AAD and Photoprotection

Henry W. Lim, MD
Former President, AAD
Department of Dermatology
Senior Vice President for Academic Affairs
Henry Ford Hospital, Detroit, Michigan, USA

AMERICAN ACADEMY of DERMATOLOGY | ASSOCIATION

Disclosure

- *Investigator:*
  - Incyte
  - L'Oréal
  - Pfizer
  - PCORI
- Consultant:
  - Pierre Fabre
  - ISDIN
  - Ferndale
  - Galderma
- Speaker, educational session:
  - Johnson & Johnson
  - Ra Medical Syteem

Photoprotection

- Environmental impact
- Photoprotection for visible light
- Photoprotection of SOC
- AAD and photoprotection

Photoprotection

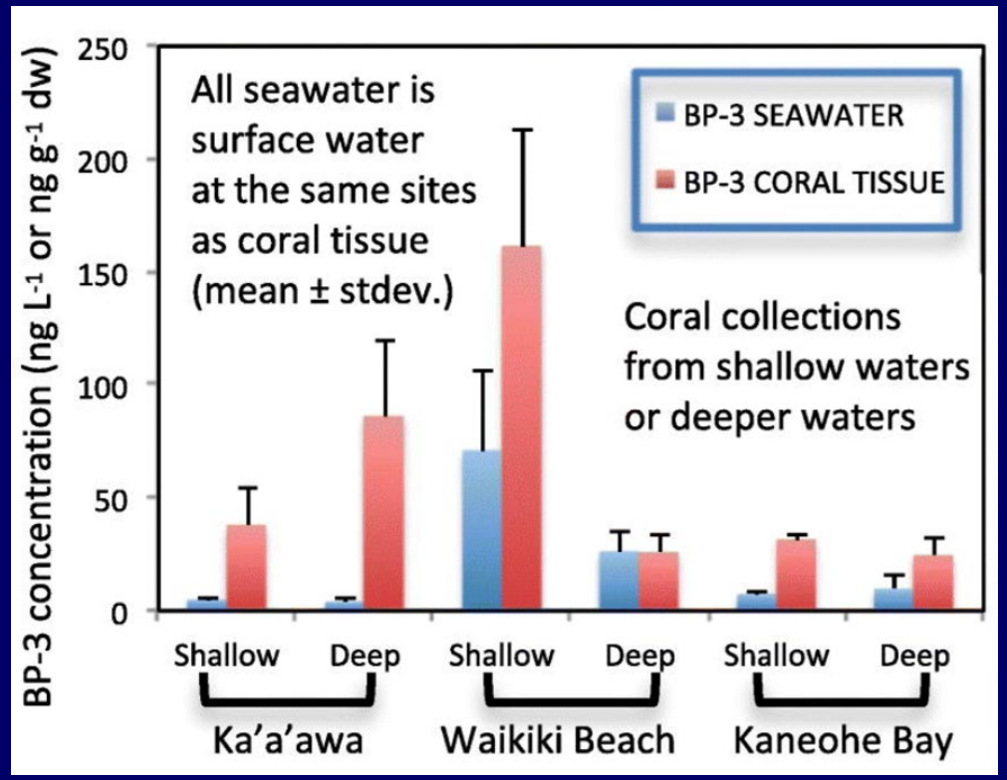
- Environmental impact

Oxybenzone

- Oxybenzone (benzophenone 3) is a short UVA and UVB filter
- Is the most common photoallergen among UV filters.
- Benzophenones: 2014 ACDS Allergen of Year
- No known safety issues in humans (has been in use in the US since 1978)
- In Europe, it has been replaced with other UVA filters in many sunscreens.
- It is still commonly used in the US because lack of other UVA filters (2018: in 2/3 of non-mineral sunscreens).

UV Filters in Water and Coral in Hawaii

(Mitchelmore, CL, et al. Sci Total Environ 2019 June; 670:398. Maryland, USA)



Range of Mean Surface Seawater Concentrations at 19 sites, Oahu, HI (parts per trillion):

- BP-3 = 0.1 to 136.2 ng L^{-1}
- EHMC (octinoxate) = not detected
- OC = < LOD to 26.9 ng L^{-1}
- OS = 33.1 to 96.0 ng L^{-1}
- HMS = 53.0 to 444.9 ng L^{-1}

Lethal concentration-50 for coral cells in vitro: 8-340 parts per billion (Downs, CA, et al. Arch Environ Contam Toxicol 2016; 70:265)

Safety of Oxybenzone

(Schneider, S, Lim, HW. JAAD 2019 Jan;80(1):266. Detroit)

- **UV filters are detected in water and coral tissues, but at magnitude lower that the lethal concentration for coral (ppt, vs ppb)**
- **Ocean warming is the major cause of coral reef bleaching**
  - *Barkley, HC, et al. Commun Biol 2018; Nov 8; 1:177. Woods Hole, MA; Honolulu, Hawaii*
  - *Cheng, L, et al. Science 2019, Jan 11; 363:128. Beijing, and Boulder, CO*
  - *Slattery M, et al. Sci Rep. 2019 May 30;9(1):8064. Mississippi, MS*
  - *Hughes TP, et al. Nature. 2019 Apr;568(7752):387. Queensland, Australia*
  - *Fisher R, et al. Nat Commun. 2019 May 28;10(1):2346. Australia*
  - *Leggat, WP, et al. Curr Biol 2019 Aug; 29:2723. Australia*

Regulations: Oxybenzone and Octinoxate

- Jan 2021: Ban in Hawaii and Key West, FL
- March 30, 2020: Ban in US Virgin Islands (oxybenzone, octinoxate, octocrylene)
- Palau (Jan 2020), Bonaire, Mexico (nature reserve)
- Being discussed in Brazil

Reef-safe sunscreens: ZnO and TiO_2

TiO_2 and ZnO Nanoparticles

(Schneider, S, Lim, HW. Photodermatol Photoimmunol Photomed 2019 Nov;35:442. [Epub: 2018 Nov 18]
Mohammed, YH, et al. JID 2019 (Feb); 139:308. Australia)

- No evidence of clinically relevant percutaneous penetration; no side effects in human
- FDA Proposed Rule (2/26/19): Category I (GRASE)
- Not sufficient data on inflamed skin where epidermal barrier function has been compromised.
- Environmental adverse effects: very low
- Whitish discoloration in SOC individuals unless it is tinted

Photoprotection

- Environmental impact
- Photoprotection for visible light

Visible Light in Photodermatology

(Mahmoud, BH,… Lim, HW, Hamzavi, IH. J Invest Dermatol. 2010 Aug;130(8):2092. Detroit Kohli, I,…, Lim, HW, Hamzavi, I. Br J Dermatol 2018 May; 178:1173. Detroit)

- **Visible light + UVA1 (≤ 2%) induces biologic effects on the skin:**
  - **Pigmentation in dark-skinned individuals.**
  - **Immediate erythema in light-skinned individuals.**
- **This might contribute to conditions that cause pigmentary alteration (melasma, PIH).**
- **Organic sunscreens do not protect against VL; other means of photoprotection are being studied**

Clinical Implications

- Tinted sunscreens could be beneficial on down-regulating the effect of VL.
  - *Boukari, F, … Passeron, J. Am Acad Dermatol. 2015 Jan;72(1):189*
- Development of new generation of filters that cover long UVA and VL region
  - *Bacqueville, D, et al. ESP-IUPB mtg. 2019*

REVIEW

Photoprotection beyond ultraviolet radiation: A review of tinted sunscreens

Alexis B. Lyons, MD,[a] Carles Trullas, MSc,[b] Indermeet Kohli, PhD,[a] Iltefat H. Hamzavi, MD,[a] and Henry W. Lim, MD[a]

Detroit, Michigan; and Barcelona, Spain

J Am Acad Dermatol. 2020 Apr 23. Online ahead of print.

Table II. Chemical formulas of pigments used in tinted sunscreens

Variable	Color			
	Iron oxide red	Iron oxide yellow	Iron oxide black	Pigmentary titanium dioxide
Chemical formula	Fe_2O_3	$FeO(OH) \cdot H_2O$	$FeO \cdot Fe_2O_3$	TiO_2
INCI name	CI 77491*	CI 77492	CI 77499	CI 77891

INCI, International Nomenclature of Cosmetic Ingredients.
*Color index (*CI*), a universally accepted nomenclature for pigments and dyes.

Lyons, A, … Lim, HW. J Am Acad Dermatol. 2020 Apr 23. Online ahead of print.

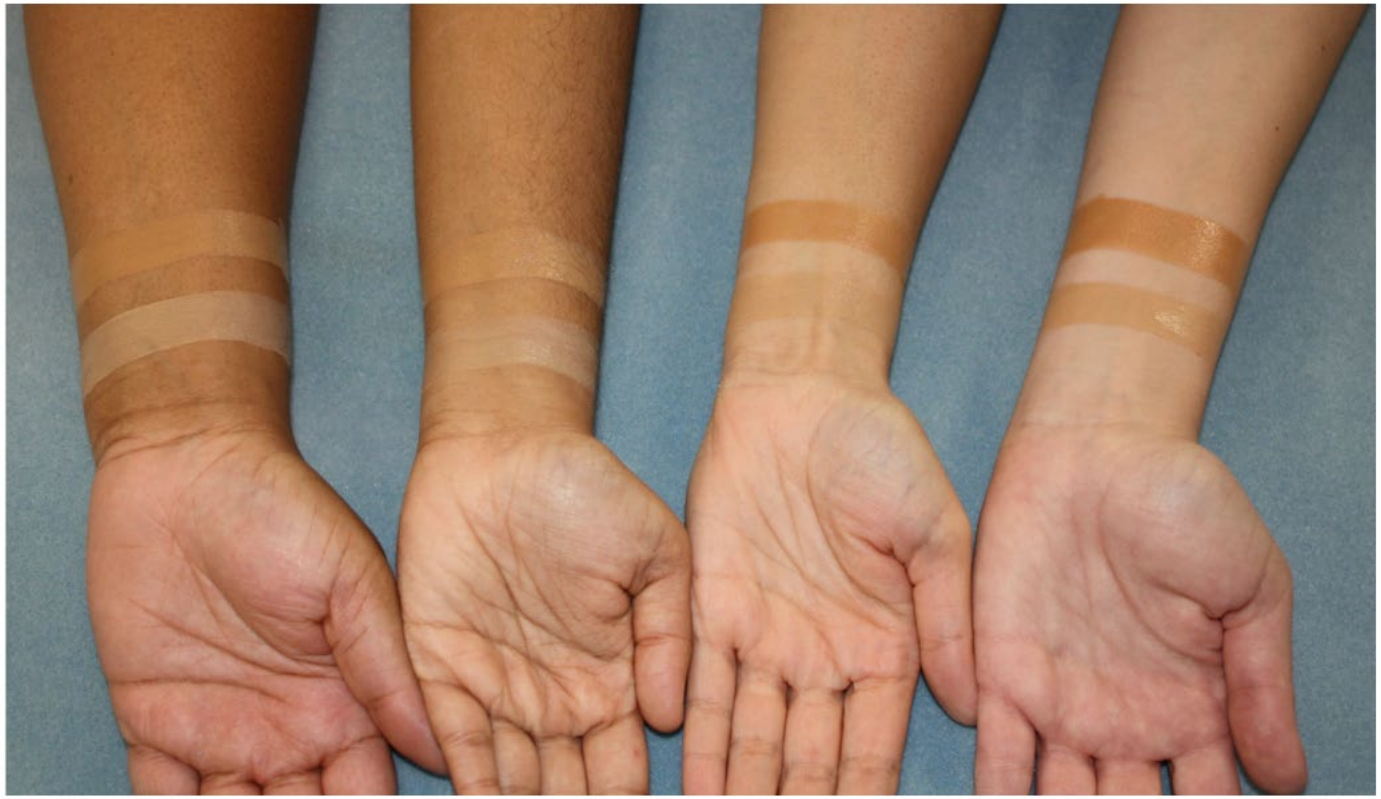


Fig 1. Two different shades of tinted sunscreens on various skin types.

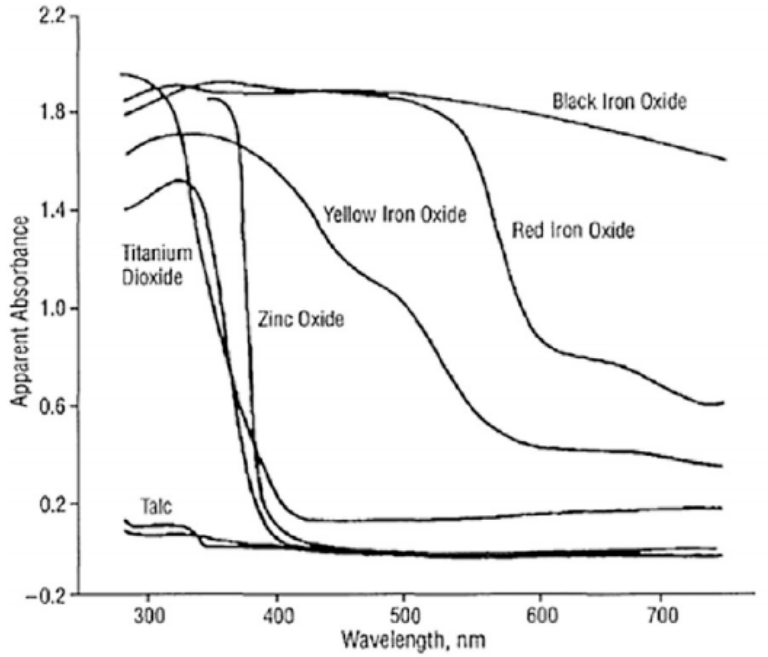


Fig 2. Absorbance profile of iron oxides and inorganic (mineral) filters. Reprinted from Sayre et al,[12] with permission.

Lyons, A, … Lim, HW. J Am Acad Dermatol. 2020 Apr 23. Online ahead of print.

Clinical Implications

- **Antioxidants might be beneficial as visible light exposure generates reactive oxygen species (*Polypodium leucotomos*, topical antioxidants)**
  - *Liebel, F, et al. J Invest Dermatol 2012; 132:1901*
  - *Mohammad, T, …Lim, HW, Hamzavi, I. J Drugs Dermatol. 2019 Dec;18:1198*
- **Afamelanotide for erythropoietic protoporphyria**
  - *Langendonk, JG, et al. N Engl J Med 2015 July 2; 373:1*

Photoprotection

- Environmental impact
- Photoprotection for visible light
- **Photoprotection of SOC**

Photoprotection in Skin of Color Individuals

- Keratinocyte carcinomas do occur in SOC individuals
- Melanoma: palms, soles, oral mucosa
- Photoprotection needs to be practiced, but probably at a modified degree compared to fair-skinned individuals
  - AAD Skin Cancer and SOC Work Group

Table 2: Calculation of MED/MPPD ratio depending on skin phototypes, considering a zenithal sun exposure and a MPPD of 15 J/cm²

Fitzpatrick Skin Phototypes	Time to achieve 1 MED	UVA dose received during 1 MED time	Equivalent of UVA MPPD during 1 MED time	Ratio MED/MPPD
I/II	15 min	5 J/cm²	1/3 MPPD	3
III	30 min	10 J/cm²	2/3 MPPD	1.5
IV	45 min	15 J/cm²	1 MPPD	1

MED: Minimal erythemal dose, MPPD: Minimal persistent pigment dose

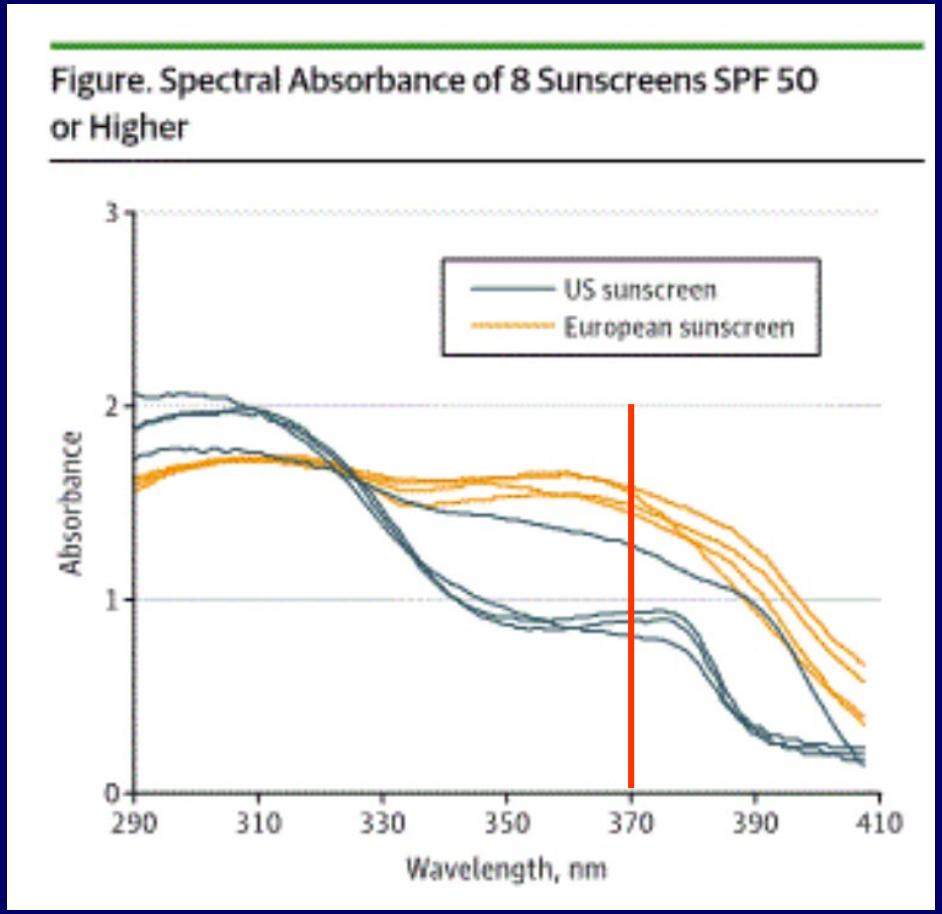
Need for a well-balanced sunscreen to protect human skin from both Ultraviolet A and Ultraviolet B damage, esp those with SOC

D. Moyal. Indian Journal of Dermatology, Venereology, and Leprology | 2012 | Vol 78 | Supplement 1, p S24-S30

Impact on New Filters in the US

(Diffey, B. JAMA Dermatol. 2016;152(5):511)

- Comparison of 4 US sunscreens with 4 sunscreens sold in Europe.
- All had SPF 50 or above
- US sunscreens: transmitted 3 times more UVA compared to the European products



FDA Proposed Rule (Feb 26, 2019)

- New broad spectrum test requirement (UVA1/UV ratio ≥ 0.7) will be added.

Photoprotection

- Environmental impact
- Photoprotection for visible light
- Photoprotection of SOC
- **AAD and photoprotection**

AAD/A Sunscreen Position and Advocacy

- Using sunscreen is one part of a comprehensive photoprotection plan.
  - AAD encourages the public to continue to protect themselves from the sun by seeking shade; wearing protective clothing, including a lightweight, long-sleeved shirt, pants, a wide-brimmed hat and sunglasses; and generously applying a broad-spectrum, water-resistant sunscreen with an SPF 30 or higher to exposed skin.
- The AADA advocates for access to safe and effective sunscreen products for the benefit of our patients and the public.
  - No position on safety testing methodology. Instead, we are encouraged to see FDA and industry working together to further access.
  - FDA is not questioning the effectiveness of sunscreen products.

What should we advise our patients?

(Schneider, S, Lim, HW. JAAD 2019 Jan;80(1):266. Detroit)

- The adverse effects of sun exposure is well established.
- Practice of photoprotection is essential:
  - Seek shade
  - Wear photoprotective clothing, wide-brimmed hat, sunglasses
  - Apply SPF>30 broad spectrum sunscreen to otherwise exposed area

What should we advise our patients?

(Schneider, S, Lim, HW. JAAD 2019 Jan;80(1):266. Detroit)

- For those concern about the environmental effect of oxybenzone or octinoxate:
  - US: Use mineral (inorganic) sunscreen. FDA: GRASE
- With practice of rigorous photoprotection: vit D 600-800 IU daily
- Photoprotection for SOC needs to be re-evaluated – good broad spectrum sunscreens

Photoprotection

- Environmental impact
- Photoprotection for visible light
- Photoprotection of SOC
- AAD and photoprotection