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Need of UV protection and evaluation of efficacy of sunscreens

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Synopsis

Sun exposure has been coupled with numerous types of acute and chronic reactions in skin, for example, sun burns, photoimmune suppression, photoaging, and skin cancer. In scrutiny of growing understanding of the potentially unfavorable long-term side effects of solar irradiation, there is a universal call for harmless and effective photoprotectants. Photoprotective agents are used for protection against ultraviolet (UV) radiations. In support of best photoprotective measures, now sunscreens are in great demand. Safeguard from UVB is quantified as a minimal erythema dose–based sun protection factor (SPF). UVA protection testing methods include evaluation of persistent pigment darkening (PPD) and critical wavelength. The rationale of this review is to present the contemporary information on the cutaneous pathophysiology of photooxidative stress, to study different UV filters with their UV spectrum and various commercially available sunscreens, with special emphasis on their active ingredients and SPFs. The characterization of different parameters to evaluate the efficacy of sunscreens, for example, SPF, immune suppression factor, photostability, and water resistance, have been described on the basis of findings from different researchers.

INTRODUCTION

Sunlight is composed of a continuous spectrum of electromagnetic radiation, that is, ultraviolet (UV) (45%), visible (5%), and infrared (50%). Furthermore, UV radiations (UVR) from the sun are classified as UVA1 (340–400 nm), UVA2 (320–340 nm), UVB (290–320 nm), and UVC (270–290 nm). UVB radiations are responsible for UV-induced skin damage. UVB suppresses immune reaction, induces tolerance toward antigens, and causes DNA damage that may further contribute to cancer. UV exposure of the skin results in the generation of reactive oxygen species (ROS), which are rapidly removed by nonenzymic (e.g., ascorbic acid, tocopherol, ubiquinol, and glutathione) and enzymic antioxidants (AO) (e.g., catalase, superoxide dismutase, glutathione peroxidase, and glutathione reductase). Excessive ROS can overcome antioxidant defense and cause oxidative stress.

UV exposure causes pigment darkening that can be immediate (occurs within seconds, disappears in 2 h after exposure), persistent where pigmentation is for 2–24 h (1), and

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delayed, that is, pigmentation is at peak at 72 h due to increase of tyrosinase activity and formation of new melanin (2).

Exposure of skin to UVA (95% of solar radiation) leads to oxidative stress because of the increase in inflammation due to infiltration of inflammatory blood leucocytes (macrophages and neutrophils); increased production of prostaglandins (PGs) as a consequence of increased lipid peroxidation (LPx); release of tumor necrosis factor-alpha, nuclear factor-κB (NF-κB), inflammatory cytokines (interleukins; IL-1α, IL-1β, IL-6); and production of ROS (3).

Responses of human skin toward UVB radiation can be acute or chronic. Acute responses include erythema, edema, pigment darkening followed by synthesis of vitamin D, delayed tanning, and thickening of the dermis and epidermis, whereas chronic effects include photoaging, immunosuppression and photocarcinogenesis (4). DNA damage by ROS leads to oxidation of 8-hydroxyguanine and pyrimidine bases that are responsible for mutagenesis and carcinogenesis (5,6). UVA penetrates deep into the epidermis and dermis. UVA and UVB are also known as tanning ray and burning ray, respectively. Long-term skin exposure to UVA can lead to skin aging (7), wrinkling, skin sagging (8), UV-induced immunosuppression (9), and burns (10). UVB absorbed by two adjacent cytosine residues in DNA causes the formation of cyclobutane pyrimidine dimers (CPD) and UVA induces the mutations at high frequency (11). UVC gets filtered by the ozone layer, as a result does not reach the earth (4). Figure 1 explains the spectrum of UV radiations as well as their hazardous effects on different layers of skin.

Sunscreens are considered a useful approach for the photoprotection of skin. Sunscreen products that can absorb, reflect or scatter UV photons are considered to be effective. Hence, they attenuate the amount and nature of UV radiations reaching viable cells in the skin. No sunscreen prevents photodamage, as it has been revealed that suberythemal

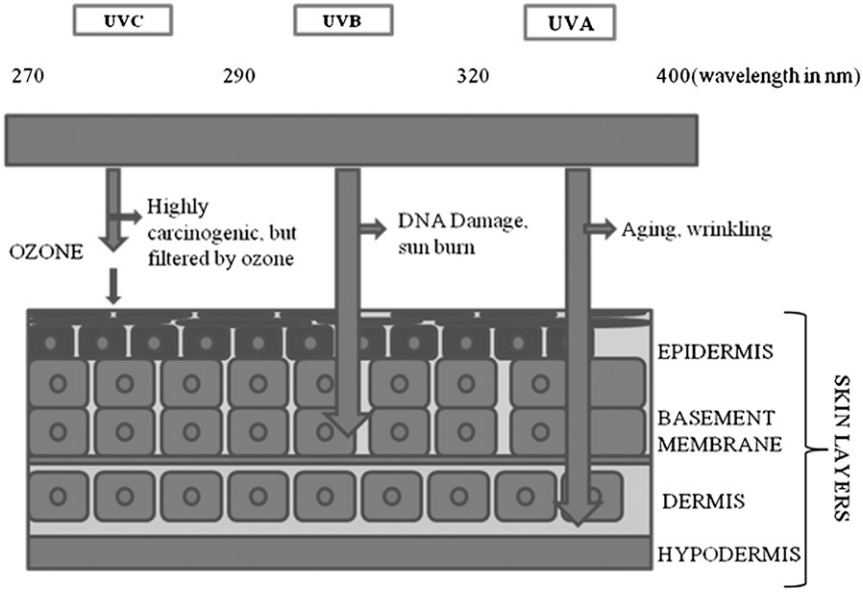

Figure 1. Effects of UV radiation after penetration through different layers of skin.

doses of UV radiations lead to a variety of molecular changes, for example, DNA damage in epidermal cells. However, the spectrum of UV radiations accessing viable epidermal cells can be altered by the use of topical sunscreens. Regular use of sunscreens has been shown to reduce actinic keratosis (12), solar elastosis, UV-induced immunosuppression (9,13), and photosensitivity in humans and prevents the formation of squamous cell carcinomas in animals.

This is well established that UV radiations are one of the major ecological causes of skin cancers; however, skin cancers can be prevented by the use of physical and chemical sunprotectives. The intervention cost of the use of sunscreen to prevent skin cancers is around AU$ 40,890 per quality-adjusted life year saved and would result in a 76% reduction in melanomas and melanoma-related deaths and 41% reduction in squamous cell carcinomas (14), whereas, the cost of treating nonmelanoma skin cancer is estimated to be in excess of US$ 650 million a year (15).

Furthermore, a thorough understanding of the mechanism of action for sunscreens, the relationship of the spectrum and sun protection factor (SPF), UV index, and different formulations containing UV filters can help users in selecting the appropriate sunscreens.

MECHANISM OF PHOTOPROTECTION

A prophylactic and therapeutic strategy against skin cancers and photoaging is defined as photoprotection (16).

MECHANISM OF PHOTOAGING

Aging is a complex, progressive process that leads to functional and aesthetic changes in the skin. The aging process can be intrinsic (i.e., genetically determined) and extrinsic (due to environmental factors). Exposure of skin to sun enhances the aging of skin, which is a continuous process. Photoaging is different from intrinsic aging. Mechanism of photoaging is explained in Figure 2.

Aging is a natural phenomenon, which is ahead of any one's control. It is a multifaceted sequence, in which there is a progressive functional decline due to the amassing of molecular damage. Human skin undergoes chronological or intrinsic aging and photoaging, that is, aging due to extrinsic factors. The skin shows a marked vulnerability to changes due to the structural and physiologic alterations that take place as a result of either intrinsic or extrinsic aging (Table I). In Figure 3, microscopic structural changes in photoaged (A, B) and intrinsically aged (C, D) skin are clearly visible. Figure 3A reveals the presence of tangled, disorganized elastic material, which consists of damaged elastin, the microfibrilar component, and fibronectin. Figure 3B depicts the basophilic degeneration of interstitial collagen, which is due to degradation by matrix metalloproteinases. Intact fibers of interstitial collagen in the Grenz zone "G" (narrow layer of upper dermis just below the epidermis, made of densely packed collagen fibrils, which is not infiltered in the same way as other layers of the dermis) are present just beneath the epidermis indicating a limited repair process. Figure 3C reveals a slight decrease in elastic fibers. Figure 3D reveals decrease in fiber thickness of interstitial collagen (7).

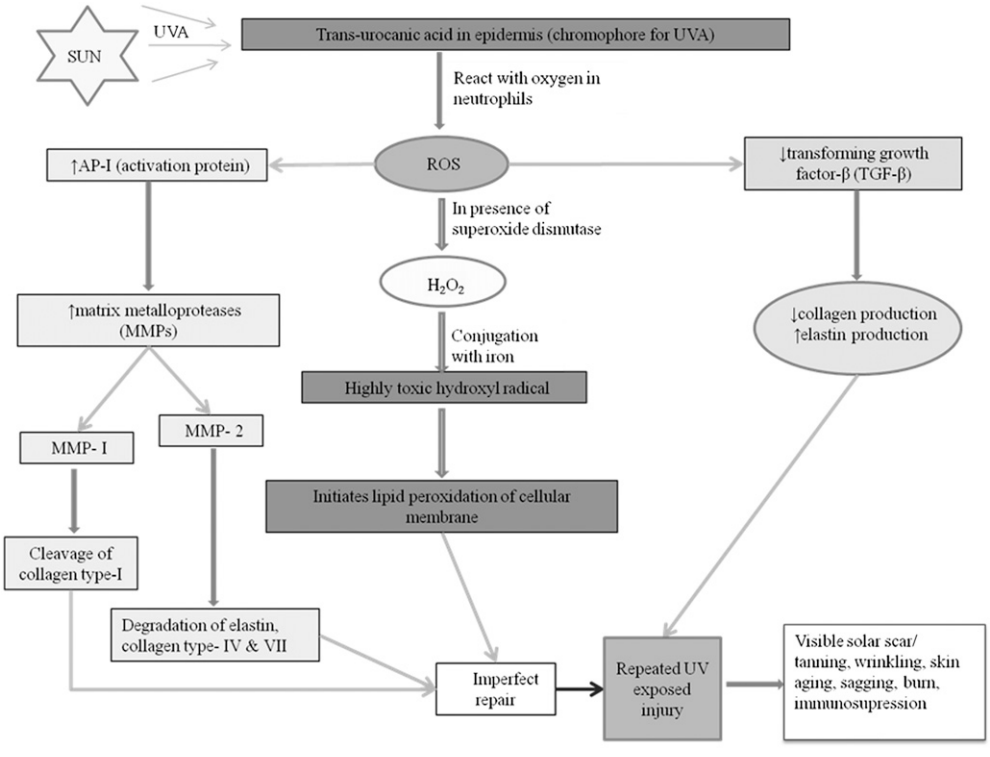

Figure 2. Signaling pathway of photoaging.

MECHANISM INVOLVED IN ALTERATION OF ELASTIC FIBERS

Wrinkling. Wrinkles on the face are prominent characteristics of photoaging. Formation of facial wrinkles is mainly due to loss of natural process of elastic properties of skin. UVB at suberythemal doses leads to reduction of elasticity and finally wrinkled skin (8). In photoaged skin, corners of eye are most susceptible and are highly associated with loss of skin elasticity (17). Neutrophil elastase (a serine proteinase) and skin fibroblast elastase (member of metalloproteinase) are major components that are responsible for the elasticity of skin (18,19). UV exposure to animal skin at less than a suberythemal dose does not cause infiltration of inflammatory cell but elicits wrinkles (20). Figure 4 summarizes the mechanism of wrinkling.

The main components of elastic fibers are elastin and fibrillin. Elastin fibers are formed in such a manner that fibrillin-rich microfibrils surrounds the cross-linked elastin, which is a central core portion (21). Various proteins in dermal or epidermal connective tissues play role in maintaining the integrity and architecture of the skin. Hence, damage to these connective tissues can be correlated to structural changes of skin, for example, wrinkling, loss of elasticity, and sagging (22). After UV irradiation, dermal keratinocytes and fibroblasts secrete cytokines, which stimulate gene and protein expression of elastase and collagen.

SUN BURN

Sun burn cells are the keratinocytes that on receiving a UVB dose (that can irreversibly or severely damage DNA) go through apoptosis. The cancer-prone phenotype can arise if

Table I
Comparison of Structural and Functional Changes in Skin during Intrinsic and Photoaging

Particular	Photoaging	Intrinsic aging
Epidermal changes	Thickness increases, acanthropic in early phase and atrophy in later stages	Thin epidermis
	Proliferative rate is higher than normal	Proliferative rate is lower than normal
	Non-uniform and random distribution of keratinocytes, polarity of cells is lost, frequent enlargement	Uniform and defined distribution of keratinocytes, polarity is maintained, usually atrophied
	Diversified melanosomes	Uniformly distributed melanosomes
	Increased number of stratum corneum (SC) cell layer	Normal cell layer
	Vitamin A content is destroyed by sun exposure	Plasma content of retinol increases
Dermal changes	Marked elastogenesis followed by massive degeneration	Elastogenesis followed by elastolysis
	Massive increase in elastic fibers	Gradual decline in production of dermal matrix
	Increased lysozyme deposition on elastic fibers	Modest lysozyme deposition on elastic fibers
	Decrease in amounts of mature collagen	Mature collagen more stable in degradation
	Increased mast cells	Decreased mast cells
	Vessels become dilated	Microvessels decrease
	Pronounced inflammation	No inflammatory response
	Marked increase in glycosaminoglycans	Slight decrease in glycosaminoglycans
Common signs and symptoms	Mild (age 28–35 years): Few wrinkles, no keratoses	Fine wrinkles, thin and transparent skin
	Moderate (age 35–50 years): Early wrinkling, sallow complexion with early actinic keratoses	Loss of underlying fat leading to hollowed cheeks and eye sockets with noticeable loss of firmness on the hands and neck
	Advanced (age 50–60 years): Persistent wrinkling, discoloration of the skin with telangiectases and actinic keratoses	Bones shrink away from the skin as a result of bone loss, which causes sagging of skin, dry skin with pruritus
	Severe (age 65–70 years): Severe wrinkling, photo aging, gravitational and dynamic forces affecting the skin, actinic keratoses with or without skin cancer	Inability to sweat sufficiently to cool the skin, faster graying of hair

these cells escape programmed cell death (10). On absorption of UVB by DNA, photoproducts (thymine dimers) are formed that lead to UV mutations (23). Signaling pathway involved in the formation of sunburn cells is explained in Figure 5.

MECHANISM OF IMMUNOSUPPRESSION

UV exposure suppresses immune responses, like contact hypersensitivity (CHS) reactions to chemical haptens (24), delayed-type hypersensitivity (DTH) reactions toward viral (25), fungal (26), or bacterial (27) antigenic attacks.

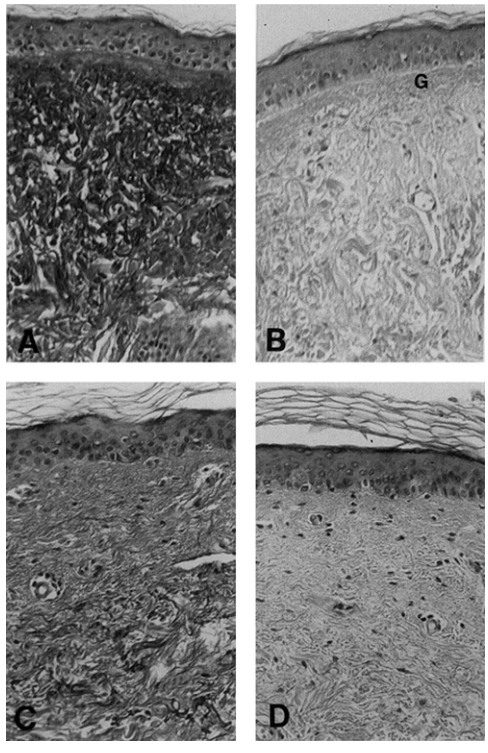

Figure 3. Histological appearance of photoaged and intrinsically aged skin. (A) Photoaged skin from the sunlight-exposed face, Elastica van Gieson staining; (B) Photoaged skin from the sunlight-exposed face, hematoxylin–eosin staining; (C) Intrinsically aged skin from the inner site of the upper branch of the same patient, Elastica van Gieson staining reveals a little reduction in elastic fibers; and (D) Intrinsically aged skin from the inner site of the upper branch of the same patient, hematoxylin–eosin staining. Adapted from Wlaschek *et al*. (7).

Chronic UV exposure may induce skin cancer or suppress the immune system. Energy from UV is absorbed and is converted to biologically recognized signal. Photoreceptors that absorb UV and initiate immunosuppression are epidermal DNA, *trans*-urocanic acid and membrane lipids (9). Mechanism of UV-induced immunosuppression has been depicted in Figure 6.

Membrane lipid peroxidation and free radical formation. Membrane LPx and ROS are the mediators of immunosuppression. Furthermore, activation of AP-1 (controls differentiation, proliferation, and apoptosis) and NF-κB (the protein complex that controls DNA transcription) leads to the formation of immune regulatory cytokines (28). ROS generated by UV exposure, leads to LPx and disturbance of redox potential. This initiates AP-1, NF-κB transcription and induces activation of cytokines (IL-4) (10). All these factors are responsible for systemic immunosuppression (9,29). Role of ROS in photoaging and immunosuppression is explained in Figure 7.

PHOTOCARCINOGENESIS

Exposure of skin to UV radiation leads to a chain of bioeffects that contribute to photocarcinogenesis. Mechanism of inflammation and immunosuppression has been explained

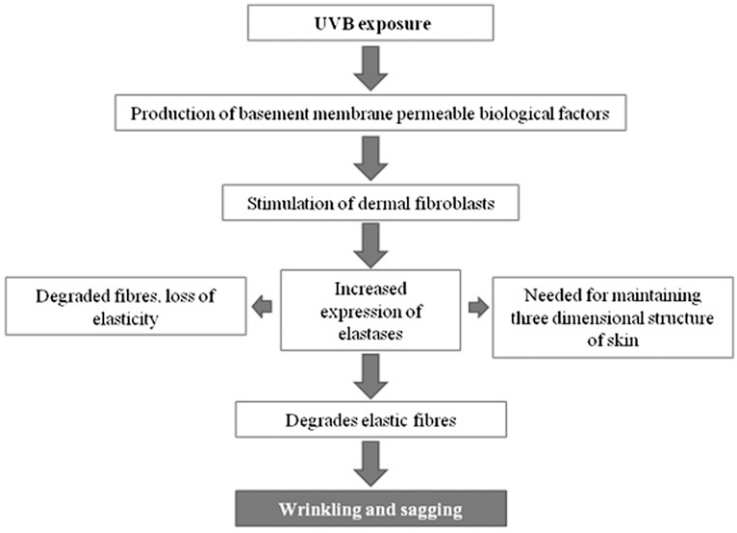

Figure 4. The mechanism involved in wrinkling through alteration of elastic fibers.

already (Figure 6). Investigations carried out by many researchers indicate that UV-induced oxidative stress leads to the development of skin cancer (3) as illustrated in Figures 8 and 9, whereas a certain level of UV exposure on skin prevents or reduces protective mechanism in the skin (3).

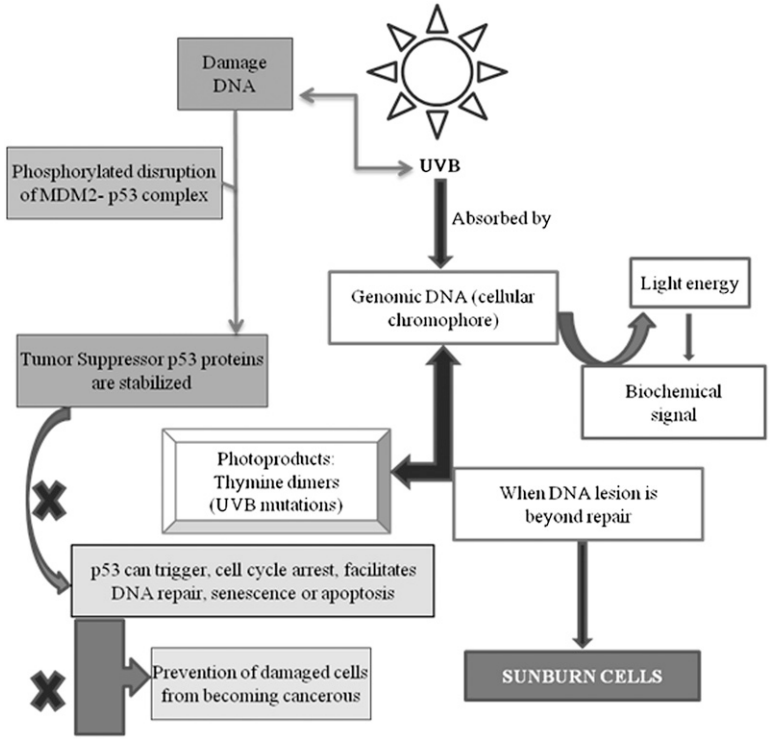

Figure 5. Signaling pathway leading to sun burn cells.

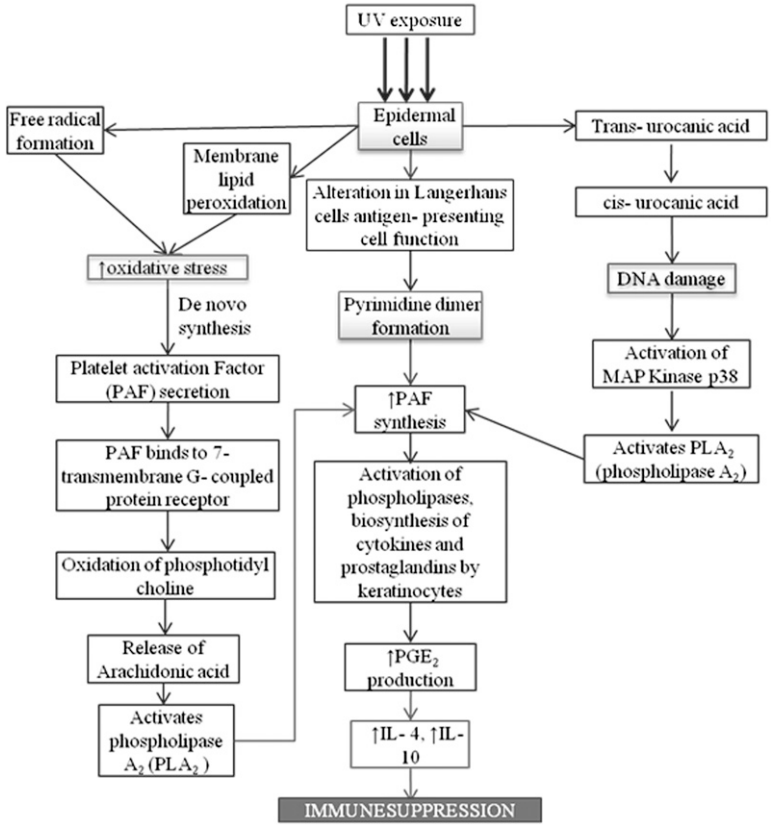

Figure 6. Mechanism of UV induced immunosuppression.

Hence, it is clear from Figures 8 and 9 that oxidative damage is important for skin carcinogenesis.

PHOTOPROTECTIVE AGENTS

Various synthetic and natural agents are available in the market for the purpose of photoprotection. Commonly used sunscreens are topical formulations. Nevertheless, various antioxidants, vitamins and minerals also claim to act as systemic photoprotective agents.

Topical sunscreens commonly have UV filters (UVA or UVB filters) and antioxidants as major components. They can act by different mechanisms like reflecting or scattering and by absorbing UV photons (30). UV filters used in sunscreens can be divided into two categories, that is, inorganic and organic sunscreens. The categorization of different types of photoprotective agents is summarized in Figure 10.

Many systemic agents with photoprotective effect have fascinated researches, as these are likely to exterminate the veritable problem by shielding the whole body. The dietary factors that claim to act as photoprotective agents are vitamin C, E, A, β-carotene. Many of systemic photoprotectants including steroids, indomethacin, etc., which are antioxidants, are not as potent as sunscreens in protecting the results of hyperpigmentation, for example, sunburn.

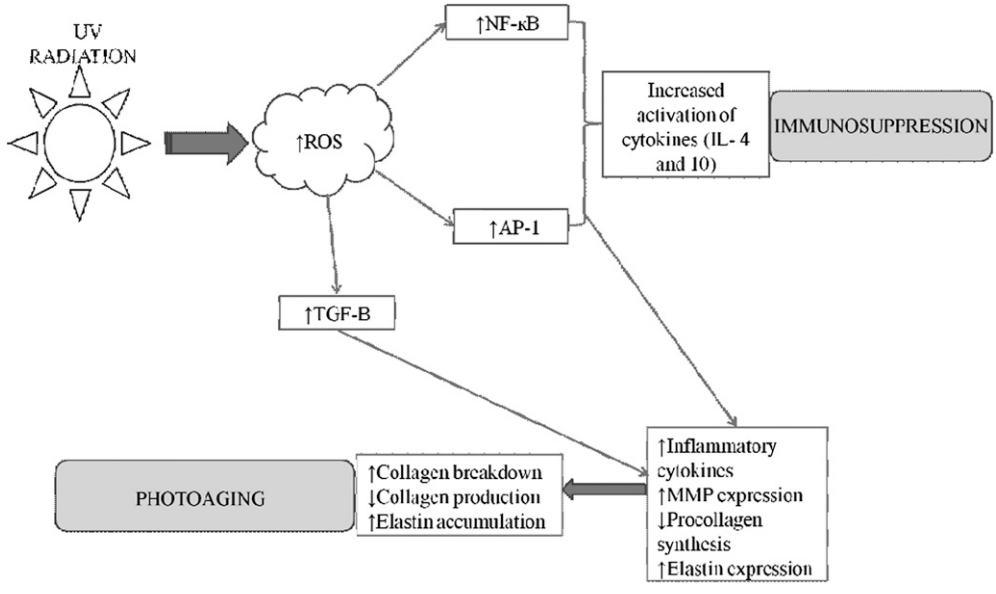

Figure 7. Role of ROS in photoaging and immunosuppression.

Chemical sunscreens are usually aromatic compounds conjugated with a carbonyl group. This structure helps in prevention of skin damage due to UV rays as it allows the molecule to absorb high-energy UV rays and release the energy as lower-energy rays (31). Furthermore, upon exposure to UV light, most of these chemical sunscreen ingredients (except avobenzone) do not undergo significant chemical changes. Para-aminobenzoic acid (PABA) is one of the initial sunscreen agents to be extensively used, however its use is associated with certain drawbacks that include the use of an alcoholic vehicle, staining of clothes etc. Its limitations have been overcome by ester derivatives, mainly padimate O or octyl dimethyl PABA. Salicylates, for example, Octisalate or octyl salicylate is a weak UVB absorber and is generally used in permutation with other UV filters and has a fine safety report. However, PABA, cinnamates, and oxybenzone may lead to contact dermatitis or photosensitivity reactions. Most of the UV absorbers used in sunscreens are photostable, which include octocrylene, Zinc oxide (ZnO), Titanium dioxide (TiO_2), Terephthalylidene dicamphor sulfonic acid, Drometrizole trisiloxane, Bis-ethylhexyloxyphenol methoxyphenyl triazine, methylene bis-benzotriazolyl tetramethylbutylphenol, etc. (4,32). Two exceptions are avobenzone and octinoxate; however, avobenzone can be stabilized by UV filters octocrylene and bemotrizinol. Furthermore, UV filter Bis-ethylhexyloxyphenol methoxyphenyl triazine improves the photostability and efficacy of sunscreens which have avobenzone and ethylmethoxycinnamate in their formulation (32). Octocrylene is also usually used in combination with other UV absorbers to accomplish superior SPF values. Oxybenzone is well intended as a broad-spectrum absorber (UVB as well as UVA2 absorber) (4). Anthranilates are weak UVB filters and they absorb mainly in the UVA2 portion of the spectrum. Avobenzone is used for true broad-spectrum UV protection as it provides a better shield against UV-A range (16). Particle size of TiO_2 used in sunscreens range between 10 and 30 nm. On the other hand, in the formulation of dispersion, the particles form aggregates of around 100 nM (4). In case of ZnO, primary particle sizes ranges between 10 and 200 nm, whereas the grades with larger particles are used in commercial

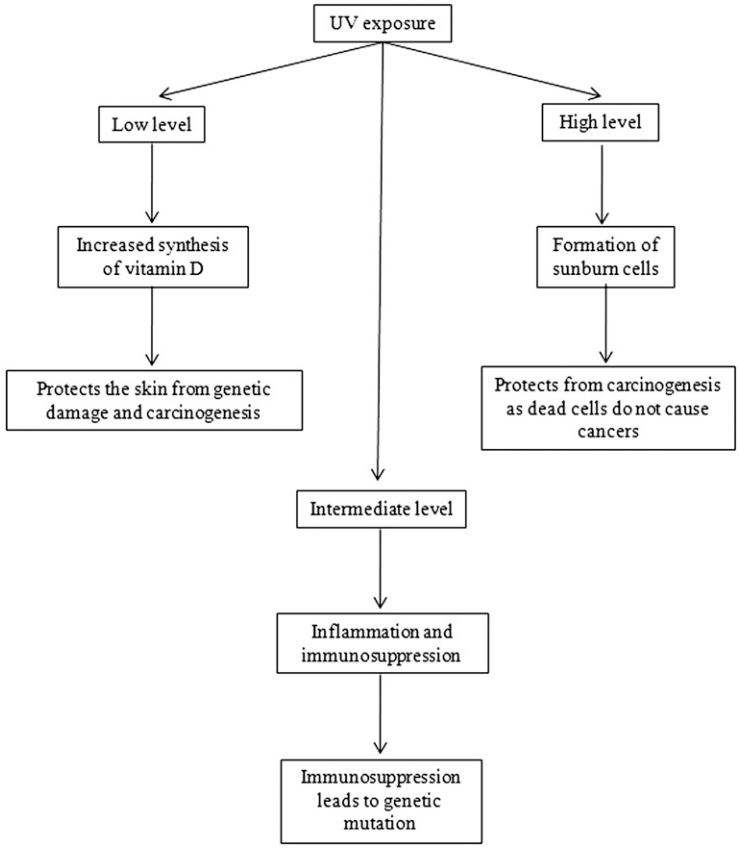

Figure 8. Broader mechanism of photocarcinogenesis.

formulation, for example, Badger; broad-spectrum SPF 30 Zinc oxide Sunscreen Cream, particle size ~ 70 nm–300 nm (33). To prevent oxygen radical formation TiO_2 is coated with aluminum oxide or silica (34).

In recent times, many oral sunscreens have also been commercialized. These products facilitate different mechanisms to prevent photodamage of skin. The majority of them own antioxidant behavior, which reload the normal antioxidant potential of the body that is lost through UV exposure after systemic loss of endogenous antioxidants. For example, a common carotenoid present in tomatoes, lycopene, is a very efficient oxygen quencher and reduces sensitivity to UV-induced erythema (35). Photoprotective and anticarcinogenic properties of dietary flavonoids and phenolics are endorsed for their antioxidant and anti-inflammatory activities, for example, polyphenol-enriched natural extract from the leaves of the fern *Polypodium leucotomos* has shown cutaneous photoprotection after single doses (36–40). Epigallocatechin-3-gallate is the major photoprotective polyphenolic component of green tea. Investigations have revealed that oral administration prevents UVB-induced skin tumor in mice mediated through the induction of immunoregulatory cytokine IL-12. In addition, oral administration of Green tea polyphenols (GTPs) to mice, also suggested that GTPs have a potential antiphotoaging effect (41,42). Omega-3 polyunsaturated fatty acid has been reported to decrease UVB-induced sunburn and inflammation (43). Classification

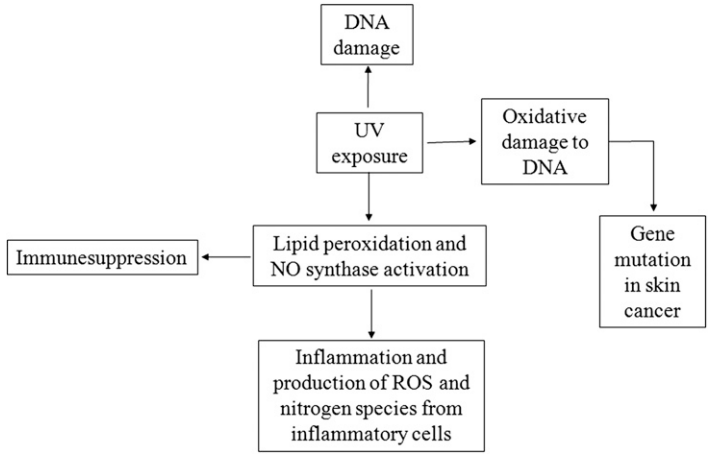

Figure 9. Role of oxidative damage in photocarcinogenesis.

of photoprotective agents has been elucidated in Figure 10. Furthermore, properties and spectrum of various photoprotective agents are summarized in Table II. It is worth mentioning that topical antioxidants have several advantages over oral antioxidants. The skin is exposed to UV rays directly hence undergoes oxidative stress conditions. Topical application of antioxidants leads to increased concentration of AOs in epidermis and dermis. Direct application of a target area increases reservoir concentration that may be continuously depleted in combating ROS. Some of the photoprotectant AOs prevent the penetration of UV rays into the skin and hence act as sunscreens (44).

Furthermore, it is desirable to keep these protectants on the skin surface for the best outcomes. However, the stability of antioxidants is an important issue which needs to be

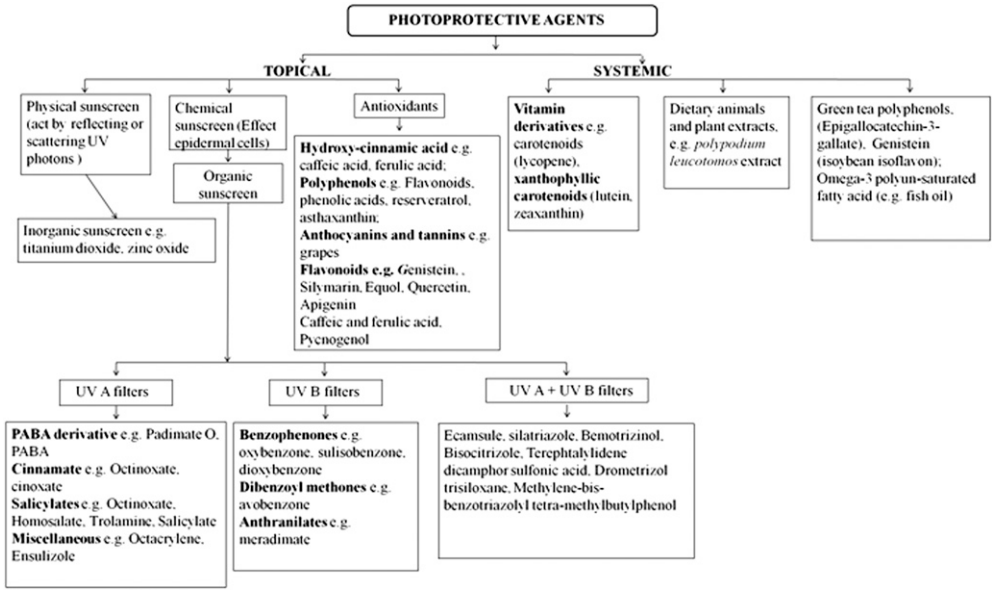

Figure 10. Classification of topical and systemic photoprotective agents.

Table II
Properties and UV Spectrum of Various UV Filters Used in Sunscreen Products

USAN/INCI	Spectral range	Maximum concentration	Function	Remarks	Regulatory status	Reference
Zinc Oxide	UVB, UVA1, UVA2	25%	Absorbs and blocks UVA and UVB rays; broad-spectrum filter	Photo stable; less likely to cause irritation, responsible for a sunscreen's white cast	FDA approved	(44,45)
Titanium Dioxide	UVB, UVA2	25%	Reflects and blocks UVA and UVB rays, does not protect against a whole range of UVA rays	Photo stable, Less likely to cause irritation, responsible for a sunscreen's white cast	FDA approved	(46,47)
Avobenzone/Butyl Methoxydibenzoylmethane (BMBM)	UVA1	3%	Absorbs full-spectrum UVA rays	Very photo unstable; oil-soluble; tends to be unstable when there is octinoxate; can be stabilized by octocrylene, 4-MBC, bis-ethylhexyloxyphenol methoxyphenyl triazine, terephthalydiene dicamphor sulfonic acid, and other UV filters or photostabilizers; not irritating to skin; microencapsulated avobenzone could minimize its degradation in sunlight	FDA approved	(48)
Bemotrizinol/ Bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT)	UVB, UVA1, UVA2	10%	Absorbs UVA and UVB rays, helps in preventing photodestabilization of other actives such as avobenzone	Very photo stable, oil soluble, minimal skin penetration	Not approved by FDA, marketed in Europe and Australia	(49, 50)
Bisoctrizole/methylene bis-benzotriazolyl tetramethylbutyl-phenol (MBBT)	UVB, UVA1, UVA2	10%	Absorbs both UVA and UVB rays, reflects and scatters some of them too, helps to stabilize other UV filters (e.g., octinoxate)	Shows little photo degradation, dissolves poorly in both oil and water, minimally absorbed by the skin, tends to be non-irritating to skin, produced as microfine particles	Not available in the United States	(48,49)

Table II Continued

USAN/INCI	Spectral range	Maximum concentration	Function	Remarks	Regulatory status	Reference
Ecamsule/terephthalylidene dicamphor sulfonic acid (TDSA)	UVA1, UVA2	3%	Absorbs UV rays and then releases the UV rays as thermal energy; no skin penetration	Photostable; water-soluble; does not protect against the entire UV spectrum, so has to be combined with other filters for good protection	FDA approved; patent held by L'Oréal and its brands	(48,49)
Ecamsule/Drometrizole trisiloxane	UVA2	3%	Absorbs UV rays; no skin penetration	Photostable, oil-soluble, used synergistically with terephthalydiene dicamphor sulfonic acid	Not yet approved by the FDA	(49)
Octinoxate/Ethylhexyl methoxycinnamate (EHMC) Octyl methoxy-cinnamate (OMC)	UVB	7.5%	Absorbs UVB rays	Water-insoluble, not photostable as most degrades over time when exposed to sunlight, can be stabilized by other UV filters such as methylene bis-benzotriazolyl tetramethylbutylphenol, there are some safety concerns are involved as absorbed by skin	FDA approved	(48,49)
Octocrylene/Octocrylene (OCR)	UVB, UVA2	10%	Absorbs UV rays	Photostable, helps to stabilize other UV filters, oil-soluble, Absorbed by skin	FDA approved	(48,49)
Octisalate/Ethylhexyl salicylate (EHS)	UVB	5%	Absorbs UV rays	Undergoes some degradation in sunlight, has emollient and water-resistant properties, Oil-soluble (so less greasy)	FDA approved	(49)
Homosalate/Homomethyl salicylate (HMS)	UVB	15%	Absorbs UV rays	Undergoes some degradation in sunlight, oil-soluble, excipient of many Coppertone sunscreens	FDA approved	(49)
Octyltriazone/Ethylhexyl triazone	UVB	5%	Absorbs UV rays	Water resistant and long lasting	Not approved by FDA	(49)

Table II Continued

USAN/INCI	Spectral range	Maximum concentration	Function	Remarks	Regulatory status	Reference
Cinoxate	UVB	3%	Absorbs UV rays	Slightly yellow, Insoluble in water	FDA approved, though no longer commonly used	(49,50)
Aminobenzoic acid	UVB	15%	Absorbs UVB rays	One of the first active ingredients in sunscreen, causes allergies, causes clothing discoloration, increased risk of cellular UV damage	Banned from sale in Europe, not used in sunscreens anymore	(49,51)
Padimate O/Ethylhexyl Dimethyl PABA (EHDP)	UVB	8%	Absorbs UVB rays	Water-insoluble PABA derivative; controversially active because after absorbing UVB rays, the active may produce indirect DNA damage; used with other chemicals to increase SPF of a product; water resistant and does not stain clothing	FDA approved, not being supported by the EU and may be delisted	(49,52)
Ensulizole/Phenylbenzimiazole sulfonic acid (PBSA)	UVB, UVA2	4%	Absorbs UVB rays	Does not degrade much in sunlight, but more studies are needed about its stability; feels lighter on skin; Used in sunscreens with less greasy finish	FDA approved	(49,53)
Dioxybenzone	UVB, UVA2	3%	Absorbs UVB rays and short-wave UVA rays	A derivative of benzophenone; Insoluble in water, so lends to water proof claims	FDA approved	(49,54)
Oxybenzone/Benzophenone-3 (BP3)	UVB, UVA2	6%	Provides effective broad spectrum protection from UV radiation, and has been approved for use since 1978	Penetrates the skin and may have some hormone-like activity in the body; 56% of sunscreens contain chemical oxybenzone	FDA approved; Approved for children older than 6 months	(49,55)

Table II Continued

USAN/INCI	Spectral range	Maximum concentration	Function	Remarks	Regulatory status	Reference
Sulisobenzone/Benzophenone-4 (BP4)	UVB, UVA2	10%	Absorbs UV rays	Photo stable; Helps stabilize other UV filters; Absorbed by skin, so its safety use in sunscreen is questionable	FDA approved	(49)
Meradimate/Menthyl anthranilate (MA)	UVA2	5%	Absorbs UVA rays	Anthranilates are weak UVB filters; absorb mainly in near UVA portion of the spectrum; less effective in this range than benzophenones, hence less widely used; no known issues in terms of toxicity; does not appear to be absorbed into the skin; in addition to sunscreens, included in lip balms, lipsticks, and facial moisturizers	FDA approved	(49,56,57)
Trolamine salicylate/ Triethanolamine salicylate	UVB	12%	Absorbs UV rays	Odorless; absorption into the skin in unknown; cannot be relied on alone as a sunscreen; water soluble, so it is frequently used in hair products that protect against UV radiation	FDA approved, in the United States and Canada	(49,58)
Enzacamene/4-Methylbenzylidene Camphor (MBC)	UVB	4%	Absorbs UV rays	May have estrogenic effect when used, but warrants further study; helps to stabilize avobenzone; Included in lip balms, lipsticks, and facial moisturizers	Approved for use in Europe and Canada, not approved by FDA or allowed in Japan	(49,59)
Bisdisulizole Disodium/Disodium phenyl dibenzimidazole tetrasulfonate (DPDT)	UVA1	10%	Absorbs UV rays	Photostable, water soluble, high molecular weight with limited dermal absorption	Approved for use in Europe, not approved by FDA	(49,60,61)

Table II Continued

USAN/INCI	Spectral range	Maximum concentration	Function	Remarks	Regulatory status	Reference
Diethylamino hydroxylbenzoyl hexyl benzoate, (DHHB)	UVA2	10%	Absorbs UVA rays	Photostable, compatible with other UV filters, may provide some protection against free radical	Approved for use in Europe and Asia	(49)
Diethylhexyl butamido triazone (DBT)	UVB, UVA1	10%	Absorbs UV rays		Approved for use in Europe and Asia, not approved by FDA	(49)
Dimethicodiethylbenzalmalonate/ Polysilicone 15 (PS15)	UVB	10%	Absorbs UVB rays	Photostable, high-molecular weight polymer with limited dermal penetration and good safety profile, Often used in hair care products	Approved for use in Europe and Asia, not approved by FDA	(49,62)
Amiloxate/Isoamyl *p*-Methoxycinnamate (IMC)	UVB	10%	Absorbs UVB rays	Most common UVB filter, used in 90% of sunscreens globally, little topical absorption and a favorable human safety profile	Approved for use in Europe and Asia, not approved by FDA	(49,62)

USAN: United States Adopted Names; INCI: International Nomenclature of Cosmetic Ingredients.

resolved as many antioxidants degrade upon UV exposure, for example, ascorbic acid (63,64) and vitamin E (65). Delivery of topical AOs has the potential to supply additional benefits to oral therapy, still, there are certain challenges associated.

EVALUATION OF EFFICACY OF SUNSCREENS

The degree and time taken for sunburn is generally affected by skin type. According to Food and Drug Administration (FDA), skin can be classified on a scale of 1 to 6. Lower number skin types (1 and 2) represent fair skin that burns rapidly and more severely, whereas higher number skin types (5 and 6), represent darker skin that does not burn easily. On the other hand, UV index is also very important as it predicts the level of UV radiation in the atmosphere. It runs from 1 to 11 and its higher value expresses a larger degree of UV irradiation and hence requires extra caution and protection (66,67).

SPF is calculated according to specifications approved by the European Commission or by USFDA. The solar simulating radiation (SSR) spectra is significant in SPF determination. The amount of UV radiation reaching a given location on earth varies according to season as well as according to geographic location e.g. intensity of UV radiation is highest at equator and high altitude and decreases with increase in latitude. Furthermore, the outcome of this extreme spectrum coupled with the high UVB dependence for erythema is that SPF is mainly a measure of UVB protection with no quantitative information on UVA.

Research data in bulk are available to confirm the use of sunscreens for sun protection along with immunosuppression but on the same point it specifies that the intensity of immune protection offered by sunscreen cannot essentially be called from its SPF. The possible justification regarding this is the difference in action spectra for erythema and immunosuppression with UVA. Hence, it is being recommended that more direct human studies should be done to corroborate this. In summation, all these effects are UVR dose dependent (68).

SUN PROTECTION FACTOR

The standard method of assessing sunscreen protection is based on erythema and is expressed as SPF. According to the FDA labeling requirement for sunscreens, mentioning of SPF is mandatory. The SPF reveals the relative amount of sunburn protection that a sunscreen can provide to the user (tested on skin types 1, 2, and 3) when used in the approved manner. SPF is the sole criterion of the protection afforded by sunscreens on which manufacturers agree to characterize sunscreen labeling.

SPF is a ratio calculated from a very simple formula, that is

SPF = MED with sunscreen/MED without sunscreen

where, MED (minimal erythema dose) is the amount of UV radiation that will produce minimal erythema on skin within few hours following exposure.

SPF 15 is the lowest grade being incorporated in sunscreens. It is observed that the claimed sun protection is often not achieved as sunscreens are applied at lower densities than that recommended by regulatory bodies (2 mg/cm^2). Furthermore, users normally misinterpret the extent of sun protection provided by different grades of SPFs. For example, users feel that SPF

30 would provide double sun protection than that provided by SPF 15. However, it is worth mentioning that SPF 15 transmits 6.66% of UVB radiation, whereas SPF 30 transmits 3.33% protection. Although the SPF ratings found on sunscreen packages apply mainly to UVB rays, many sunscreen manufacturers include ingredients that protect the skin from some UVA rays as well. These "broad-spectrum" sunscreens are highly recommended.

IMMUNOSUPPRESSION FACTOR

The immunosuppressive effect of UVB radiation has been acknowledged for a long time and it is thought to affect the progress of skin cancers; however, a few discrepancies are due to the different UV sources. There are different patterns of sun exposure coupled with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Different mechanisms of immunosuppression have already been explained via Figure 6. The statistics pertaining to skin cancer risk drop by regular sunscreen use are inconsistent, for example, one randomized assessment of sunscreen worth demonstrated statistically significant protection for the development of SCC but no protection for BCC (69), whereas another randomized study verified a poorer trend for manifold occurrences of BCC among sunscreen users (70) but no noteworthy decline in BCC or SCC prevalence (71).

Immunosuppression also contributes to the formation of nonmelanoma (keratinocyte) skin cancers. This amplified threat has been coupled to the intensity of immunosuppression and UV exposure. Risk of cutaneous malignancy increases with the increased interval and dose of immunosuppressive agents; the reverse effect is seen with decreased dosage, or after the removal of immunosuppressive factors.

SPF is based on erythema, which is a poor indicator of immunosuppression (72). This brings up the subject whether the immune protection factor (IPF) of a sunscreen is equivalent to its SPF? According to few studies, sunscreen may provide insufficient immunoprotection in the prevention of skin cancer. Hence, the capacity of sunscreens to shield laboratory animals and humans against the immunosuppressive effects of UV radiation has been the area under discussion and great disagreement (73–75). The dose providing 50% immunosuppression (D50%) was calculated to be about five MEDs (76).

Wolf and Kripke (1998) brought out that application of different sunscreens with SPFs ranging from 3.5 to 5.7 afforded full immunoprotection up to 8 MED, whereas only one did so at 12 MED. They also concluded erroneously that sunscreens protected beyond their SPF. However, this conclusion generated much criticism, including major criticism being that IPFs were not determined in the investigation (76).

Peguet-Navarro *et al.* (2000) ranked IPFs according to the sunscreen SPF. Research included determination of dose of UVB providing 50% inhibition of the mixed epidermal cell/lymphocyte reactions (D50%), in the presence or in the absence of the different sunscreens graphically. The IPFs for the sunscreens were determined as the ratio of D50% in the presence of sunscreen/D50% in the presence of the respective vehicle. In the same manner, the IPFs for the vehicles were estimated as the D50% in the mien of the vehicle/D50% in the absence of any discussion. It is a really hard task to relate the SPF value of sunscreen to its IPF. Both values refer to a different biological occurrence and depend significantly on their particular action spectra (77).

The IPF of a sunscreen can be determined using the induction or the elicitation arm of the local CHS or DTH response, and the systemic DTH response. Therefore, in order to understand fully the relationship between SPF and IPF, it is essential that UVR dose–response studies should be carried out with and without sunscreen.

QUANTIFICATION OF CHS RESPONSES

Sensitization of skin is carried out using 2,4-dinitrochlorobenzene (DNCB) 24 h after irradiation. Sunscreen control groups can be treated with sunscreen and sensitized with ethanol only (in the center of the sunscreen-treated site) to determine the nonspecific irritant effects of DNCB challenge (72). After a specific period, elicitation sites were quantified as mentioned below. The dermal thickness of each elicitation site was determined using a high-frequency 20 MHz ultrasound scanner (78).

The percent increase in dermal thickness for each elicitation site is plotted versus DNCB challenge dose (*x*-axis), and the dose–response relationship can be determined using linear regression analysis. The CHS response is represented by the slope of the linear regression line. The steeper the slope the stronger is the response.

Theoretically, IPF = SPF (i.e., IPF/SPF = 1) especially if erythema and immunosuppression have common chromophore(s) and both endpoints have similar dose–response curves. However, *in vivo* SPF for sunscreens are not predictive of the sunscreen's IPF, determined using nickel CHS model. Immune protection seems to be independent of erythemal protection. Investigations carried out by Poon *et al.* (2003) revealed that the range of SPF of selected sunscreens was found to be between 6 and 20, whereas the range of IPF was between 2 and 21. The sunscreen with the highest SPF did not have the highest IPF, whereas the sunscreen with the lowest SPF did not have the lowest IPF (78). Thus, SPF may not predict the ability of sunscreens to protect the immune system.

The paradigm is based on analysis of investigational data; sunscreen containing 2% octylmethoxy cinnamate is expected to have an *in vivo* SPF around 2 (5.7 found *in vitro*), sunscreen having 2% *o*-PABA—an SPF of 2.5 (4.5 found *in vitro*), and sunscreen with 6% ZnO—SPF of 5 (3.8 found *in vitro*) (79). So, the conclusion that the formulation that provides the highest immune protection is the formulation with highest *in vitro* SPF is valid only for an *in vitro* situation and particular model of evaluation. Table III summarizes different *in vivo* techniques used to calculate IPF of sunscreen products.

UVA-PROTECTION FACTOR DETERMINATION

SPF is first and foremost a measure of UVB protection as UVB is 1000 times more erythemogenic than UVA. Presently, there is no agreement about the paramount method for measuring UVA protection. A variety of methods have been proposed. *In vivo* methods have been developed among which persistent pigment darkening (PPD) is more broadly used. PPD is measured 2 h after irradiation of the skin with 30 joules/cm^2 of UVA.

Application method and UV irradiation protocol used for UVA-protection factor (PF) determinations are similar to that used for SPF testing. The only exception is that UVA spectrum should be used for UVA-PF determination. The results may be observed at a

Table III
Different *In Vivo* Techniques Used for IPF Calculation from CHS Response via Suppression of Induction and Elicitation Studies

Antigen used	Quantification of responses via suppression of induction	IPF calculation via suppression of induction studies	Reference
DNCB	Ultrasound measurement & reaction diameter calculation. Determined average CHS response of all elicitation sites. Linear relationship between CHS response and DNCB concentrations	From CHS responses; IPF = SSR dose that induced 50% immunosuppression (ID50) in unprotected group/SSR dose that induced ID 50 in protected groups. Or IPF = SSR dose responses modeled curves for CHS responses with sunscreen/SSR dose–responses-modeled curves for CHS responses with sunscreen without sunscreen	(80)
DNCB	Determined percentage increase in dermal thickness instantly by 20 MHz ultrasound image analysis and scans were performed immediately before and 48 and 72 h after the challenge. Slope of the DNCB dose–response is a measure of CHS	Percentage increase in dermal thickness = Difference in dermal thickness at 72 h and 0 h × 100 Dermal thickness at 0 h	(72)
DNCB	Determined increase in skin-fold thickness (SFT) at each elicitation site, and an overall score per volunteer was given by the sum of the SFT of all elicitation sites. Each challenge site was measured before and after patch application	Individual CHS responses were expressed as a total millimeter increase in SFT and total North American Contact Dermatitis Group (NACDG) score were plotted against total UV dose delivered in joules/cm^2. Nonlinear regressions were generated from the different UV dose–response curves	(81)

Table III
Continued

Antigen used	Quantification of responses via suppression of induction	IPF calculation via suppression of induction studies	Reference
Kit containing seven antigens (tetanus toxoid, diphtheria toxoid, Streptococcus, tuberculin, *Candida albicans*, *Trichophyton mentagrophytes*, and *Proteus mirabilis*)	Summed the mean diameter of each positive reaction to each recall antigen to obtain a total score for each volunteer. Reaction borders were defined by redness and induration	Could not calculate IPF, but determined whether the IPF was equal to or not to the SPF by comparing each pre- and post-SSR DTH score with a paired *t*-test. Then, comparisons between sunscreen and non-sunscreen groups were compared by analysis of variance and Tukey's tests	(82)
Nickel	Quantified the CHS response to nickel by determining an erythema index (EI) by reflectance spectroscopy. After subtraction of the background (absence of nickel patch), the EI of the exposed sites (with or without sunscreen) was compared with the EI of the appropriate unirradiated nickel-patched sites. The results are expressed as ΔEI = EI (unirradiated control) − EI (test site)	Compared the EI induced by the nickel CHS response (minus the skin background color) at non-SSR exposed sites with the EI at test sites. Statistical significance was assessed by the paired *t*-test to determine the amount of SSR to achieve immunosuppression. The SSR doses that reduced the mean EI of the unirradiated skin by 20% were calculated, for both protected and unprotected sites, and were defined as minimal immunosuppressive doses (MISD) IPF = MISD of protected skin/MISD of unprotected skin. A calculation used pooled rather than individual volunteer data	(83)

specific interval after irradiation, and the minimal persistent pigment darkening dose (MPD) is determined as the lowest UV dose that produces substantial tanning with clearly defined borders. The UVA-PF is calculated as the ratio of the MPD of sunscreen protected to unprotected skin, as described by Chardon *et al.* (84).

SUNSCREEN ABSORBANCE DETERMINATION

An *in vitro* method proposed by Diffey *et al.*, 1994, is based on the shape of the absorption spectrum of a sunscreen product, which is obtained using spectrophotometry The spectral absorbance profiles of different sunscreens is obtained using a UV-1000 SPF analyzer with sunscreen applied at 2 mg/cm^2 on to a quartz plate substrate profiled with the topography of skin samples (85).

Two different methods of rating UVA protection can be calculated from the absorbance spectra. The Diffey critical wavelength is that wavelength below and including which 90% of the total UV is absorbed by a sunscreen from 290 nm to 400 nm (85). Higher critical wavelengths, therefore, indicate better UVA protection. The critical wavelength determination does not promote the fake belief of UVB and UVA as split entities, but rather as part of the uninterrupted electromagnetic range. The Boots UVA ratio is the ratio of the total absorption by a sunscreen in the UVA region compared with that in the UVB region.

A significant positive correlation was observed between IPF and the Diffey critical wavelength. Similarly, there was also a significant positive correlation between IPF and the Boots UVA ratio. Both these parameters measure the breadth of a sunscreen's protection and thus show that the spectral broadness of a sunscreen is an important factor for immunoprotective capability (79).

A complete description of a product's photoprotective distinctiveness fallout when the critical wavelength is used in concurrence with SPF. However, this *in vitro* spectrophotometry measurement lacks the significance to a scientific/biological endpoint easily grasped by the public. IPF possibly has a better correlation with the UVA protectiveness of sunscreen than with the SPF. Furthermore, a more elementary method for measuring sunscreen's immunoprotective capacity is required.

PHOTOSTABILITY OF SUNSCREENS

The photostability of active ingredients of a sunscreen product is also of foremost apprehension. As discussed before, sunscreen ingredients absorb or reflect and scatter radiation throughout the episode they are anticipated to offer a shield for, and consequently they ought to be stable photochemically. However, several chemical filters show signs of some photoreactivity (negligible or noteworthy) and lead to formation of photoproduct(s) that might still act as a filter (e.g., photoisomerization reaction) or presence of such products may lead to diverse protection spectra for different sunscreens and consequently influence their safeguard. Photostability depends on the main filter, presence of other filters, and on solvent or vehicle of the sunscreen product. In order to achieve an effective formulation, it is important to find photostable excipients.

In case of photo-unstable sunscreens, photoprotective efficacy gets reduced on UV exposure. Thereafter, LPx leads to generation of potentially toxic breakdown products that reside on skin besides the presence of sunscreen on the skin. For example, butyl methoxydibenzoyl methane on UV exposure undergoes cleavage and generates ROS. These toxic products also interact with other excipients present in sunscreen and with skin components and increase the thiobarbituric acid reactive species level depicts LPx (86).

The question here is that what are the challenging photoreactions that lead to breakdown? Previous investigations have disclosed photodecomposition of dibenzoylmethanes into complex mixtures in solution, loss of an *N*-methyl group from *N*,*N*-dimethylaminobenzoate (87), photooxidation of dibenzoylmethanes and photodimerization of dibenzoylmethanes (88).

Gonzalez *et al.* (2007) investigated photostability of seven commercial sunscreens with absorption spectrum analysis. Sunscreen product (0.5 mg/cm^2) was placed between plates of silica, and the area under the curve (AUC) in the spectrum was calculated for UVA (320–400 nm), UVA1 (340–400 nm), UVA2 (320–340 nm), and UVB (290–320 nm) before (AUC_{before}) and after (AUC_{after}) UV artificial exposure (UV_{art}) (980 kJ/m^2 UVA and 12 kJ/m^2 of UVB) and before and after UV natural (UV_{nat}).

AUC Index (AUCI), that is, AUCI = AUC_{after}/AUC_{before}, was >0.80, then sunscreen was considered photostable. Here, joules/cm^2 = J/cm^2 and kilojoules/cm^2 = kJ/cm^2.

The investigations revealed that several commercially available sunscreens are not photostable. Instability was noticeable in the absorption region in the UVA range. Sunscreens with TiO_2 particles appeared to be more photostable. UVA absorber butyl methoxydibenzoylmethane, which was present in three out of six sunscreens in the study, was degraded during UV exposure (89).

Avobenzone is not photostable and hence encouraged the need to stabilize the formulation so as to improve efficacy. After UV exposure, avobenzone molecule gets transformed into a molecule that does not absorb UVA radiation; consequently, UVA protection decreases with the time spent under the sun (88). To make it a commercially viable product, manufacturers have developed systems to stabilize avobenzone in the final formulations, for example. The combination of avobenzone with octocrylene, salicylates, methylbenzylidene camphor, micronized ZnO/TiO_2 (90), or Bis-ethylhexyloxyphenol methoxyphenyl triazine (32) makes avobenzone photostable. A combination of diethylhexyl 2,6-naphthalate, avobenzone, and oxybenzone is a constituent of various sunscreens (Table IV). Dometrizole trisiloxane is effective for mid-range UVA protection. The addition of dometrizole trisiloxane to terephthalylidene dicamphor sulphonic acid improves UVA protection in a synergistic manner.

Tarras-Wahlberg *et al.* (1999) investigated UV spectrum of some photoactive organic species common in sunscreens before and after irradiation with UVA and UVB light. Possible presence of breakdown products was determined using gas chromatography mass spectrometer (103).

Moyal *et al.* (2002) utilized diffuse reflectance spectroscopy technique that allows measurement of the UVA efficacy of sunscreen products *in vivo* on human volunteers. The absorption spectrum of the product is obtained by measuring the change in reflection of the skin with and without product. The obtained absorption spectrum helps in revealing

Table IV
Composition of Few Commercially Available Sunscreens Marketed by Pharmaceutical Companies

Product (Brand name)	Active ingredients	Company	SPF	PA factor (UVA coverage)	Ref. (website)
ANSOLAR Gel cream	Avobenzone, Bis-ethylhexyloxyphenol methoxyphenyl triazine, octyl triazone, octocrylene and isoamyl *p*-methoxycinnamate	Stiefel	SPF 30	PA+++	(91)
Ansolar Lotion	Methylene bis-benzotriazolyl tetramethylbutylphenol, Octyl Methoxycinnamate, Homosalate, Octyl Triazone	Stiefel	SPF 60	PA+++ protection; Nongreasy, Hypoallergenic, noncomedogenic, water resistant	(91)
Spectraban sun screen serum control gel	Cyclopentasiloxane, dimethicone cross polymer	Stiefel	SPF 40	PA+++ (PPD 13); prevents skin darkening and helps to reduce brown spots/pigmentation, offers high protection against UVA rays, protects against photoaging	(92)
Spectraban sensitive cream	Methylene bis-benzotriazolyl tetramethylbutylphenol, octyl methoxy cinnamate	Stiefel	SPF 30	PA++; water-resistant properties	(91)
Suncros Aqua Gel	Octinoxate	Ranbaxy Laboratories Ltd.	SPF 26	-	(93)
Suncros Aqua Lotion	Zinc oxide, octinoxate, avobenzone and oxybenzone	Ranbaxy Laboratories Ltd.	SPF 50	-	(94)
Sunkare Lotion	Avobenzone, octinoxate, oxybenzone	Unichem Laboratories Ltd.	SPF 26	-	(95)
Sunban Lotion	Octyl methoxycinnamate, oxybenzone, titanium dioxide	Hh Pharmaceuticals Pvt Ltd.		-	(96)
Photoban	Avobenzone, octyl Methoxycinnamate, oxybenzone	Micro Labs Ltd.	SPF 30	-	(97)
Melagard 50	Avobenzone, octinoxate, oxybenzone, zinc oxide	Nicholas Piramal India Ltd.	SPF 50	-	(98)

Table IV
Continued

Product (Brand name)	Active ingredients	Company	SPF	PA factor (UVA coverage)	Ref. (website)
Hyclean	Octinoxate, oxybenzone	Ranbaxy Laboratories Ltd.	-	-	(99)
Melalite 15 cream	Hydroquinone, octinoxate, oxybenzon	Piramal Health care	SPF 15	-	(100)
Vanicream	Titanium dioxide, zinc oxide	Pharmaceutical Specialties, Inc.	SPF 50+	Broad spectrum but PA factor not mentioned on the label, conforms to the maximum quantity of water resistance (80 minutes)	(101)
Vanicream Sunscreen Sport	Zinc oxide, octinoxate	Pharmaceutical Specialties, Inc.	SPF 35	Broad spectrum but PA factor not mentioned on the label, meets the maximum amount of water resistance (80 minutes)	(102)

the UVA protective efficacy of the test product depending on the type of appropriate source and biological action spectrum (104).

Hojerová *et al.* (2011) assessed photostability of 15 products using three indicators, that is, AUCI for the total UV range, and UVB, UVA, UVA2, UVA1 range separately and the residual effectiveness of *in vitro* SPF and UVA-PF. All sunscreens were photostable in the 15 UVB region. Seven products exhibited photoinstability in the total UV range (290–400 nm); all of them contained a combination of the ethylhexyl methoxycinnamate (EHMC) and butylmethoxydibenzoylmethane (BMBM) together with other UV filters. Eight products lacked their stability in the UVA1 range (340–400 nm), thus confirmed that photodegradation of some current sunscreens is primarily a problem of this region. Sunscreens S1 (EHMC, BMBM, and phenylbenzimidazole sulphonic acid) and S6 (EHMC, BMBM, phenylbenzimidazole sulphonic acid, and ethylhexyl triazone [EHT]) showed maximum photoinstability and their AUC-UVA1 Index was 0.15 only. Excellent UVA1 photostability was shown by sunscreen S8 (EHMC, EHT, and methylene bis-benzotriazolyl tetramethylbutylphenol) and its AUC-UVA1 Index was 1.00. Three sunscreens showed very good UVA1 photostability (AUC-UVA1 Index ranged from 0.98 to 0.93). Comparison of the residual usefulness of *in vitro* SPF and UVA-PF values with the AUC-Index showed that methods give a similar ranking of the sunscreen's photostability (105). Hence, photostability studies should be a mandatory requirement before the marketing of sunscreen for a safer and better sunscreen protection.

WATER RESISTANCE TEST

In vitro test has been performed by few International industries for evaluating water resistance of sun blockers. The test involved assessing SPF of sunscreens before and after water immersion and then determining percentage of SPF retention. If SPF resistance is more than 50%, then the product is marked as water resistant, otherwise not. The products were applied to polymethyl methacrylate (PMMA) plates in place of skin. According to the investigators, conductivity of water affects the water resistance of the products. Ahn *et al.* (2007) also determined *in vitro* water resistance test and concluded that rate of flow of water for washing off the product from substrate and strength or properties of substrate are critical parameters. According to the investigations, stirring rate of 150 rpm for 60 min simulated sufficient *in vivo* conditions (106).

$$\%\mathrm{WRR} = [\mathrm{SPFwet} - 1]/[\mathrm{SPFdry} - 1] \times 100\%$$

where, WRR = water resistance retention SPFwet = SPF after water immersion and SPFdry = SPF before water immersion.

In the United States, *in vivo* determination involves the ability of a product to withstand water immersion for 20 min, and SPF should not change. Very or extra water resistant products should offer the same protection after four cycles of 20-min immersions. Each immersion cycle is followed by a 20-min rest and an air dry period until the total water exposure time is reached. According to European guidelines, SPF after a 40- and 80-min water immersion period is compared to the original SPF before water exposure. The product is declared as water resistant or extra water resistant if SPF after 40- or 80-min immersions, respectively, is greater or equal to 50% of the pre-immersion SPF. Consequently, SPF number specified on label for European sunscreen products is pre-water exposure,

whereas in the United States, the SPF on the label corresponds to the measurements after the water immersion cycles (106).

CONCLUSION

Remedial and marketable interest in the effects of UVA radiation on skin has stimulated efforts to compute and illustrate the worth of sunscreen products in the broad spectrum. However, for appropriate protection against the UV spectrum, contemporary sunscreens should retain this efficiency for the duration of the whole period of exposure to the sun according to labeled SPF. Consequently, it is significant to doubt whether sunscreen is photostable when subjected to sunlight. Changes in labeling guidelines have made it easier for consumers to estimate the echelon of UVA safeguard provided by sunscreens. Yet, advanced research is desirable in many areas including the role of visible light, systemic absorption of sunscreens, and function of vitamin D and sun exposure in preventing diseases.

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