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Sunscreen- The Double Edged Sword

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Editorial

Sunscreens have long being recognized as substances to provide effective protection against the detrimental effects of solar radiation. The deleterious effects of sun exposure can be either acute (e.g. sunburn and drug-induced photo toxicity) or chronic (potential long-term risks of repeated sun exposures like solar elastosis, keratoses, induction of skin cancers, and alteration of immune responses and functions)[1]. Due to growing incidences of skin cancer, dermatologists are regularly recommending sunscreens to their patients. Action spectra of normal and abnormal reactions of solar radiationare variable, which can serve as a deciding factor in prescribing the appropriate sunscreens catering to individual patient needs. Increased recognition of the harmful effects of ultraviolet (UV) radiation on the skin has triggered development of two main types of sunscreens namely Physical and Chemical, based on the nature of UV filter present in them. The physical also known as Inorganic sunscreen protects our skin by deflecting or blocking the sun's rays and usually contains Titanium dioxide (TiO_2) and Zinc oxide (ZnO) as active ingredients. They are generally stable with lesser chances of degradation. TiO_2 having a pitiable UVA protection with an excellent UVB defence may lead to skin eruptions in predisposed individuals. While Zinc oxide with a superior defence against the entire spectrum of UVB and UVA rays is generally well tolerated and can be used even on delicate skin. Both are FDA approved but cosmetically physical sunscreens are less tempting as being thick and opaque and they leave a white cast.

Chemical Sunscreen also referred to as organic sunscreen works by absorbing the solar radiation. While a few chemical filters can scatter sun rays, most of them work by absorption. The following UV filters or the active ingredients are most commonly used: Octylcrylene, Avobenzone, Octinoxate, Octisalate, Oxybenzone, Homosalate, Helioplex, 4-MBC, butyl methoxydibenzoylmethane (*BMDBM*), Mexoryl SX and XL, Tinosorb S and M, Uvinul T 150 and Uvinul A Plus. Most of them are photostable and have a better coverage against UVA and UVB rays than physical sunscreens, but the range of protection depends on the active ingredient and its stability. Although more acceptable, it can potentially irritate the sensitive skin and eyes. Not all the marketed Chemical sunscreens are FDA approved and themajority of marketed sunscreens contain both physical and chemical UV filters. McLean DI, *et al.* [2] in 1998 discussed on the common myth in the public health sunscreen message like sunscreens prevent all types of skin cancer, andthat it prolongs the stay time in the sun. In Matsuoka LY, *et al.* [3] favoured the hypothesis that sunscreens suppress synthesis of vitamin D3. From then numerous other similar studies worked up to give dissimilar result regarding safety of sunscreen. Martincigh, *et al.* drew attention to the detrimental effect of sunscreens as photosensitizers, with propensity to photopotentiate dangerous reactions in the skin, especially the dimerization of thymine [4]. Gonzalez H, *et al.* [5] showed that BMDBM, one of the most widely used UV-A filter, undergoes decomposition under sunlight exposure and it was noticed that photostability of the sunscreen in the UVA range is not always adequate since it depends on factors like preservatives, oxygen radical scavengers, and base formulation. Despite emerging trends, safety of titanium dioxide and zinc oxide nanosized particles has come under scrutiny. And thus the question of safety of physical sunscreen containing titanium dioxide came in picture when a study conducted by Brezová V, *et al.*[6] found creation of reactive oxygen species upon photoexcitation of sunscreens containing titanium dioxide. This reaction significantly depends on the sunscreen composition, as the additives present (antioxidants, radical-scavengers, solvents) can transform the reactive radicals generated to less harmful alternatives. Recently there is a renewed interest in sunscreens containing metal oxide nanoparticles which are thought to provide excellent protection against sunburn and being transparent on the skin have a better cosmetic appeal [7,8]. A significant study by Gulson B, *et al.* [8] found that a small quantity of zinc from zinc oxide particles in sunscreens is absorbed through human skin. Further blood and urine zinc level from nano

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sunscreen group was higher than those receiving the bulk sunscreen which might be due to the fact that nano-sized particles potentially release more ionic Zn due to their larger surface area [9]. Tan MH, *et al*. [10] in a pilot study on the percutaneous absorption of microfine titanium dioxide found a higher level of titanium in the epidermis and dermis of subjects who applied micro fine titanium dioxide sunscreen to their skin. Although, studies with larger cohorts are necessary to establish if this absorption is statistically significant but this landmark finding can create awareness among a lot of people applying microfine titanium dioxide sunscreen. Further *in vitro*studies on insoluble nano sized particles suggested possible cell uptake, oxidative cell damage or genotoxicity.

An extremely significant proposition is UVA barring sunscreens cause more damage to human skin as UVA radiation and/or visible light has the propensity to attenuate certain damage induced by UVB. This is supported by van Weelden, *et al.* in 1984 when they demonstrated that UV A radiation can decrease UVB induced erythema in human skin. Further Sutherland, *et al.* in 1980; D'Ambrosio, *et al.* in 1981; Eggset, *et al.* in 1983; and Roza, *et al.* in 1991 supported reduction in UVB-induced thymine dimmers following exposure to UVA and/or visible light in humans. Giokas DL, *et al.* [11] emphasized that photo-induced decomposition cannot be the sole reason of gradual attenuation of protective capacity of UV filters applied on the skin surface and concluded that systematic absorption through the skin surface do play some role.Gustavsson GH, *et al.* [12] emphatically demonstrated that Benzophenone-3 (BZ-3) which is a commonly used chemical UV filter following per cutaneous absorption undergoes conjugation in the body to make it water soluble before urinary excretion. Thus babies should be ideally stay away from chemical sunscreens keeping in mind their immature liver conjugation capacity, which can lead to potential toxicity.Janjua NR, *et al*. [13] in 2008 also demonstrated the common chemical UV filters namely Benzophenone-3 (BP-3), Octyl-Methoxycinnamate (OMC) and 3-(4-methylbenzylidene) camphor (4-MBC) have detectable plasma and urine concentration after 2 hours of the first application. Further *in vitro and animal studies have shown* endocrine-disrupting effects of these ingredients leading to disruption of endogenous reproductive hormone levels. Studies on experimental animals reveal UV-filters can potentially lead to developmental/reproductive toxicity and disturbances of hypothalamic–pituitary–thyroid axis [14]. Suzuki T, *et al*. [15] compared benzophenone and 16 of its derivatives with hormone-responsive reporter assay in various cell lines to crack estrogenic and antiandrogenic activities of the former. They found hydroxylated benzophenones exhibited estrogenic activity in human breast cancer cell line MCF-7 and also 4-hydroxyl group on the phenyl ring of benzophenone derivatives is essential for high hormonal activities, and the existence of other hydroxyl groups distinctly alters its function. Liardet S, *et al.* [16] in 2001, questioned the safety of sunscreens as they challenged that high level of DNA damage can be induced even without the warning sign of erythema. It was postulated that prevention of actinic erythema does not prevent other deleterious effects of UV radiation and a high rate of DNA damage can take place even in the protected skin which in long run can lead to frank malignancy. Marinus C.G. Van Praag MCG, *et al.* [17] favours the view that UV- induced fall of allo-activating capacity is not prevented by local application of sunscreen. There is an imperative implication of lack of correlation between defence against erythema and immune suppression since it encourages the user to stay in the sun longer, thus increasing the risk of immune suppression, which is associated with an increase incidence of cutaneous malignancies. Autier P, *et al.* [18] based on their study proposed that sunscreens do not protect against melanoma. This might be due to their ability to hold-up or evade sunburn episodes, which lead to prolonged exposure to unfiltered ultraviolet radiation.Krause M, *et al.* [14] in 2012 review a number of selected chemical UV filters like benzophenone-3 (BP-3), 3-benzylidene camphor (3-BC), 3-(4-methyl-benzylidene) camphor (4-MBC), 2-ethylhexyl 4-methoxy cinnamate (OMC), Homosalate (HMS), 2-ethylhexyl 4-dimethylaminobenzoate (OD-PABA), 4-aminobenzoic acid (PABA) and found fewer convincing results for defence against melanoma skin cancer by sun protective topical preparations. On further review of human studies and animal data, suspected role of sunscreen in causation of melanoma skin cancers was suggested, which was further supported by a rapidly rising incidence of malignant melanoma despite of ever increasing use of sunscreens.

For UV protection of both normal individuals and of patients with photosensitivity-related problems, various methods apart from overhyped use of sunscreen can be effective. WHO in its Ultravioletradiation and the INTERSUN Programme recommends use of protective clothing, limiting the mid-day sun as UV rays are the strongest between 10 a.m. and 4 p.m. Mind the Shadow rule "Watch your shadow – Short shadow, seek shade!" and watching for UV index to predict the exposure level can prove quite beneficial and free from potential side effects.

Skin cancer is an increasing problem worldwide with excessive UVR exposure as the major risk factor. All subjects when outdoors should adopt a comprehensive approach to effective photoprotection. If they do a decrease in skin cancerincidence in future will be a reality.

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