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SUNSCREENS: THE CURRENT SCENARIO

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Abstract

The increasing incidence of cutaneous malignancies and detrimental effects caused by ultraviolet radiation (UV) has increased the use of sunscreens. Many organic and inorganic filters are used as a measure of photoprotection, but their efficacy and safety profile still raise questions. Concerns have been raised regarding safety of nanotechnology in sunscreen, detrimental effects on environment, photocarcinogenic potential of UV filter to name a few. New developments in formulations of sunscreens along with changes in the guidelines of the regulatory bodies like The United States Food and Drug Administration and European Union have prompted us to revisit this topic. Continuous public education is still needed about proper application technique of sunscreen along with behavioral measures. In this article, the authors try to shed light on classification, pharmacological actions, various related terminologies, indications, emerging concerns and correct application technique as well as usefulness of oral sunscreens.

Key Words - Ultraviolet radiation, sunscreen, photoprotection, controversies.

Introduction

Photoprotection is crucial to prevent detrimental effects of ultraviolet (UV) radiations like photo-carcinogenesis, photoageing and photosensitivity. Sunscreens have become an integral part of not only the dermatologists' therapeutic armamentarium but are also distributed as over the counter and cosmetic products because of increasing awareness against harmful impact of radiations. Nevertheless, we need to continue educating the general population about photo protective measures as there are concerns of inadequate application of sunscreen. In this article we attempt to compile basic aspects of sunscreens along with an effort to understand debatable issues associated with it.

Why do we need photo protection?

Ultraviolet radiations (wavelength 200-400nm) are a small part of electromagnetic radiation spectrum, classified as UVA, UVB and UVC. Most detrimental and probably extensively studied part of UV radiations is its role as a major causal factor of skin cancer.[1]Unprotected chronic sun exposure leads to development of non melanoma skin cancers.[2] Direct photochemical damage to DNA is caused by UVB leading to gene mutations by means of pyrimidine dimers and development of precancerous and cancerous lesions while UVA penetrates deeper into skin; acting indirectly at cellular level by generation of free radical species.[3] Ultraviolet radiations cause both acute and chronic effects on skin which are elaborated in [Table 1].[4],[5]

Majority of current research and preventive strategies are centered around detrimental effects of UV radiations on skin due to its higher photon energy and relatively visible macroscopic changes. However, visible light which has been less studied so far, has a significant role in disease pathogenesis like solar urticaria, porphyria and idiopathic photodermatoses.[6] Infrared

Table 1: Effects of ultraviolet radiations on skin.

Ultraviolet radiation spectrum (200-400nm)			
	UVC	UVB	UVA
Wavelength (in nanometers)	200-290	290-320	UVA1=340-400 UVA2=320-340
Sea level solar radiation	0% (Completely absorbed by ozone)	Approximately 2-5%	95-98%
Molecular and cellular effects		• Cyclobutane pyrimidine dimer • 6-4 pyrimidine-pyrimidone dimer • Epidermal sunburn cell • Skin hyperplasia • Vitamin D synthesis	• Reactive oxygen species •Immuno-suppression •Cyclo butane pyrimidine dimer (weak)
Clinical effects Acute		• Erythema (peaks 24 hours), Oedema • Pigment darkening • Delayed tanning	• Immediate pigment darkening (fades within 15 minutes)
Chronic		• Photocarcinogenesis • Photoageing • Immunosuppression (weak)	• Photoageing •Immunosuppression • Photocarcinogenesis (weak)

A (IRA) can cause photoageing and photocarcinogenesis through its ability to induce gene alterations.[7] Education about wholesome photo protective measures is needed to attain overall protection against solar radiations.

Sunscreen usage: indications

Sunscreens have become an integral part of day to day activity, primarily used for protection against immediate and long term ill effects of ultraviolet radiations. With current trends of leisure activities like sunbathing, tan beddings and increased awareness of skin cancers, markets are flooded with more and more sunscreens. Sunscreens are primarily indicated in prevention and management of freckling, sunburn, photoageing, photocarcinogenesis, photosensitive and photo-aggravated dermatoses. Sunscreens have become indispensable in procedure driven dermatology to prevent post procedural hyper pigmentation. Strict photoprotection is needed to prevent development or aggravation of certain dermatoses, few examples of which are tabulated [Table 2].

Table 2. Indications of strict photoprotection.

- Dysplastic naevus syndrome
- Systemic lupus erythematosus
- Dermatomyositis
- Genetic skin cancer syndromes (xeroderma pigmentosum, Gorlin syndrome)
- Bloom syndrome, Cockayne syndrome
- Previous or current non-melanoma skin cancer
- Previous melanoma
- Previous exposure to arsenic or ionizing radiation
- Patients on systemic immunosuppressive therapy
- Porphyrias

Sunscreen: classification and characteristics

Sunscreen agents are broadly divided into topical and systemic. According to the Food and Drug Administration (FDA), topical sunscreens are classified as organic and inorganic, discarding the previously used terms like chemical and physical sunscreens [Figure 1]. An organic sunscreen agent is an active chemical which depending on their chemical characteristic absorbs UV radiation thereby moving into higher energy state from ground state. Depending on the fate of higher energy excited state, these are further divided into photo-stable, photo-unstable and photo-reactive.

- *Photo-stable sunscreen:*
  - » It returns to the ground state after dissipating its absorbed radiation to the environment as heat.
  - » Subsequently becomes capable of absorbing UVR again (recycles).
- Photo-unstable sunscreen:
  - » It degrades or undergoes conformational change after absorbing UV energy.
  - » It cannot enter in next cycle.
- *Photo-reactive sunscreen:*
  - » These agents produce free radicals by interactions of their excited state to surrounding biological molecules.
  - » They can exert unwanted biological effects.

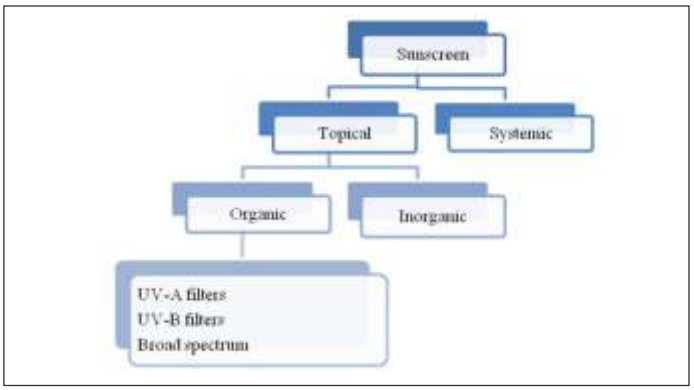

Figure 1. Classification of sunscreens.

Inorganic agents exert their protective function by means of reflecting, scattering or absorbing UV radiation. To enhance user's experience their "whitening effect" may be lessened by using their micronized or ultrafine particles.[8] Incorporation of inorganic particulates has an added advantage of scattering light from the upper layers of epidermis thus enhancing the sunburn protection factor (SPF) value.[9],[10]

On the basis of photo protective quality against particular wavelengths, topical sunscreens are classified as UVA filters, UVB filters and broad spectrum sunscreens. Sunscreen agents are recognized by three widely used nomenclatures which are the US adopted name (USAN), International Nomenclature Cosmetic Ingredient (INCI) name, and trade name [Table 3].[11]

Sunscreen related terminology:

For a long time the labeling information over sunscreens was misleading and confusing, making claims like sweat proof, water proof etcetera. Regulatory agencies like the FDA and European Union (EU) issued guidelines to regulate labeling of sunscreens hence enabling people to choose effective agents, to provide optimal sun protection without being misguided by lucrative claims of pharmaceuticals.[12] The FDA has discarded the terms like sweatproof, waterproof and sun blocks for the same reasons. These terminologies have been replaced by water resistant and very water resistant which are adequately defined. According to the FDA, manufacturers should display the effective duration of water resistance and need of reapplication over the sunscreen label. Water resistant sunscreens should be applied before activities like swimming or excessive sweaty conditions. False claims like immediate protection after application or longstanding efficacy of product (lasting >2 hours) are forbidden if not supported by enough evidence. Consumers can confidently choose a product suitable to their needs with help of this information over label and be realistic about photo protective efficacy of the product. The FDA has also made it mandatory to test a product for both UVB and UVA protection before using the terminology 'broad spectrum' on the label.

Water resistant- withstand 2 sequential water immersion of 20 minutes (40 minutes total) while maintaining claimed SPF value.

Very water resistant- maintains claimed SPF after immersion in water for 20 minutes, 4 times (80 minutes total).

Critical wavelength- wavelength at which 90% of the total area under the absorbance curve occurs.

Broad spectrum- sunscreen with critical wavelength ≥ 370nm with UVA protection factor ≥ 4.

Table 3. Classification and nomenclatures of topical sunscreen agents.

USAN	*INCI*	*Trade name*
Broad-spectrum and UVAI (340-400 nm)		
Bemotrizinol	Bis-ethyl hexyl oxyphenol mmethoxy phenyltriazine	Tinosorb S
Bisoctrizole	Methylene bis-benzotriazolyl tetramethylbutylphenol	Tinosorb M
Silatriazole	Drometrizole trisiloxane	Mexoryl XL
Ecamsule	Terephthalylidene dicamphorsulfonic acid	Mexoryl SX
Avobenzone	Butyl methoxydibenzoyl methane	Parsol 1789
	Diethylamino hydroxybenzoyl hexyl benzoate	Uvinul A Plus
Bisdisulizole	Disodium phenyl dibenzimidazole tetrasulfonate	Neo Heliopan AP
Zinc oxide	Zinc oxide	ZnO(nanox)
UVB (290-320 nm) and UVAII (320-340 nm)		
Enzacamene	4-Methylbenzylidene camphor	Eusolex 6300
Oxybenzone	Benzophenone-3	
Padimate O	Ethyl hexylrimethyl PABA	Eusolex 6007
Octinoxate	Ethyl hexylmethoxycinnamate	Uvinul MC 80
Octisalate	Ethyl hexyl salicylate	Neo heliopan OS
Amiloxate	Isoamyl p-methoxycinnamate	Neo heliopan E1000
Octyltriazone	Ethyl hexyltriazone	Uvinul T 150
Sulisobenzone	Benzophenone -4	Uvinul MS40
Octocrylene	Octocrylene	Uvinul N 539 T
Homosalate	Homomenthyl salicylate	Eusolex HMS

The efficacy of sunscreen agents is determined by two main indices; SPF and UV protection factor. There are several in vivo and in vitro methods to determine these. Protection against erythemogenic spectrum of UV light (UVB and UVA2) is measured by sunburn protection factor (SPF).[12]

The sunburn protection factor is measured as a ratio of the amount of UVR necessary to burn the protected skin (with sunscreen) to that required to burn the same non protected skin (without sunscreen) with all other parameters being constant. The required amount of UVR is known as MED (minimal erythema dose) which is defined as the minimum UV dose required to produce perceptible erythema of the skin with well defined margins at 16 to 24 hours after UV irradiation.[12] This means that a SPF 30 sunscreen protected skin can tolerate the same amount of UV radiation 30 times more than the unprotected skin. The grading of SPF is done as low (SPF 2-15), medium (SPF 15-30), high (SPF 30-50) and highest (SPF >50).

For measurement of UVA protection, various testing methods have been developed by regulatory bodies in Japan, the European Union (EU), United Kingdom (UK) and Australia.

UVA protection indices:

1. Australian/New Zealand Standard: In vitro method. 8-µm and 20-µm thick layers of the product should not transmit greater than 10% and 1% of radiation of 320 to 360 nm, respectively.
2. Japanese standard (persistent pigment darkening): In vivo test. It is a ratio of UVA required to induce persistent pigment darkening (PPD) 2 to 24 hrs after irradiation in sunscreen protected skin to unprotected skin. Ratings- PA+, PA++, PA+++, PA++++ (PA= protection grade from UVA).
3. European Union guidelines: Based on PPD method. It requires UVA protection factor to be ≥ 1/3 of labeled SPF.
4. Boots star rating system (United Kingdom): In vitro method. It measures ratio of UVA absorbance to mean UVB absorbance.

Since 2012, the FDA has mandated that only sunscreens having SPF≥15 and critical wavelength ≥370 nm, can display their claim about protection against development of skin cancers.[12]

Ideal sunscreen: The notion of ideal sunscreen is that it should provide maximum photo-protection while maintaining its compliance quality. An ideal sunscreen should possess 'spectral homeostasis', which refers to uniform protection against UVA

and UVB radiations spectrum.[13] The characteristics of an ideal sunscreen also include cosmetic acceptability and non-irritant nature, among others [Figure 2].

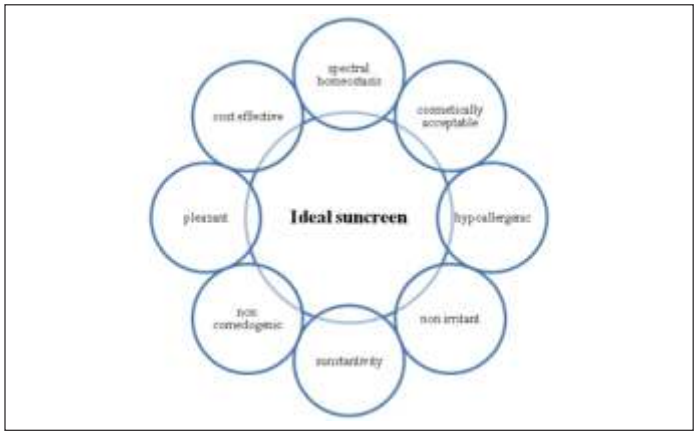

Figure 2. Ideal sunscreen

Guidelines for application:

Apart from SPF and substantivity, the other major factor that determines the protective efficacy of a given sunscreen is its adequate application. There is a lack of basic knowledge about correct application, leading to attainment of only one third to quarter of the recommended dose of photoprotection.[14] Sunscreen needs to be applied about half an hour before going outdoor, in a density of at least 2 mg per square centimeter which can be further simplified by following the "Tea spoon rule."[15] The rule recommends application of 1 teaspoon of sunscreen to the face/head/neck, 1 teaspoon to each upper limb, 2 teaspoons to trunk (front and back), and 2 teaspoons to each lower limb. The protective efficacy can be boosted significantly by reapplication 20 minutes later, thus correcting the areas of inadequate application.[6]

Sunscreen should always be used along with complete photoprotection package which includes seeking shade, protective clothing, wide-brimmed hat and sunglasses. A continuous effort in public education is required concerning its correct application, reapplication and prevention of unnecessary sun exposure.

Systemic sunscreens:

There is a growing interest in use of orally active ingredients to counter the inherent photochemical reaction, by decreasing free radical injuries. Antioxidants act by reversing the oxidative stress developed by UVR and infrared radiations. Their protective efficacies have been reported in various studies. Still larger studies are needed to confirm their level of protection and long term safety profile. Carotene, antimalarials, vitamin A, C and E, green tea extracts, selenium, retinol and many more have been reported to have photo protective qualities.[8] Three widely used and studied systemic sunscreens are polypodium leucotomos extract, afamelanotide and nicotinamide.

Polypodium leucotomos, belonging to fern group of plants, has been shown to decrease psoralen plus UVA and UVB phototoxicity.[16],[17] The oral administration of the drug as 240 mg twice a day provides a SPF value of 3-8, and has been shown it to be protective against erythemogenic spectra of UVR.[18]

The melanocortin-1 receptor agonist, afamelanotide exerts its photoprotection via increasing synthesis of eumelanin. It has been approved as an adjuvant in adult patients of erythropoietic protoporphyria by the European Union to prevent phototoxicity and has to be administered as 16 mg subcutaneously every 2 months.[19]

When taken orally, nicotinamide (active form of niacin) has been shown to be photo protective by enhancing intracellular adenosine triphosphate,[20] DNA repair and boosting cell energy.[21],[22] Its broad photoprotective effect against development of premalignant lesions is being studied currently.

Sunscreens related controversies:

1. Hormonal effect:

There are rising concerns about possible hormonal disruption of sunscreen agents benzophenones specially oxybenzone, which is in widespread use since 1970s. Initial in vitro studies have shown its antiandrogenic and estrogenic effects.[23],[24] However in recent in-vivo studies the claims were not substantiated about cause and effects.[25] Careful observation and further human studies are needed to clarify this aspect.

2. Role of antioxidants:

Nowadays, many sunscreen manufactures are using antioxidants beside active ingredient to decrease the adverse effects of free radicals, generated by UV exposure. In vivo studies have shown decreased matrix metalloproteinase-1 activity and less pigment induction with use of stabilized antioxidants[26] but a recent study has proven otherwise because of lack of stability of antioxidants used in sunscreens.[27]

3. Nanoparticulate sunscreen:

There are concerns about rising use of nanotechnology in sunscreens (to make it cosmetically elegant) as nanoparticles can produce free radicals on UV irradiation.[28] Various studies have shown that the confinement of nanoparticles is limited to stratum corneum. In addition, the use of coated nanoparticles has made it safe for usage in humans.[29] However application at sites with severely impaired barrier function should be minimized till further data are available.

4. Photocarcinogenic potential of retinyl palmitate (RP):

It is a storage form of vitamin A which was approved by the FDA to use in cosmetics and edibles. In view of rising concerns about photo carcinogenicity of compound, Wang et al[30] concluded in-depth review on this topic in addition to a large in-vivo study conducted by the FDA. None of the above could establish conclusive evidence about photo-carcinogenicity of RP. Also there is long standing history of safety profile of the product in humans.[11]

5. Vitamin D deficiency:

There have been concerns of vitamin D deficiency regarding universal use of sunscreens as ninety percent of vitamin D production in skin happens as a result of UV exposure. However, review of literature by Norval et al[31] concluded that deficiency doesn't occur with normal usage of sunscreen most likely due to insufficient application of sunscreen by most individuals. Unprotected exposure to UVR is not recommended to obtain vitamin D and supplementation in individuals at risk is advised as supported by the Institute of Medicine.[19]

6. Pediatric population and sunscreen:

Although there are no deleterious effects of sunscreen documented with use in early age, still it is advisable to use sunscreens containing inorganic filters over exposed area, in

adjunction to other sun protective measures.[11]

7. Environmental issues:

The effects of organic sunscreens on environment have become a burning issue since water sources are found to be contaminated with sunscreens specially oxybenzone in various studies.[32] They can react to chlorine in pools to form brominated transformation products which are hard to remove by usual water filters. In addition to this, studies have indicated possible role of oxybenzone in coral bleaching.[33] The adverse impact is still being studied.

8. Role of higher SPF:

The labeling restriction of SPF value more than 50 as SPF50+ by the US FDA has created a stir about significance of higher SPF. Various studies have shown that sunscreen with higher SPF has provided better protection against sunburn and UV induced phototoxicity.[34] The higher SPF can compensate the efficacy of a product in actual use as there are enough evidences to suggest that on an average only one third amount of a given SPF is attained due to insufficient and improper application.[14]

9. Sunscreen and special populations

There has always been confusion about prescription of sunscreen in Fitzpatrick skin type IV to VI as these skin types are less prone to sun damage because of inherent protective quality of melanin. However, enough evidence of photodamage including photo ageing has been documented.[35] In addition, malignant melanoma carries a poorer prognosis in POC (people of colour) despite low prevalence. Hence it is recommended to use regular sunscreen with other sun protective measures the same way as in other skin types. Broad spectrum sunscreen with SPF ≥30, specially containing inorganic filters are better suited for POC as they are more acceptable.[36]

Use of regular sunscreen with other photo protective behavior measures should be followed in patients of organ transplantation and dialysis to decrease the risk of premalignant and malignant changes in skin.[37]

10. Sunscreen and cosmetics:

Besides conventional sunscreen cream and lotion, now a day active ingredients are seen as foam, gel, mousse, spray, pastes, oils, butters, sticks and ointments. The pharmaceuticals and cosmetic giants are using sunscreen in range of over the counter products and cosmetics like foundation, compact, shampoo, lipstick, lip balm and wipes, with claim of varied SPF. The efficacy of these are not well established and not approved by the FDA yet. The spray forms are being promoted as convenient to use in children and over relatively non accessible sites like back in adults. For acne prone skin, gel and sprays forms are tolerated well. Sprays have also shown to retain active compounds to superficial layers of epidermis thus decreasing the risk of deeper penetration.[38]

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References

1. Gilchrest BA, Eller MS, Geller AC, Yaar M. The pathogenesis of melanoma induced by ultraviolet radiation. N Engl J Med 1999;340:1341-48.
2. van Kranen HJ, Westerman A, Berg RJ, Kram N, van Kreijl CF, Wester PW, et al. Dose-dependent effects of UVB-induced skin carcinogenesis in hairless p53 knockout mice. Mutat Res 2005;571:81-90.
3. Rhodes LE. Topical and systemic approaches for protection against solar radiation-induced skin damage. Dermatol Clin 1998;16:75-82.
4. Forestier S. Rationale for sunscreen development. J Am Acad Dermatol 2008;58:133-8.
5. Young AR. Photobiology. In: Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's Textbook of Dermatology. 9th ed. West Sussex (UK): Wiley-Blackwell; 2016. p.9.5-9.7.
6. Rai R, Shanmuga SC, Srinivas C R. Update on photoprotection. Indian J Dermatol 2012;57:335-42.
7. Calles C, Schneider M, Macaluso F, Benesova T, Krutmann J, Schroeder P. Infrared A radiation influences the skin fibroblast transcriptome: mechanisms and consequences. J Invest Dermatol 2010;130:1524-36.
8. Kaimal S, Abraham A. Sunscreens. Indian J Dermatol Venereol Leprol 2011;77:238-43.
9. Lademann J, Schanzer S, Jacobi U, Schaefer H, Pflücker F, Driller H, et al. Synergy effects between organic and inorganic UV filters in sunscreens. J Biomed Opt 2005;10:14008.
10. Vergou T, Antoniou C, Patzelt A, Richter H, Schanzer S, Sterry W, et al. Transfer of ultraviolet photon energy into fluorescent light in the visible path represents a new and efficient protection mechanism of sunscreens. J Biomed Opt 2011;16:105001.
11. Jansen R, Osterwalder U, Wang SQ, Burnett M, Lim HW. Photoprotection: part II. Sunscreen: development, efficacy, and controversies. J Am Acad Dermatol 2013;69:867-e1.
12. Latha MS, Martis J, Shobha V, Shinde RS, Bangera S, Krishnankutty B, et al. Sunscreening agents: a review. J Clin Aesthet Dermatol.2013;6:16-26.
13. Diffey B. The need for sunscreens with broad spectrum protection. In: Urbach F, editor. Biological responses to ultraviolet a radiation. Overland Park (KS): Valdenmar Publication Co; 1992. pp. 321-8.
14. Wang SQ, Dusza SW. Assessment of sunscreen knowledge: a pilot survey. Br J Dermatol 2009;161:28-32.
15. Isedeh P, Osterwalder U, Lim HW. Teaspoon rule revisited: proper amount of sunscreen application. Photodermatol Photoimmunol Photomed 2013;29:55-6.
16. Gonzalez S, Pathak MA, Cuevas J, Villarrubia VG, Fitzpatrick TB. Topical or oral administration with an extract of Polypodium leucotomos prevents acute sunburn and psoralen-induced phototoxic reactions as well as depletion of Langerhans cells in human skin. Photodermatol Photoimmunol Photomed 1997;13:50-60.
17. Middelkamp-Hup MA, Pathak MA, Parrado C, Garcia-Caballero T, Rius-Díaz F, Fitzpatrick TB, et al. Orally administered Polypodium leucotomos extract decreases psoralen-UVA induced phototoxicity, pigmentation, and damage of human skin. J Am Acad Dermatol 2004;50:41-9.
18. Nestor MS, Berman B, Swenson N. Safety and efficacy of oral Polypodium leucotomos extract in healthy adult subjects. J Clin Aesthet Dermatol 2015;8:19-23.
19. Lim HW, Arellano-Mendoza MI, Stengel F. Current challenges in photoprotection. J Am Acad Dermatol 2017;76:91-9.
20. Park J, Halliday GM, Surjana D, Damian DL. Nicotinamide prevents ultraviolet radiation-induced cellular energy loss. Photochem Photobiol 2010;86:942-48.
21. Surjana D, Halliday GM, Damian DL. Nicotinamide enhances repair of ultraviolet radiation-induced DNA damage in human keratinocytes and ex vivo skin. Carcinogenesis 2013;34:1144-49.
22. Thompson BC, Surjana D, Halliday GM, Damian DL. Nicotinamide enhances repair of ultraviolet radiation-induced DNA damage in primary melanocytes. Exp Dermatol 2014;23:509-11.
23. Schlumpf M, Schmid P, Durrer S, Conscience M, Maerkel K, Henseler M, et al. Endocrine activity and developmental toxicity of cosmetic UV filters- an update. Toxicology 2004;205:113-22.
24. Ma R, Cotton B, Lichtensteiger W, Schlumpf M. UV filters with antagonistic action at androgen receptors in the MDA-kb2 cell transcriptional-activation assay. Toxicol Sci 2003;74:43-50.
25. Janjua NR, Mogensen B, Andersson AM, Petersen JH, Henriksen M, Skakkebaek NE, et al. Systemic absorption of the sunscreens benzophenone-3, octyl-methoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and

reproductive hormone levels in humans. J Invest Dermatol 2004;123:57-61.
26. Matsui MS, Hsia A, Miller JD, Hanneman K, Scull H, Cooper KD, et al. Non-sunscreen photoprotection: antioxidants add value to a sunscreen. J Investig Dermatol Symp Proc 2009;14:56-9.
27. Wang SQ, Osterwalder U, Jung K. Ex vivo evaluation of radical sun protection factor in popular sunscreens with antioxidants. J Am Acad Dermatol 2011;65:525-30.
28. Newman MD, Stotland M, Ellis JI. The safety of nanosized particles in titanium dioxide and zinc oxide based sunscreens. J Am Acad Dermatol 2009;61:685-92.
29. Livraghi S, Corazzari I, Paganini MC, Ceccone G, Giamello E, Fubini B, et al. Decreasing the oxidative potential of TiO(2) nanoparticles through modification of the surface with carbon: a new strategy for the production of safe UV filters. Chem Commun 2010;46:8478-80.
30. Wang SQ, Dusza SW, Lim HW. Safety of retinylpalmitate in sunscreens: a critical analysis. J Am Acad Dermatol 2010;63:903-6.
31. Norval M, Wulf HC. Does chronic sunscreen use reduce vitamin D production to insufficient levels? Br J Dermatol 2009;161:732-6.
32. Cuderman P, Heath E. Determination of UV filters and antimicrobial agents in environmental water samples. Anal Bioanal Chem 2007;387:1343-50.
33. DiNardo JC, Downs CA. Dermatological and environmental toxicological impact of the sunscreen ingredient oxybenzone/benzophenone-3. J Cosmet Dermatol 2018;17:15-9.
34. Williams JD, Maitra P, Atillasoy E, Wu MM, Farberg AS, Rigel DS. SPF 100+ sunscreen is more protective against sunburn than SPF 50+ in actual use: Results of a randomized, double-blind, split-face, natural sunlight exposure clinical trial. J Am Acad Dermatol 2018;78:902-10.
35. Del Bino S, Bernerd F. Variations in skin color and the biological consequences of ultraviolet radiation exposure. Br J Dermatol 2013;169:33-40.
36. Agbai ON, Buster K, Sanchez M, Hernandez C, Kundu RV, Chiu M, et al. Skin cancer and photoprotection in people of color: a review and recommendations for physicians and the public. J Am Acad Dermatol 2014;70:748-62.
37. Ulrich C, Degen A, Patel MJ, Stockfleth E. Sunscreens in organ transplant patients. Nephrol Dial Transplant 2008;23:1805-8.
38. Durand L, Habran N, Henschel V, Amighi K. In vitro evaluation of the cutaneous penetration of sprayable sunscreen emulsions with high concentrations of UV filters. Int J Cosmet Sci2009;31:279-92.