Sunscreen: Scientific Advisory and Regulatory Assessment

July 13,2022

I. What is sunscreen

Sunscreens are products used to prevent sunburns, from excessive exposure to sunlight. These products are designed to block the harmful ultraviolet (UV) radiation, from being absorbed by the skin. The UV rays can cause skin burns, it can also damage the cells under the dermis which may lead to premature ageing of the skin as well as some types of skin cancers.

II. How Does UV Radiation Affect My Skin? What Are the Risks?

Sunlight reaching the earth's surface consists of ultraviolet radiation (UV) (290–400 nanometres). UV radiation, a known carcinogen, can have a number of harmful effects on the skin. The ultraviolet wavebands are further subdivided into UVB (290–320 nanometres), UVA (320–400 nanometres). These two types of UV radiation that can affect the skin—UVA and UVB— both have been linked to skin cancer and a weakening of the immune system. They also contribute to premature aging of the skin, and cause skin color changes.

UVA Rays, which are not absorbed by the ozone layer, penetrate deep into the skin and heavily contribute to premature aging. Up to 90 percent of the visible skin changes commonly attributed to aging are caused by sun exposure.

UVB Rays, these powerful rays, which are partially absorbed by the ozone layer, mostly affect the surface of the skin and are the primary cause of sunburn.

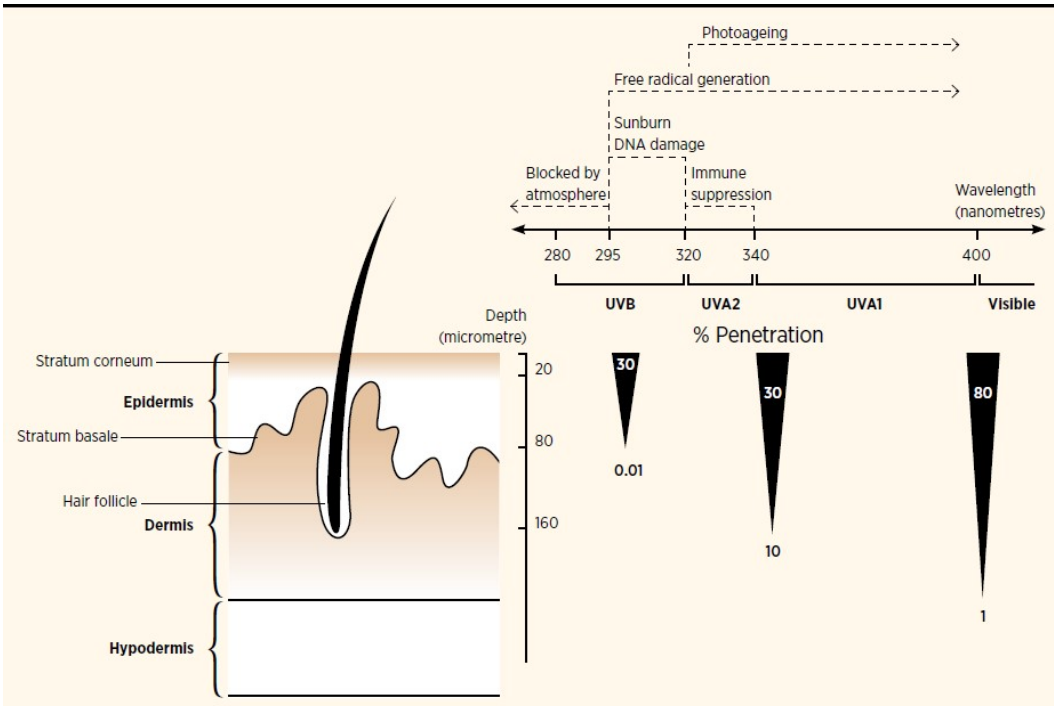

Figure 1: *Schematic cross section of skin showing dermal penetration and biological effects of different wavelengths of UV radiation*

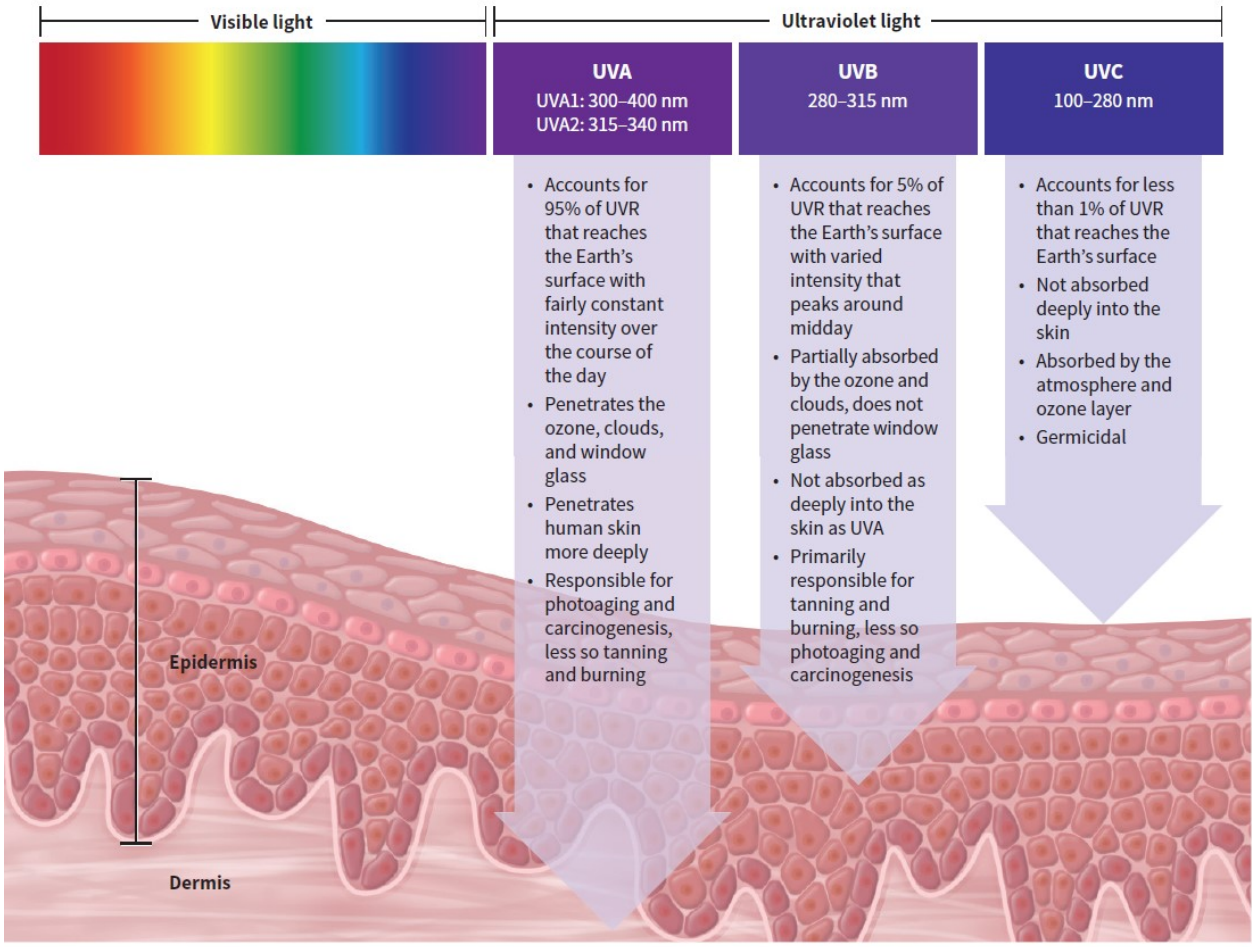

Figure 2: *Schematic representation of the electromagnetic spectrum of light, emphasizing ultraviolet radiation (UVR) frequencies and their effect on human skin. Generally, the shorter the wavelength of radiation, the greater the potential for biological damage. Note: UVA = ultraviolet A, UVB = ultraviolet B, UVC = ultraviolet C. Sunscreen filters are active against UVA1, UVA2 and UVB radiation*[1]

III. Sunscreen ingredients

Sunscreen ingredients protect the skin either by absorbing and/or reflecting the UVB/UVA rays. These ingredients are divided into organic (consisting of synthetic organic chemical's) and inorganic sunscreens. The FDA requires that all sunscreens contain a Sun Protection Factor (SPF) label. The SPF reveals the relative amount of sunburn protection that a sunscreen can provide an average user.

IV. What is SPF & how is it measured

The level of sun protection provided by sunscreen products is estimated using the Sun Protection Factor or 'SPF' test, which uses the erythemal response of human skin, in vivo, to ultraviolet

radiation (UVR). The SPF value is a ratio calculated from the energies required to induce a minimum erythemal dose (MED) response with and without sunscreen product applied to the skin of human volunteers. The protocol specifies the use of UVR (full-spectrum, solar-simulated) from an artificial source.

a. **Calculation of individual sun protection factor (SPF_i)**
SPF_i is a ratio of the MED on product-protected skin (MED_p) to that on unprotected skin (MED_u) in the same subject.

$$SPF_i = \frac{\text{MED (protected skin)}}{\text{MED (unprotected)}} = \frac{MED_p}{MED_u}$$

Since the SPF metric is a ratio (MED_p/MED_u), each subject acts as their own control and the SPF value obtained is independent of skin type. The final SPF is an average of individual SPF, determined on at least 10 subjects. The use of MED values in the determination of SPF provides a relative level of protection versus an absolute level (in practice) and is, therefore, suitable for all skin types, where higher numbers are indicative of greater protection from erythemally-effective UVR.
Even though the MED in darker-skinned subjects requires higher doses of erythemally-effective UVR, solar UVR still causes damage to skin of all human subjects and, therefore, sun protection is needed, regardless of skin type.

V. Standards for determination of SPF

Specifically, the as rest of the world, Indian population also needs sun protection and sunscreens should play a frontline role in public health in India. The International Standards Organizations (ISO), In-Vivo SPF Test Method ISO24444, (together with the UVA methods, ISO24443 and ISO24442) are validated International standards to measure sunscreen efficacy, based on state-of-the-art science and developed by global experts.

Sunscreens are an important way of protecting the skin against the sun's harmful UVR radiation (UVR). India has many Sunscreen products already in market with Sun Protection Factor (SPF) claims. In order to make these claims, a validated, robust test method is necessary.
SPF is an in vivo, human scientific method, which measures the amount of protection provided by a topically-applied sunscreen against erythemally-effective UVR.
The test provides a SPF metric, derived from comparing the amount of time / energy/dose needed to cause barely-perceptible reddening of the skin (erythema), 24 hours after exposure to solar-simulated UVR, with and without sunscreen (applied at 2mg/cm2).

a. **SPF = minimum erythema dose with sunscreen / minimum erythema dose without sunscreen**
While an *in vitro* SPF method is currently under development, the ISO24444 SPF test method is the only *in vivo* method currently available, developed and published by International Standards (ISO). Globally, most geographies have adopted ISO24444 for measuring *in vivo* SPF values.
In the absence of any specific locally-developed method, the ISO method is the most relevant, validated reference method to make fair claims on SPF in India.

b. Adoptability of the ISO methods to Indian population

Before we look at the adoptability of ISO test methods to Indian population, let us first understand the various skin types. Across the Globe the skin differentiation is assessed by the Fitzpatrick model. The Fitzpatrick skin type (or phototype) describes a way to classify the skin by its reaction to exposure to sunlight. The Fitzpatrick skin type (or phototype) depends on the amount of melanin pigment in the skin. This is determined by constitutional colour (white, brown, or black skin) and the effect of exposure to ultraviolet radiation (tanning). Pale or white skin burns easily and tans slowly and poorly, therefore it needs more protection against sun exposure. Darker skin burns less and tans more easily.

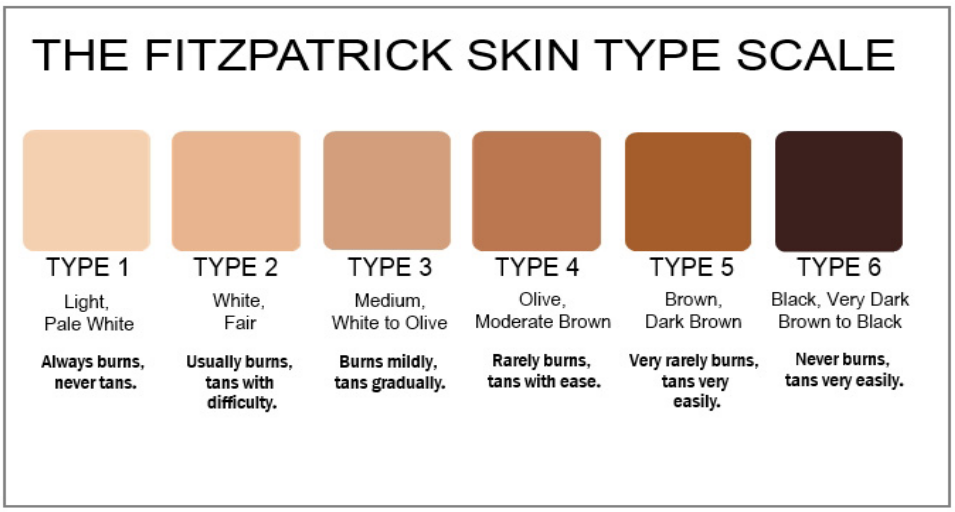

Figure 3: *Fitzpatrick skin type scale*

The Fitzpatrick (FP) skin type describes a way to classify the skin. The skins are classified 6 types, wherein Indian population is classified under skin type IV-VI

There is currently a proposal under circulation, on extrapolation of SPF test conducted on skin types I, II, III to types IV & V; based on the below justification.

i. Differences in skin colors and their classification:

Selection of volunteers for the ISO 24444:2019 test method is based on the use of an objective tool; an instrument called a spectrophotometer which yields colour measurement in the CIE (1976) L*a*b* color space. Using these data, skin color can be characterized by its Individual typology angle or ITA°. Based on this classification the skin colors of the world can be broadly classified into 6 groups as depicted in the below table

Table 1: Skin Color Categories & their ITA values

Skin color category	Skin phototype	ITA
Very Light	I	>55°
Light	II	>41° to 55°
Intermediate	III	>28° to 41°
Tan or matte	IV	>10° to 28°
Brown	V	>-30° to 10°
Black	VI	≤-30°

ii. Reaction of different skin color categories to erythemally-effective UVR

Besides the inherent color, there are differences across phototypes in Minimum Erythema Dose (MED - the dose of erythemally-effective UVR needed to elicit barely-perceptible reddening of skin 24hr after exposure). The darker the skin phototype, the greater the MED[2]. Hence, e.g., a phototype IV would generate an MED of 550-700mJ/cm^2, while a phototype III would require 390mJ/cm^2 and Type II requires 280mJ/cm^2

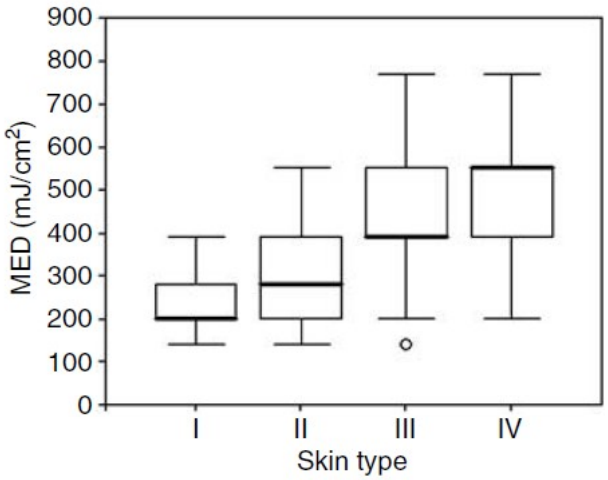

Figure 4: *The relationship between MED and skin type. The MED was associated with skin type (P < 0.001).*

The relationship between an individual's skin color (as reflected by their ITA° value) with their sensitivity to burning from UVR, independent of their ethnicity, was further established. Regression analysis of all data points (dashed line) yielded a correlation coefficient (r2) equal to 0.40. A separate regression analysis using composite weighing (where average values were used across the 12 laboratories, in 5o increments) yielded a separate correlations (solid line)[4].

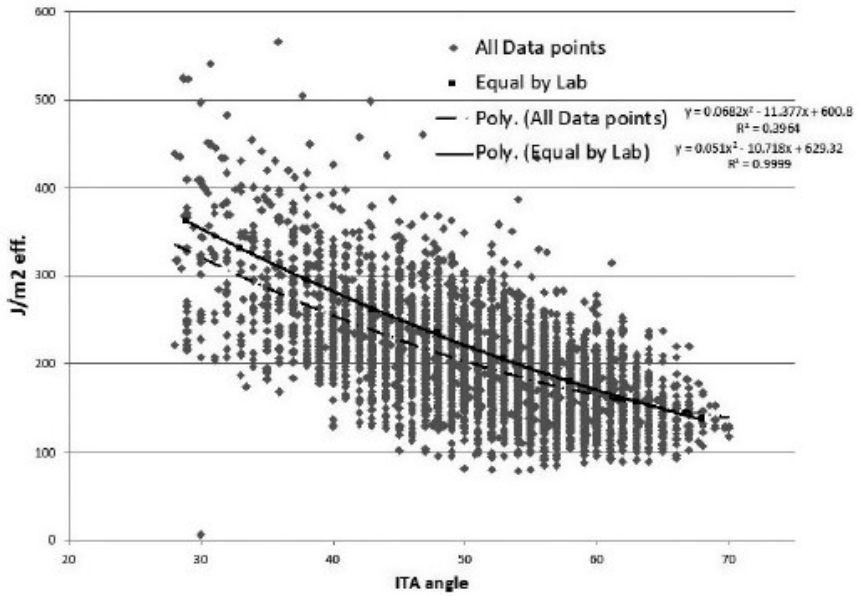

Figure 5: *The relationship between ITA and MED (J/m²)*

Similar results have also been observed by Indian researchers on Indian skin types[3] :

Table 2: The mean MED for each skin type was as shown below

		Mean	Std. deviation	Minimum	Maximum
Skin type	3	40.00	-	40.00	100.00
	4	51.22	11.88	40.00	100.00
	5	68.29	16.11	40.00	100.00
	6	78.00	14.76	60.00	100.00
Total		61.51	17.25	40.00	100.00

The mean MED ± SD for solar simulated irradiation, including UVB, for the 100 subjects was 61.5 ± 17.25 J/cm².

Hence, it should be clear that the difference is only in the dose required to generate the MED, irrespective of skin type.

Further support for the use of ISO SPF test methods in Indian skin types was presented in the paper[5]; the workers compared the action spectra of erythema and melanogenesis in heavily-pigmented individuals to those in fair-skinned individuals and showed that those with Skin Type V (relevant to the Indian population) will certainly exhibit erythema, as well as persistent pigment reactions, when exposed to UVR.

The UV doses to induce these reactions in skin type V was compared to Caucasian skin types I-II. The ratio of MED values between skin types V and skin types I and II was 2.29, which is close to the ratio of melanin pigment in these skin types.

Most importantly, the shape of the erythema action spectrum was found to be the same between skin type V and skin types I-II, indicating a common erythemal (sunburn) response to erythemally-effective UVR between skin types I-II and skin type V (relevant to Indian skin).
To conclude, if the nature of the erythemal (sunburn) response is the same between these different skin types, then the protection measured in skin type I-III may be extrapolated to darker skin types.

Table 3: Proposal to modify the ISO24444 requirement to meet Indian population type, refer below

Parameters/ Concerns	**Existing Method Requirement (ISO24444)**	**Modified Validated Method (Extrapolation Requirement)**
Skin Colour of the test subject	**1. Minimum ITA°** value ≥28° And untanned on test area	Broadening of the Average value: Panel should have ITA° value from 25° to 55°
	2.Average test Subject Panel should have ITA° value:41° to 55°	
	3.Inclusion: Subjects with ITA° in each of the three ITA° bands 28° to 40° (**Skin Type III**), 41° to 55° (**Skin Type II**) and >56° (**Skin Type I**)	

References:

1. *Megan Sander MD, Michael Sander DMD, Toni Burbidge MD, Jennifer Beecker MD; The efficacy and safety of sunscreen use for the prevention of skin cancer, CMAJ 2020 December 14;192:E1802-8. doi: 10.1503/cmaj.201085*
2. *Roy A. Palmer1, Susan Aquilina1, Peter J. Milligan2, Susan L. Walker1, John L.M. Hawk1 and Antony R. Young1 "Photoadaptation during Narrowband Ultraviolet-B Therapy Is Independent of Skin Type: A Study of 352 Patients" Journal of Investigative Dermatology (2006) 126, 1256–1263.*
3. *Vandana Mehta Rai, S. D. Shenoi, C. Balachandran, Sathish Pai "Minimal erythema response (MED) to solar simulated irradiation in normal Indian skin" Indian J Dermatol Venereol Leprol September-October 2004 Vol 70 277-279*
4. *Curtis Cole; Global data of unprotected skin minimal erythema dose relationship with Individual Topology Angle; Photodermatol Photoimmnnol Photomed. 2020; 36:452-459*
5. *N. Kollias, Y. H. Malallah, H. Al-Ajmi, A. Baqer, B. E. Johnson, S. Gonzalez; Erythema and melanogenesis action spectra in heavily pigmented individuals as compared to fair-skinned Caucasians; Photodermatol Photoimmunol Photomed, 1996: 12: 183-188*

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