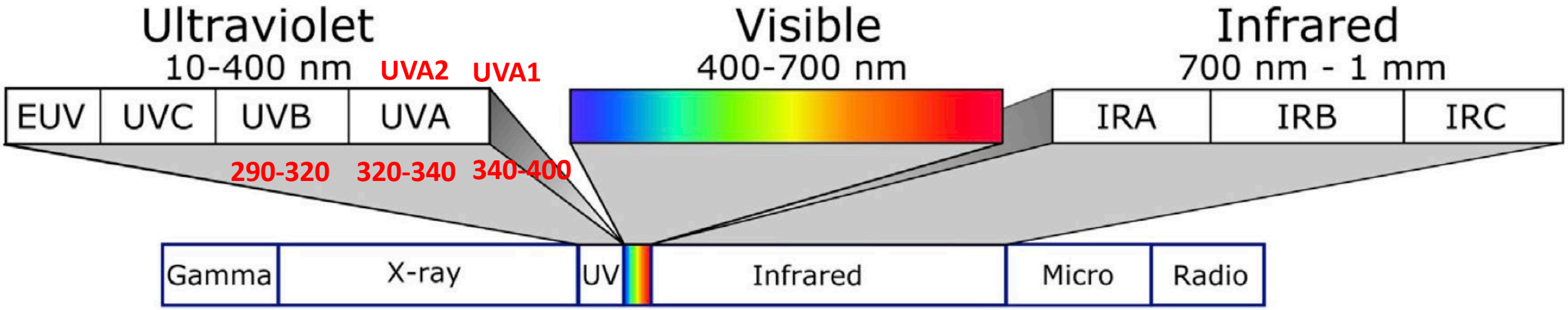
Disclosures

- Bristol Myers Squibb
- Castle Biosciences
- Dermavant Sciences
- DermTech
- Galderma
- LEO Pharma
- Lilly
- National Eczema Association
- Ortho Dermatologics
- Pfizer
- RBC Consultants
- Verrica Pharmaceuticals

Electromagnetic Spectrum



- Actinic dermatitis
- Cutaneous malignancies
- Photodermatoses (e.g. lupus, PMLE)
- Solar urticaria (mast cell-mediated)
- Photoaging

- **Hyperpigmentation**
  - **Redistribution of melanin from basal layer to upper epidermis**
- Erythema
- Oxidative stress
- Actinic dermatitis (rarely)
- Solar urticaria (mast cell-mediated)
- Porphyrias
- PMLE (rarely)

***Blue light emitted from devices is low-intensity and cumulative dose is not sufficient to cause hyperpigmentation**

The Algebra of Sunscreen

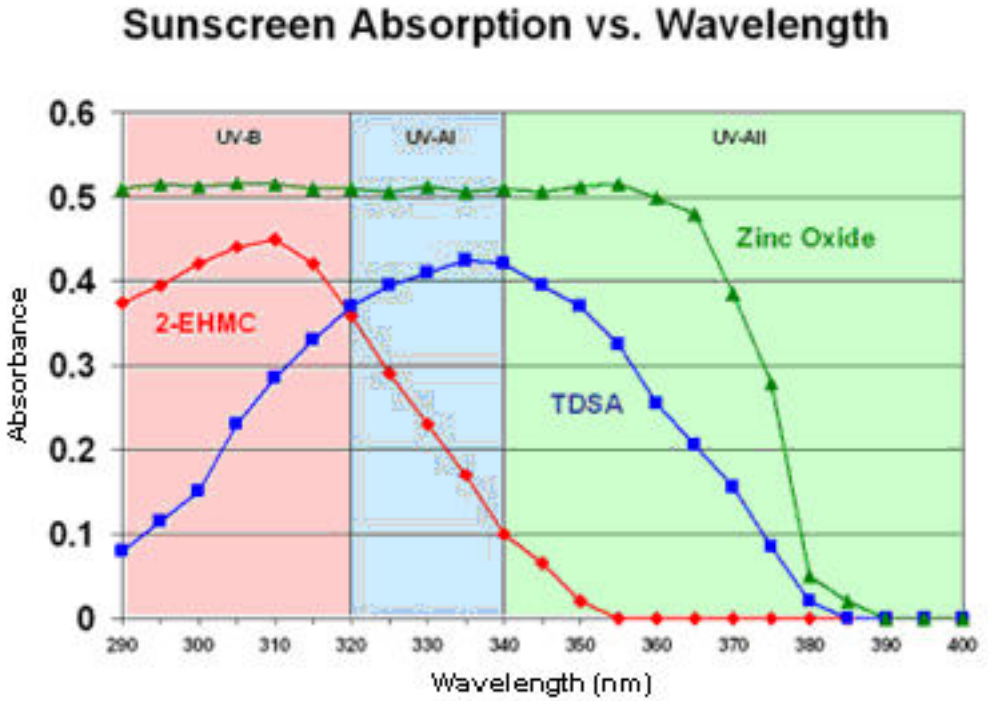
Sunscreen = (Filter) * (Filter pharmacokinetics) * (Vehicular elegance) +/- (Tint) +/- (Bioactive add-ons)

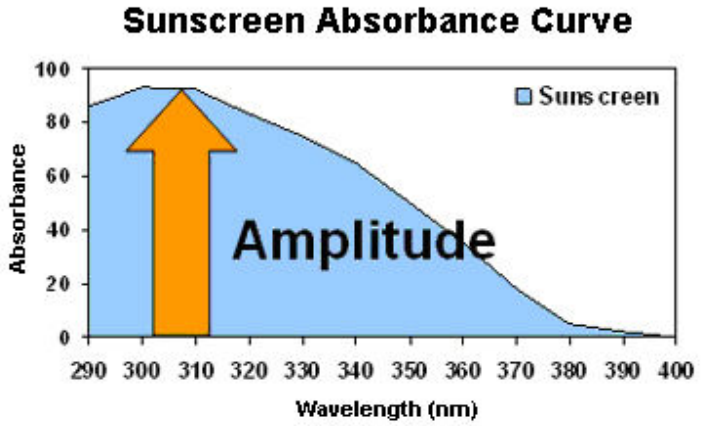
- Filter = UVA, UVB, Visible light
  - Sun protection factor (SPF) based on human UV erythemal action spectrum
  - Critical wavelength 370nm
  - "Broad-spectrum" = covers entire UV spectrum
    - US 2019 designation: "A UVA I/UV ratio of 0.7 or higher, indicating that the product provides a minimum measure of UVA I radiation absorbance relative to total UV radiation (i.e., UVB + UVA) absorbance, in addition satisfying to the 370 nm critical wavelength requirement"
    - Broad-spectrum products would have more uniform amount of radiation protection against UVA1, UVA2 and UVB ranges
  - Understanding of filter and filter metabolite(s) pharmacodynamics (e.g. endocrine disrupting effects?)
- Filter pharmacokinetics
  - Avoiding absorption/penetration through skin is critical
  - Vehicle formulation is critical for elegance, filter photostability, filter solubility & distribution a
    - Encapsulation techniques with nanotechnology, alginate microparticles, cyclodextrins
    - Semi-crystalline polymers
- Vehicular elegance
  - Spreadability, application into hair-bearing areas
- Tint
  - Iron oxides (Fe_2O_3) added to cover VL spectrum and different skin colors are mimicked using a combination of different oxidation states of iron oxide
- Bioactive add-ons
  - Anti-oxidants for synergy (reduction of ROS), hyaluronic acid
  - Repair enzymes (i.e. photolyase)

Sun Protection Factor (SPF)

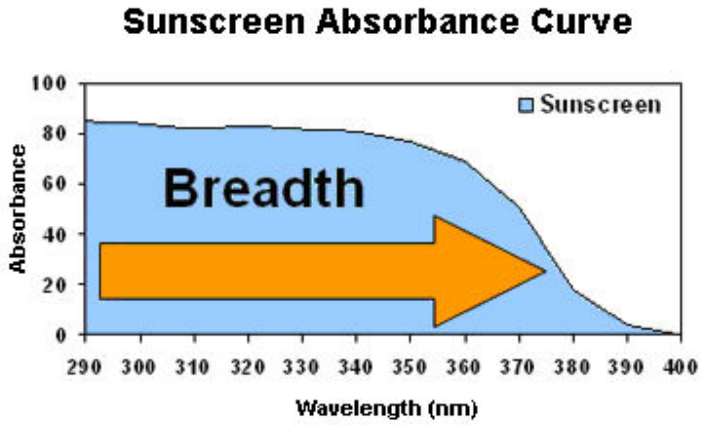
- Measures effectiveness of sunscreen at blocking UVB (erythema)
- No consensus on how to measures UVA protection yet
- UVA1 (340–400 nm) preferentially induces CPD in the basal layer, which contains stem cells and melanocytes,63 as well as damaging DNA repair enzymes.64
- Studies in vivo or in 3D skin models, have shown that for a given SPF a high UVA-PF sunscreen offers better protection against pigmentation, photoageing and DNA damage compared with low UVA-PF

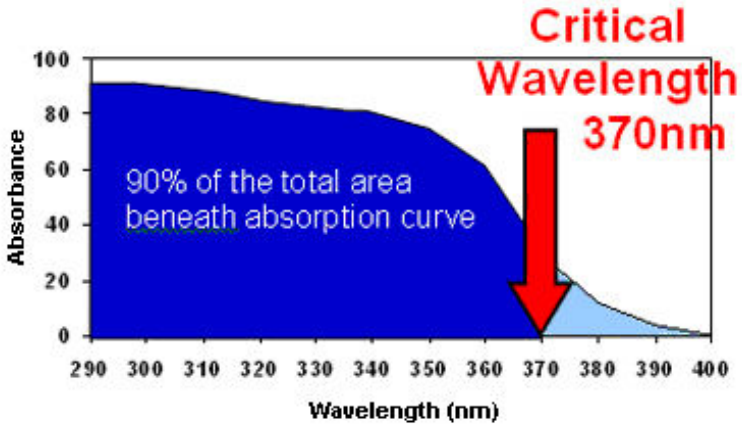
Critical Wavelength





***SPF describes amplitude of protection in UVB range**

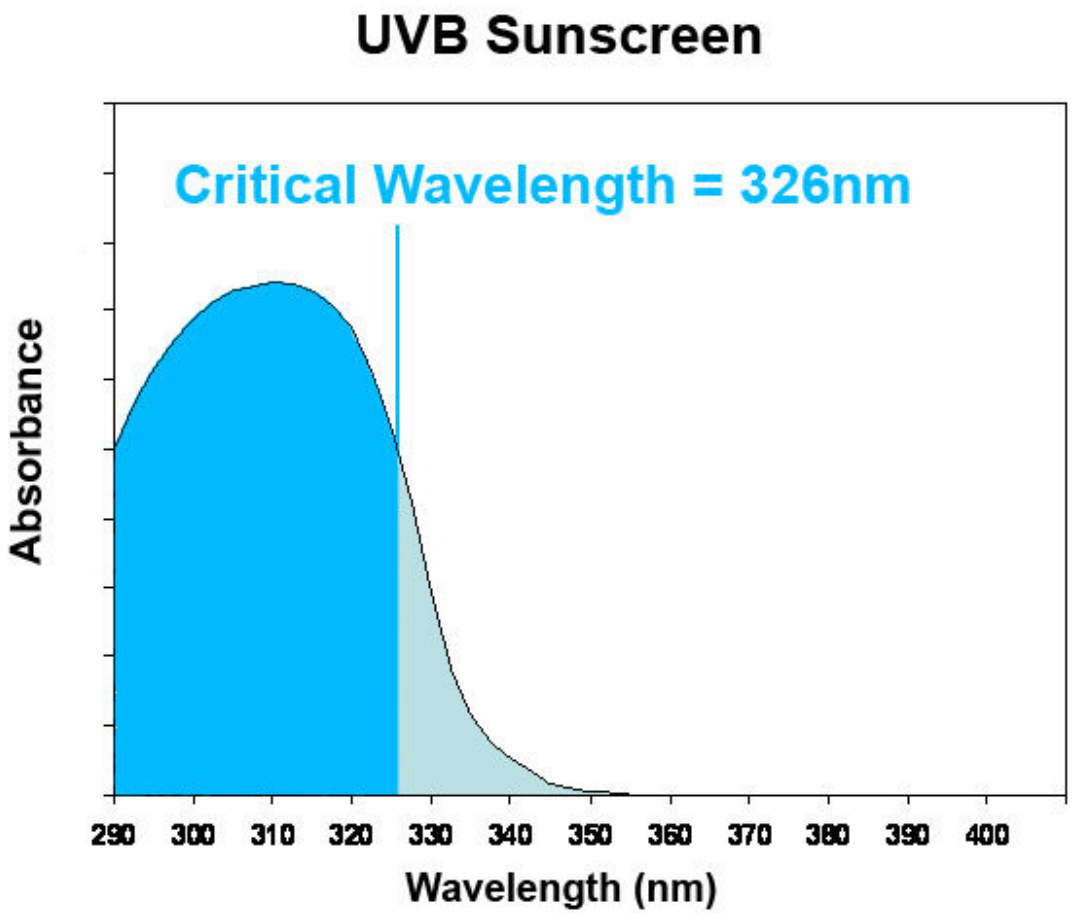


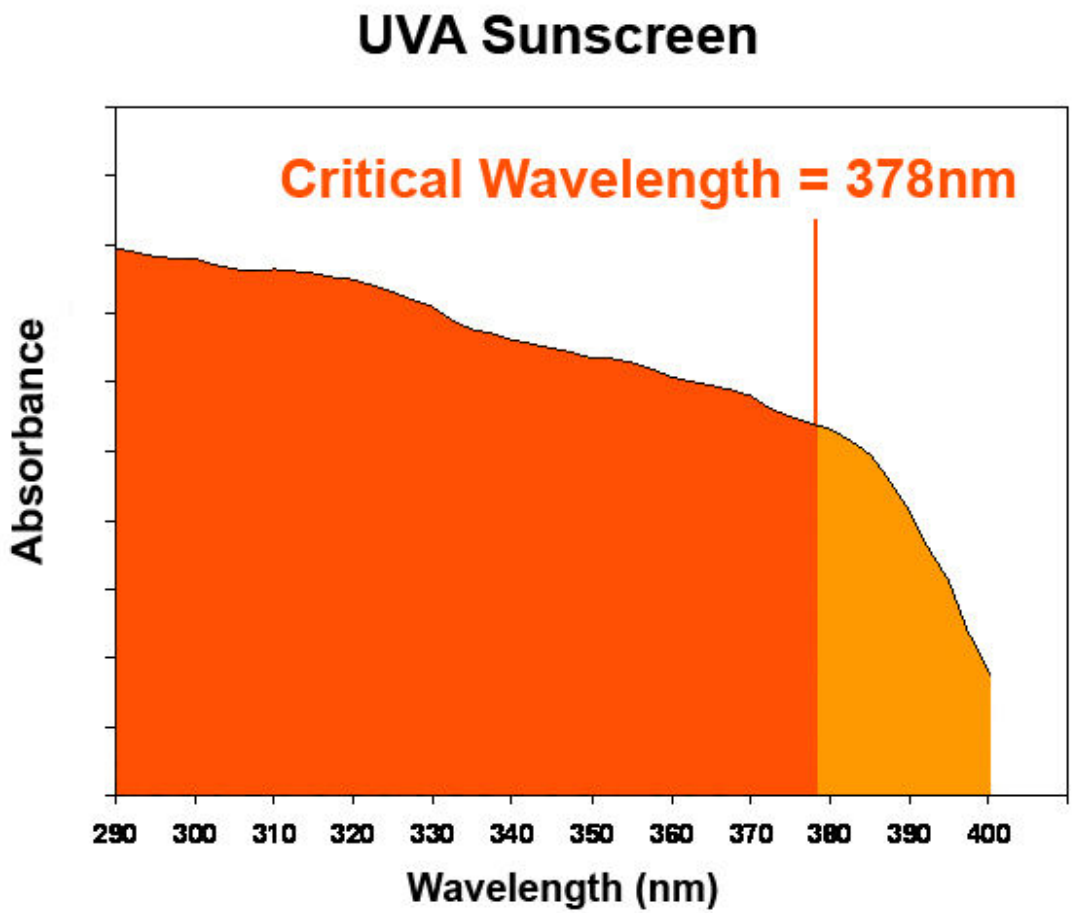


***FDA requires 370nm for "broad spectrum" coverage.** Higher critical wavelength ensures MORE UV PROTECTION (especially longer UVA)

https://drdembny.com/critical-wavelength-and-broad-spectrum-uv-protection/

Critical Wavelength





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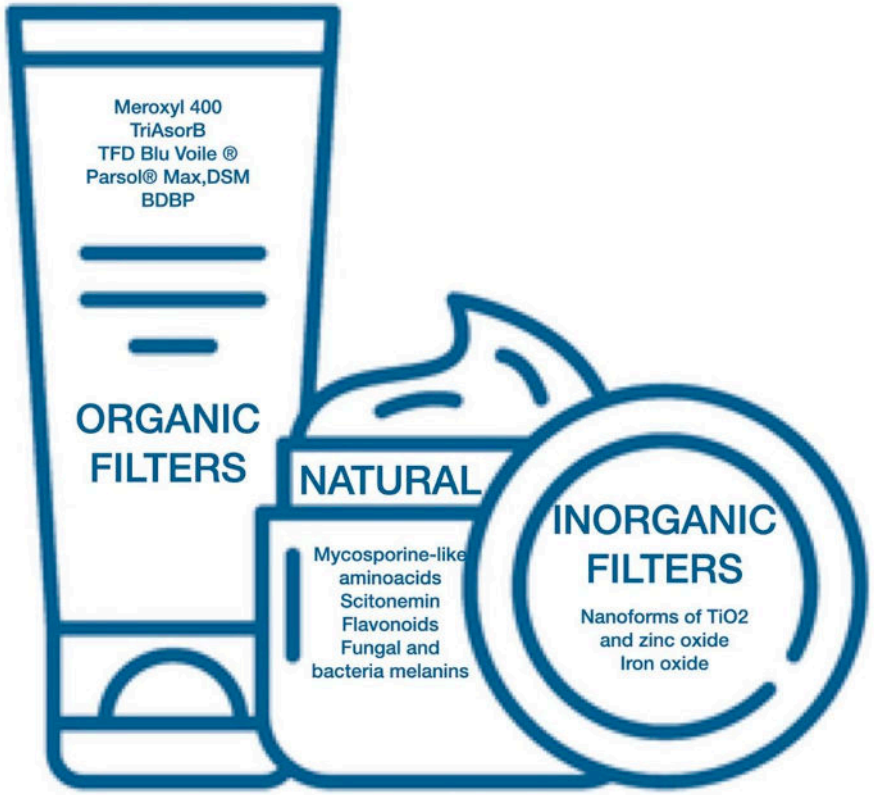
Filters



Photochemical & Photobiological Sciences (2023) 22:2473–2482
https://doi.org/10.1007/s43630-023-00453-x

REVIEWS

New developments in sunscreens

José Aguilera[1] · Tamara Gracia-Cazaña[2,3] · Yolanda Gilaberte[2,3]

Visible light. Part II: Photoprotection against visible and ultraviolet light

Amaris N. Geisler, BS,[a] Evan Austin, BS,[b,c] Julie Nguyen, MD,[b,c] Iltefat Hamzavi, MD,[d] Jared Jagdeo, MD, MS,[b,c] and Henry W. Lim, MD[d]
New York and Brooklyn, New York; and Detroit, Michigan

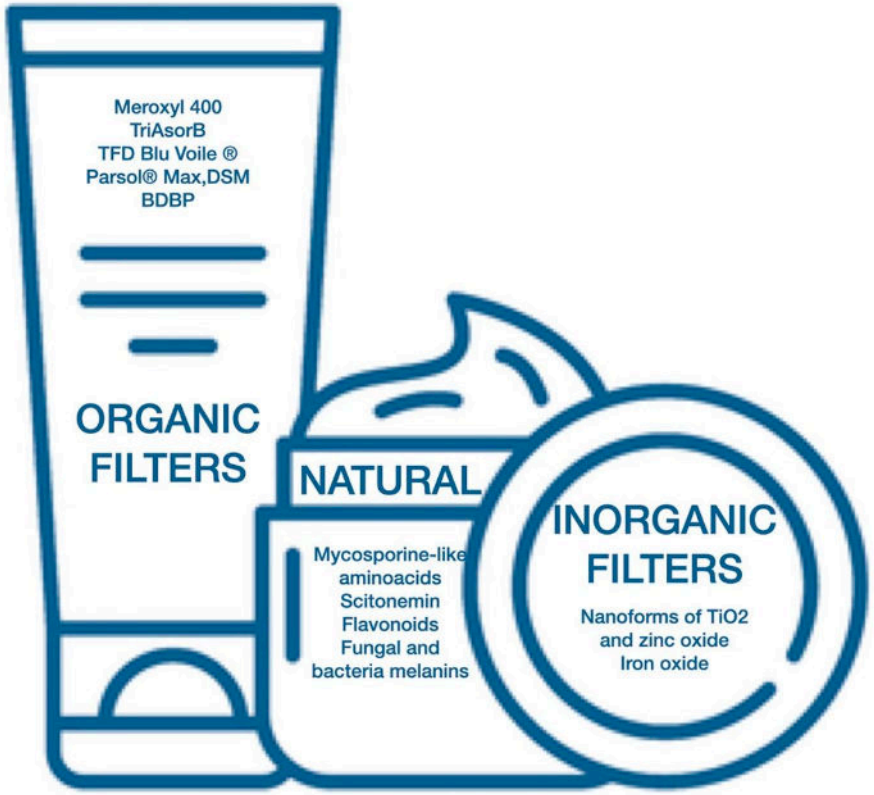
Table I. Approved UV filters listed in the 1999 United States Food and Drug Administration sunscreen monograph[30,46,73]

Light filter	Maximum approved concentration (%)	Peak absorption (nm)	Action spectrum
Organic filters			
PABA derivatives			
PABA	15	283	UVB
Padimate O	8	311	UVB
Benzophenones			
Dioxybenzone	3	352	UVB, UVA2
Oxybenzone	6	288, 325	UVB, UVA2
Sulisobenzone	10	366	UVB, UVA2
Salicylates			
Homosalate	15	306	UVB
Octisalate	5	307	UVB
Trolamine salicylate	12	260-355	UVB
Cinnamates			
Cinoxate	3	289	UVB
Octinoxate	7.5	311	UVB
Other			
Avobenzone	3	360	UVA2, UVA1
Ensulizole	4	310	UVB
Meradimate	5	340	UVA2
Octocrylene	10	303	UVB, UVA2
Inorganic filters			
Titanium dioxide	25		UVB, UVA2, UVA1
Zinc oxide	25		UVB, UVA2, UVA1

Filters

10-year retrospective analysis of ~24,000 patch-tested patients revealed ~0.9% had a sunscreen allergy, of which 70% were due to OXYBENZONE

Oxybenzone named contact allergen of the year by the American Contact Dermatitis Society. European Scientific Committee on Consumer Safety recommends replacing with other filters.



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Filters

NO **natural organic sunscreens are currently included in the lists of approved sunscreen filters of different international regulatory agencies.**

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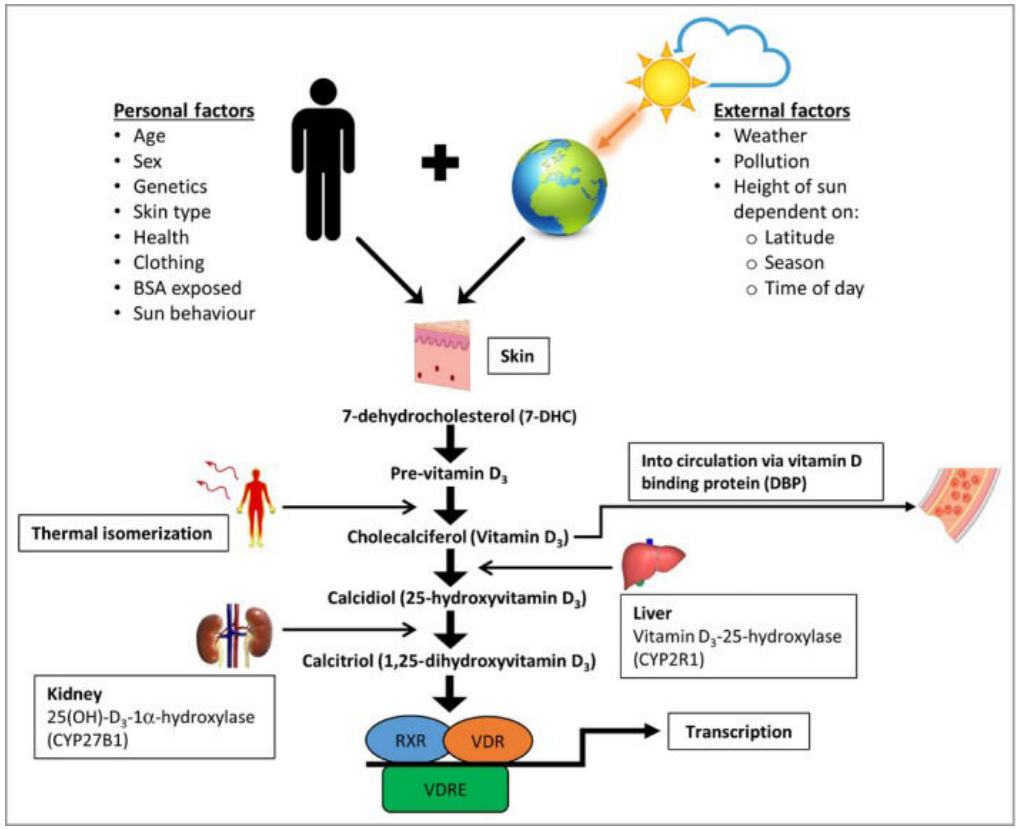
Prevention of Skin Penetration

Organic Filters and Endocrine Disruption?

Sunscreen & Natural Vitamin D Production

- UVB mainly responsible for Vit D synthesis
- UVA2 may cause Vit D degradation
  - High UVA-PF showed greater Vit D synthesis than low UVA-PF
- Studies show that serum 25(OH)D can be increased with repeated **suberythemal UVB** exposure that is transmitted through sunscreens
- Recommendation from Passeron et al (2019) (international panel consensus):
- ***Sunscreen use for daily and recreational photoprotection need not compromise skin vitamin D synthesis, even when applied under optimal conditions. Increasing the UVA-PF for a given SPF improves vitamin D3 production.***
- AAD and the National Council on Skin Cancer Prevention recommend both receiving vitamin D through the diet and oral supplements and avoiding intentional UV radiation exposure



REVIEW ARTICLE

BJD
British Journal of Dermatology

Sunscreen photoprotection and vitamin D status*

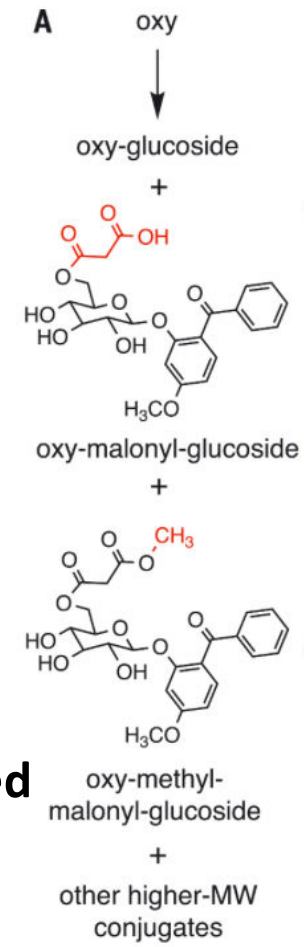
T. Passeron,[1,2] R. Bouillon,[3] V. Callender,[4] T. Cestari,[5] T.L. Diepgen,[6] A.C. Green,[7,8] J.C. van der Pols,[9] B.A. Bernard,[10] F. Ly,[11] F. Bernerd,[12] L. Marrot,[12] M. Nielsen,[10] M. Verschoore,[10] N.G. Jablonski[13] and A.R. Young[14]

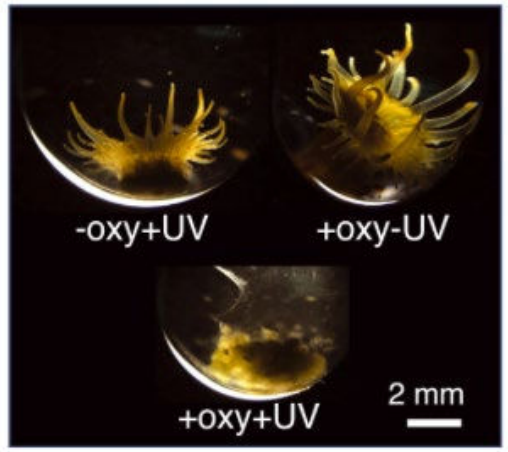
Visible light. Part II: Photoprotection against visible and ultraviolet light

Amaris N. Geisler, BS,[a] Evan Austin, BS,[b,c] Julie Nguyen, MD,[b,c] Iltefat Hamzavi, MD,[d] Jared Jagdeo, MD, MS,[b,c] and Henry W. Lim, MD[d]
New York and Brooklyn, New York; and Detroit, Michigan

Sunscreen & Coral Reefs

- Estimated ~14,000 tons of UV filters released annually
- Oxybenzone metabolized into phototoxic glucoside conjugate in coral and cause reef bleaching
  - Symbiont algae help sequester these metabolites
- Similar concerns for other organic UV filters
- Hawaii has strictest ban in USA
  - 2021: oxybenzone, octinoxate (cinnamate ester)
  - 2023: avobenzone, octocrylene added
  - Maui: non-mineral sunscreen
- Reef-safe alternatives = mineral sunscreens (ZnO, TiO)
  - ***Careful as ”reef-safe” and “reef-friendly” terms are NOT regulated
- **HOWEVER! Study done in Oahu, HI showed that concentrations detected in seawater were 1000-fold LOWER than those reported to be cytotoxic to coral reefs in vitro**
- **Ocean water warming is a major contributing factor**





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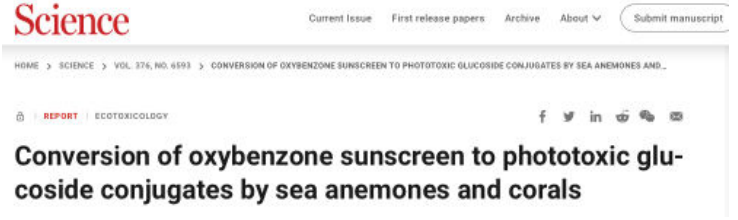
Science

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HOME › SCIENCE › VOL. 376, NO. 6593 › CONVERSION OF OXYBENZONE SUNSCREEN TO PHOTOTOXIC GLUCOSIDE CONJUGATES BY SEA ANEMONES AND...

REPORT | ECOTOXICOLOGY

Conversion of oxybenzone sunscreen to phototoxic glucoside conjugates by sea anemones and corals

2019 Key West, FL attempted to pass bill to ban sale of sunscreens containing oxybenzone and octinoxate but Gov. Ron DeSantis signed bill in 2020 that prevented it from going into effect.

Florida's coral reefs valued at ~$8.4 billion annually…

Florida Phoenix

EDUCATION HEALTH POLITICS & LAW ENVIRONMENT CULTURE & SOCIETY WORKING & THE ECONOMY

ENVIRONMENT HEALTH WORKING & THE ECONOMY

DeSantis signs bill prohibiting Florida cities from banning any sunscreens – even those that threaten corals

BY: **LAURA CASSELS** - JUNE 30, 2020 2:10 PM

Nanoparticle ZnO & TiO Safe?

Ultraviolet Protective Clothing (UPF)

- Standardized in vitro measurement of UVA and UVB protection of clothing
- Qualities of fabric that render sun protection:
  1. Construction: thicker, denser, tightly woven fabrics transmit less UVR
  2. Color: dark saturated or brighter reflective
  3. Material:
  4. Treatment: some chemicals/dyes may be added to absorb UVR
     - Chemicals/dyes may be removed with washing cycles so UPF rating may decrease over time

UPF RATINGS

HOW THE UPF SCALE WORKS

A regular cotton t-shirt typically has a UPF rating of only 5-7. Roughly 20% of UV rays pass through.

GOOD
UPF 15

93.3% UVA and UVB Radiation Blocked
6.7% Effective UV Transmission.

Anything less is not considered protective.

A UPF rating of 30 means that only 1 in 30 units of UV that reach the fabric will pass through to you.

Look for clothing that is **at least rated UPF 30 or higher** and bears the Skin Cancer Seal of Recommendation.

VERY GOOD
UPF 25-35

BEST
UPF 50-50+

98% of rays blocked
Less than 2.5% Effective UV Transmission

RECOMMENDED
SKIN CANCER FOUNDATION
ACTIVE

UPF 30+ Required for Seal of Recommendation

Oral Photoprotection - *Polypodium leucotomos* extract

- OTC fern extract
- Rich in polyphenols: ferulic acid, caffeic acid, etc.
- Multiple in vitro & in vivo studies showing anti-oxidative and anti-inflammatory effects
- NOT functioning as a filter (no SPF) but affecting post-UV/VL cellular effects

Table 1 Effects of *Polypodium leucotomos* extract on ultraviolet radiation-induced photoaging in vitro and in vivo

References	Cell types/substrates	Effect of PLE following UV exposure
In vitro studies		
Philips et al. [10]	Fibroblasts, keratinocytes	↓LDH release (fibroblasts only) ↓MMP-1 ↑Elastin
Philips et al. [28]	Fibroblasts	↑TGF-β ↑Type I collagen ↑Type V collagen
Philips et al. [12]	Keratinocytes	↓Elastase ↑TIMP-1 ↑TIMP-2 ↑Fibrillin-1 ↑Fibrillin-2 ↑TGF-β ↑HSP-27 and HSP-70
Alonso-Lebrero et al. [31]	Fibroblasts, keratinocytes	↑Cell survival (fibroblasts and keratinocytes) ↑Cell proliferation (fibroblasts and keratinocytes) ↓Cytoskeletal disorganization (fibroblasts only)
Capote et al. [32]	Trans-urocanic acid, Fibroblasts	↓Cis-UCA (± H_2O_2) ↓Trans-UCA photodecomposition (in the presence of TiO_2) ↑Fibroblast survival
Janczyk et al. [35]	Keratinocytes	↓TNF-α ↓NO

Table 2 Effects of *Polypodium leucotomos* extract on visible light-induced photoaging in vitro and in vivo

References	Cell types/substrates	Effect of PLE following VL exposure
In vitro studies		
Delgado-Wicke et al. [36] Gonzales et al. [38]	Zamarron et al. [45] Fibroblasts	Delayed morphologic abnormalities ↓MMP-1 ↓Cell death rates ↓Cathepsin-K (trend) ↑Fibrillins ↑Elastin
References	Model	Effect of PLE following VL exposure
In vivo studies		
Mohammad et al. [47]	Human	↓COX-2 ↓MMP-2 (trend) ↓MART-1 (trend) ↓MMP-1 (trend) ↓MMP-9 (trend) ↓Persistent pigment darkening ↓Delayed tanning
Truchuelo et al. [48]	Human	↓MMP-1

Photochemical & Photobiological Sciences
https://doi.org/10.1007/s43630-021-00087-x

REVIEWS

The potential effect of *Polypodium leucotomos* extract on ultraviolet- and visible light-induced photoaging

Aunna Pourang[1] · Mohsen Dourra[2] · Nneamaka Ezekwe[1] · Indermeet Kohli[1] · Iltefat Hamzavi[1] · Henry W. Lim[1]

Hair Photoprotection?

- Solar radiation affects human hair: color change, loss of gloss, loss of mechanical strength
- Gray hair lacks photoprotective melanin
- Colored / dyed hair damaged more quickly than natural hair (synthetic pigment)
- Wet hair particularly prone to UV radiation
- UVR → oxidation of lipids & proteins in shaft → ROS → keratin denaturation
- Many organic filters do not adhere well to hair surface
- products usually contain silicones, which are responsible for the even filters distribution on the hair surface, antioxidants to neutralize free radicals, and organic filters. Despite the use of coating substances, such as silicones, products in the form of aerosols and mists are not evenly distributed on the surface of the hair shafts. Unfortunately, the inability to cover every millimeter of hair thoroughly, limits the effectiveness of the cosmetics.

Skin Research & Technology
Open Access
ORIGINAL ARTICLE | Open Access

Assessment of the photoprotection properties of hair cosmetics using the hemispherical directional reflectance method

Anna Stolecka-Warzecha, Sławomir Wilczyński, Małgorzata Bożek, Sylwia Libionka, Łukasz Chmielewski

First published: 15 October 2023 | https://doi.org/10.1111/srt.13443

UV Radiation Damage

- Reactive oxygen species (ROS) → inflammation, collagen/elastin degradation, pigmentary alterations, cellular apoptosis
  - Superoxide, Hydrogen Peroxide
  - Depletion of enzymatic and non-enzymatic antioxidant systems
- Cyclobutane pyrimidine dimers (CPDs) → actinic keratoses, cutaneous malignancies

Antioxidants

- Scavenge UV-induced reactive oxygen species (ROS)
- UV organic filters unstable in presence of ROS, so **antioxidants may increase filter photoprotective effects via stabilizing**
- Enzymatic:
  - Catalase
  - Superoxide Dismutase
  - Glutathione peroxidase
- Non-Enzymatic:
  - α-tochopherol (Vitamin E) and derivatives tocopheryl acetate, tocopherl glucoside
  - Ascorbic acid (Vitamin C) and derivatives ascorbal palmitate, ascorbal tetraisopalmitate, 3-O-ethyl ascorbic acid, ascorbyl glycoside
  - Niacinamide
  - Coenzyme Q (CoQ10) – Ubiquinone (oxidized), Ubiquinol (reduced)
  - Glutathione
  - Oxothiazolidine
  - Ferulic acid and derivatives erythl ferulate, ehtylhexyl ferulate
  - Ectoine
  - Polyphenols, flavonoids
  - Ubiquinone

Research Article

Coenzyme Q_{10} Sunscreen Prevents Progression of Ultraviolet-Induced Skin Damage in Mice

Haiyou Wu,[1,2] Zhangfeng Zhong,[1] Sien Lin,[1,3] Chuqun Qiu,[1] Peitao Xie,[2] Simin Lv,[4] Liao Cui,[1] and Tie Wu[1,4]

cosmetics

MDPI

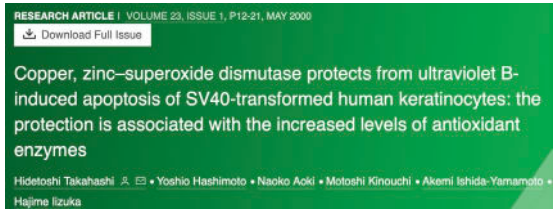
Commentary

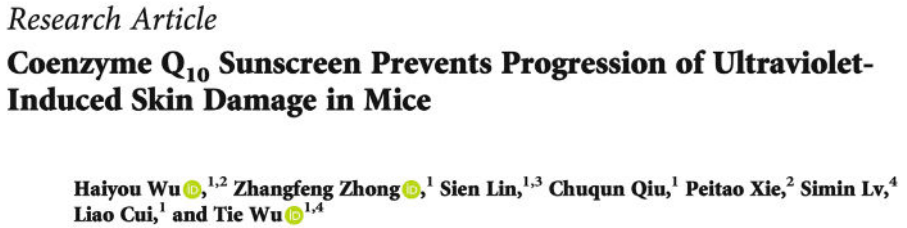
Benefits of Anti-Aging Actives in Sunscreens

Karl Lintner

Enzymatic Antioxidants: Superoxide Dismutase (SOD) & Catalase

- Scavenge UV-induced reactive oxygen species (ROS)
  - SOD: superoxide; Catalase: hydrogen peroxide
- **UV irradiation depletes SOD & Catalase → oxidative stress**
- Can counteract by:
  - Increasing SOD/Catalase expression endogenously in keratinocytes
    - Some antioxidants such as CoQ10 can do this!
  - Increase proteins (i.e. heat shock protein, HSP) that protect SOD/catalase
  - Exogenously applying enzymes SOD/catalase
    - Difficult to formulate, may have regulatory hurdles
  - Develop mimetics (i.e. from other organisms *Thermus thermophile* bacteria)





Cannabidiol (CBD) and Photoprotection?

- Dose-dependent protective effect on both keratinocyte and melanocyte viability in presence of UVB irradiation
- Possibly acting as an anti-oxidant, reverse apoptotic pathways

Contents lists available at ScienceDirect

Redox Biology

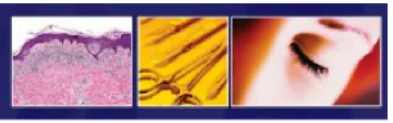
journal homepage: www.elsevier.com/locate/redox

Research Paper

Cannabidiol protects keratinocyte cell membranes following exposure to UVB and hydrogen peroxide

S. Atalay [a], I. Dobrzyńska [b], A. Gęgotek [a], E. Skrzydlewska [a,*]

JCD Journal of Cosmetic Dermatology Open Access



LETTER TO THE EDITOR

Novel cannabidiol sunscreen protects keratinocytes and melanocytes against ultraviolet B radiation

Pranjal Gohad MS, PhD, John McCoy PhD, Carlos Wambier MD, PhD, Maja Kovacevic MD, Mirna Situm MD, Andrija Stanimirovic MD, PhD, Andy Goren MD

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

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Therapeutic application of cannabidiol on UVA and UVB irradiated rat skin. A proteomic study

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Photoprotective Effects of Cannabidiol against Ultraviolet-B-Induced DNA Damage and Autophagy in Human Keratinocyte Cells and Mouse Skin Tissue

by Yanmei Li [1,2], Dan Hao [1,2], Danfeng Wei [1,2], Yue Xiao [1,2], Lian Liu [1,2], Xiaoxue Li [1,2], Lian Wang [1,2], Yu Gan [3], Wei Yan [1,2,*], Bowen Ke [3,*] and Xian Jiang [1,2,*]

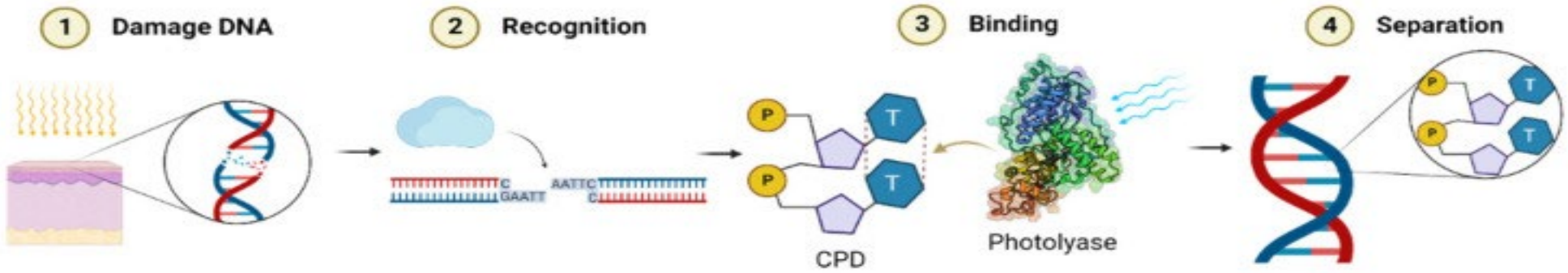
Actively Reversing Sun Damage?

- Incorporating **photolyase and other DNA repair enzymes** directly into sunscreen product
- **RECRUITING** DNA repair enzymes

Photolyase

molecules
MDPI
Review
Photolyase Production and Current Applications: A Review

- Naturally occurring DNA repair enzyme
- Use light-dependent process to restore DNA integrity
- **Reverse cyclobutene pyrimidine dimers (CPDs) and pyrimidine-pyrimidone (6-4) photoproduct (6-4PP), prevent apoptotic cell death, and treat actinic keratoses**
- Reduce photoaging via reduction of pro-inflammatory cytokine IL-6 and MMP1 (degrade collagen and elastin)
- Absent in humans and placental animals
  - Humans can only repair DNA lesions using **nucleotide excision repair (NER)**



Supplementary Material

Appendix I: How to Identify Commercial Products with DNA Repair Enzymes

DNA repair enzymes used in cosmetics and consumer products are most often listed on the label by either their tradename or their common industry-assigned name, as follows:

Photolyase: Photosomes® / plankton extract

UV Endonuclease: Ultrasomes® / micrococcus lysate

OGG1: Roxisomes® / arabadopsis thalania extract

T4 endonuclease V in liposomes is not currently available commercially.

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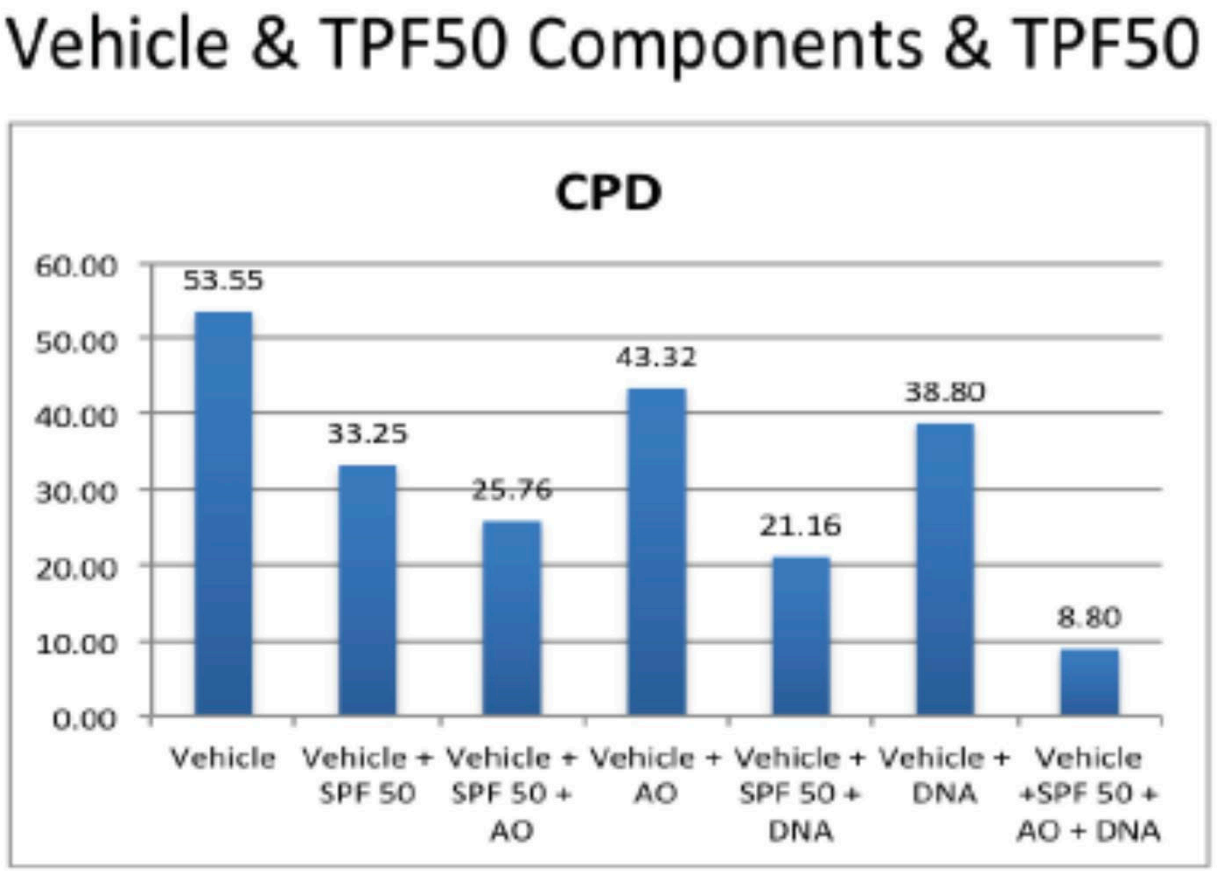
REVIEW

Six critical questions for DNA repair enzymes in skincare products: a review in dialog

Combination of UV Filter, Anti-Oxidants, and DNA Repair Enzymes is Synergistic!

FIGURE 1. Amount of CPDs after experimental irradiations in the 8 study arms.



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An Experimental Double-Blind Irradiation Study of a Novel Topical Product (TPF 50) Compared to Other Topical Products With DNA Repair Enzymes, Antioxidants, and Growth Factors With Sunscreens: Implications for Preventing Skin Aging and Cancer

Enzo Emanuele MD PhD,[a] James M. Spencer MD MS,[b] and Martin Braun MD[c]

Recap Photoprotection Objectives

- Understand clinical relevance of electromagnetic spectrum
  - UVC, UVB, UVA2, UVA1, Visible Light (VL), Infrared (IR)
- Understand what goes into making effective sunscreen formulations and what SPF is
- Identify and classify sunscreen UV filters approved by the FDA
  - Appreciate the development of novel UV filters (i.e. plant-based)
  - Learn about photoprotection against visible light Appreciate safety of organic sunscreen UV filters with respect to endocrine disruption and coral reefs
- Recognize that natural vitamin D production occurs despite sunscreen usage
- Appreciate UPF clothing
- Recognize utility of scalp hair photoprotection
- Appreciate oral forms of photoprotection
- Understand the adjunctive role of antioxidants in sunscreen formulations
- Be aware of enzymes (i.e. supraoxide dismutase) included in sunscreens that act as antioxidants
- Be aware of enzymes (i.e. photolyases) included in sunscreen products that simultaneously reverse UV-damaged skin (i.e. reverse CPD dimers)
- Appreciate that combination products may exhibit synergistic photoprotective effects

Thank You!

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