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Review Of Sunscreen In UVA Protection And Preventing Skin Cancer

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ABSTRACT

The promotion of sunscreen products as a means to mitigate skin damage from ultraviolet radiation (UVR) is widely supported by healthcare professionals. However, there is a pressing need to thoroughly understand both the efficacy and safety of these products. The current method for evaluating sunscreen efficacy, the sun protection factor (SPF), primarily measuresprotection against UVB rays (290-320 nm). This assessment does not fully account forprotection against long-wavelength UVA1 (340-400 nm) rays. Furthermore, there is no universally accepted method for evaluating UVA efficacy, which is critical as consumers increasingly demand broad-spectrum UVB and UVA protection.UVB radiation causes significant damage to keratinocytes by inducing DNA damage that can lead to malignant transformation. The body's defense mechanisms include the immediate death of severely damaged cells and the blockage of cell-cycle progression in less affected cells, allowing for DNA repair through nucleotide excision repair (NER). Successfully repaired cells survive, while irreparably damaged keratinocytes undergo apoptosis, forming "sunburn cells."Sunscreens are designed to protect the skin from excessive UVR exposure. They are often recommended for their ability to prevent UV-induced sunburns and reduce the risk of premature skin aging and skin cancer. However, current sunscreen labeling may overstate the protective benefits, potentially misleading consumers into feeling safer to extend their sun exposure.This approach emphasizes practical usage over mere reliance on product labeling, ensuring more effective sun protection and reducing the risk of UVR-related skin damage.

KEYWORDS

Skin, Sunscreen, Organic filters, Natural Products, Inorganic filters.

INTRODUCTION

The use of sunscreens as photoprotective agents for UV protection is becoming very popular. A sunscreen preparation is defined as a formulation which, when applied topically, protects the treated area from sunburn. Sunscreens aid the body's natural defense mechanisms against harmful UV radiation from the sun. Their function is based on their ability to absorb, reflect, or scatter the sun's rays.

The SPF is calculated from the formula: $SPF = \frac{MED\ with\ sunscreen}{MED\ without\ susncreen}$.

Where, MED = Minimal erythema dose.

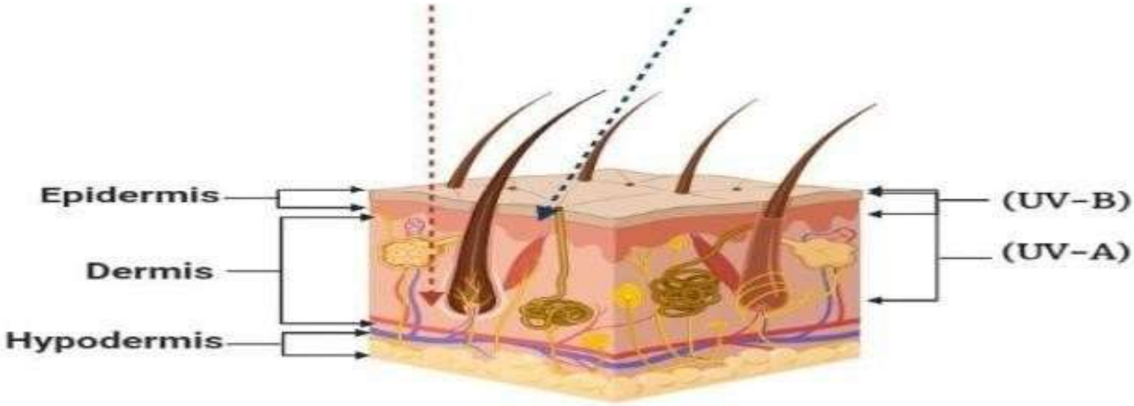

Fig.1:Anatomy of skin layers and showing penetration of UVA and UVB radiation intoskin layers

Frequent exposure to solar ultraviolet (UV) radiation is well known to cause damage to exposed surfaces, leading to the fading and aging of paints, fabrics, and plastic coatings, as well as sun-related skin cancer, which are major industrial, environmental, and health concerns. Advancing the field of UV protection involves protecting against the broadest possible spectrum of UV radiation, including ultraviolet-A (UVA) (400–320 nm) and ultraviolet-B (UVB) (320–290 nm) wavelengths of sunlight. This advancement includes optimizing the photostability of protective molecules and trapping reactive species before photochemical damage occurs.

This review presents some of the recent innovations in UV-protective technology, including advancements in nanoparticles, nanoencapsulation, and nanocomplexation. It also explores recent novel applications and potential future directions, such as incorporating antioxidants and natural products, to enhance UV protection. Beyond these technological advancements, the review discusses novel applications such as integrating antioxidants and natural products into UV-protective formulations. Antioxidants can mitigate oxidative damage induced by UV radiation, while natural products offer potential benefits such as biocompatibility and reducedenvironmental impact.

LITERATURE REVIEW

1. Francis P. Gasparro

These studies collectively underscore the necessity of UVA photoprotection. The findings prompt further investigation into identifying chromophores that are sensitive to longer UVA wavelengths and potentially shorter visible light wavelengths. Although action spectra determinations frequently emphasize this aspect, pinpointing a specific chromophore isuncommon. Nevertheless, these studies highlight which wavelengths exhibit potentiating effects. Although continued investigations will certainly be fruitful, existing in vivo animal and human studies are remarkably consistent in their conclusion that sunscreens are both safeand effective. One criticism has been that sunscreens block only a portion of the UVR spectrum. However, now that true broad-spectrum protection is possible, this should no longerbe an issue.

2. Devanjali Bhattacharjee

From this, we can conclude that sunscreens made of natural products are better than those formulated with synthetic ingredients. Ultraviolet rays damage skin function, with UV-B affecting the upper layer of the skin and causing sunburn. To treat this, sunscreen agents are used. While synthetic products in formulations are effective, they have side effects such as endometriosis, cytotoxicity, and genotoxicity. To overcome this problem, natural products areused in sunscreens, offering minimal side effects and being as efficacious as synthetic products.

3. K. Morabito

We have reviewed the traditional components, the use of nanoparticles, and the emerging technologies of UV protection in considerable detail. New techniques in this field are providing significant advancements in terms of improved UV protection, enhanced safety, and increased photostability. Particularly promising developments include the polymeric encapsulation of UV absorbers, which ensures better stability and effectiveness of the active ingredients. Additionally, there is a notable shift from relying solely on chemical absorbers to incorporating antioxidants and other natural product additives. These natural additives not only offer protection against UV radiation but also bring additional benefits such as reduced side effects and enhanced skin health. This move towards more natural and safer formulationsreflects a growing trend in the industry aimed at meeting consumer demands for products thatare both effective and safe for long-term use.

4. Bibi Petersen

The studies reviewed clearly indicate a discrepancy between the amount of sunscreen typically applied during testing and what occurs in real-life scenarios. SPF testing uses 2 mg/cm^2 because it yields more consistent results than the smaller amounts (0.5–1.0 mg/cm^2) commonly applied in everyday situations. The relationship between sunscreen application thickness and SPF can vary depending on the product and may not always follow a straightforward exponential pattern.When considering the reality of sunscreen use, current labeling practices tend to overestimate the protective effectiveness of sunscreens. This can mislead consumers into feeling overly protected, potentially leading them to extend their sun exposure beyond safe limits. Educational efforts aimed at improving sunscreen application have shown modest success, with studies demonstrating that reapplication can increase the effective sunscreen layer to 0.95–2.01 mg/cm^2.

5. Priyanka Kantivan Goswami

This study suggest that, for a long time, chemicals have been commonly used as photoprotective agents in sunscreen formulations. However, due to increasing concerns about their harmful effects, their popularity is declining. In recent years, natural sunscreens have garnered significant attention from researchers due to their safety profile, diverse biological effects on the skin, and cost-effectiveness. The phytoconstituents found in plants contribute additional properties that make them highly suitable for sunscreen formulations. These plant-derived actives are preferred over chemical sunscreens because they offer broad-spectrum UV absorption capabilities. Moreover, they provide protective effects against oxidative stress, inflammation, and even skin cancer. The shift towards natural sunscreens reflects a growing recognition of their benefits in terms of safety and broader skin health advantages beyond UV protection alone. This trend underscores the potential of plant-based ingredients in offering effective and safer alternatives in the field of sun protection.

6. Mark E. Burnett

There is significant overlap between the UV absorption profiles of sunscreens and the actionspectrum required for vitamin D synthesis in the skin. In theory, the correct application of sunscreens could potentially reduce vitamin D levels. However, in practice, this does not seemto be the case. Numerous studies have shown that sunscreens are often not applied correctly—in terms of amount, frequency, and coverage. As a result, under real-world conditions, improper sunscreen use or extended sun exposure may actually lead to vitamin D productionamong sunscreen users. Factors such as season, latitude, obesity, and age also influence the cutaneous synthesis of vitamin D from UVB exposure. Despite the potential for sunscreen toinhibit vitamin D synthesis, it's important to note that adequate levels of vitamin D can still be achieved through dietary supplementation. This suggests that while sunscreen use plays a role in sun protection and may impact vitamin D synthesis, it can be managed alongside otherstrategies to ensure sufficient vitamin D levels in the body.

IDEAL PROPERTIES

- It must absorb or filter out the rays causing sunburn, specifically those in the regionfrom 2900 to 3300 Angstroms.
- There should be no chemical breakdown that results in decreased efficacy or increasedtoxicity or irritation due to byproducts.
- It should have suitable properties for formulation with a cosmetic base and shouldpenetrate the skin easily.
- Frequent reapplication of sunscreens should not be required for effective results.
- It should be effective at low concentrations.
- It should have very slight or no absorption for long ultraviolet rays beyond 3400 Angstroms, which are thought to produce tanning without appreciable erythema.
- The compound and any decomposition products produced under conditions of useshould be nontoxic and nonirritating.
- It should be nearly neutral to avoid untoward effects from the presence of acid or baseon the skin.
- It should have good solubility in the ointment base or vehicle in which it is formulatedand low water solubility to prevent rapid removal by perspiration.
- It should be relatively nonvolatile to avoid evaporation under conditions of use.
- It should not be rapidly absorbed through the skin.

CLASSIFICATION

The classification of sunscreen agents is based on their composition and mechanism of action.Sunscreen agents work by different methods, including blocking, reflecting, and scattering UVradiation. Chemical (organic) sunscreens contain compounds that absorb UV radiation and convert it into heat, which is then released from the skin. Physical (inorganic) sunscreens, suchas those containing zinc oxide and titanium dioxide, act as physical barriers that reflect and scatter UV radiation away from the skin. Hybrid sunscreens combine both chemical and physical agents to provide broad-spectrum protection, leveraging the benefits of each method to maximize UV defense while minimizing potential drawbacks.

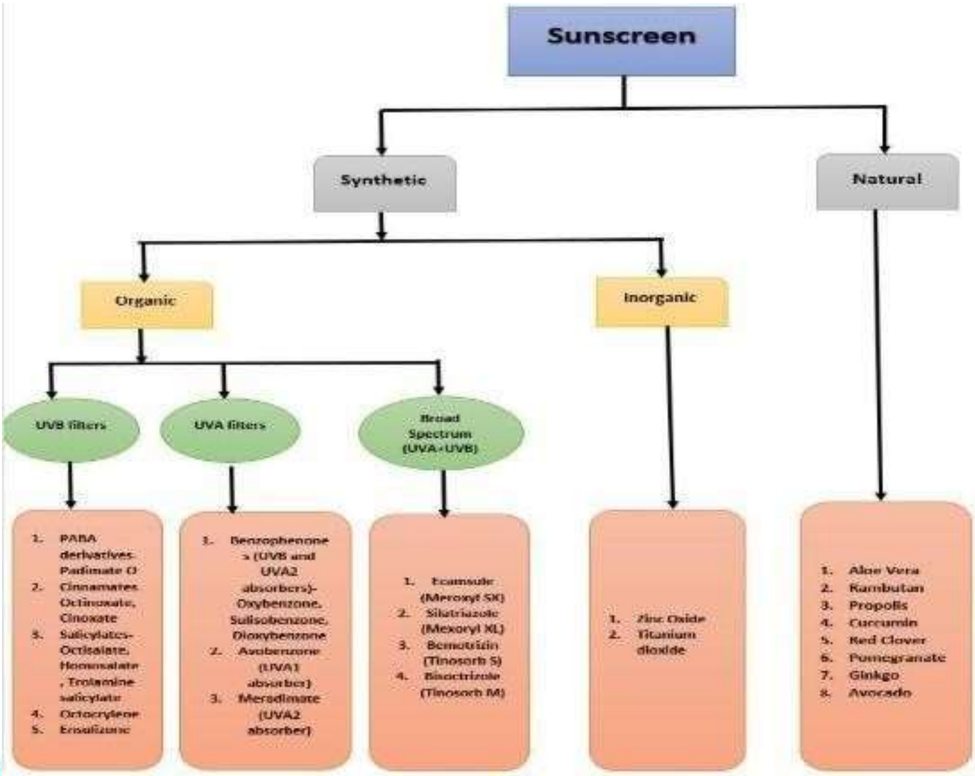

Fig.2:Classification of Sunscreen

SYNTHETIC SUNSCREEN

Synthetic sunscreens typically combine organic and inorganic filters to achieve comprehensive UV protection. Chemical sunscreens, categorized under organic filters, work by absorbing UV rays, particularly high-energy UV rays, and converting them into heat. They are effective across a broad spectrum of UV rays. In contrast, physical blockers, represented by inorganic compounds like zinc oxide and titanium dioxide, reflect and scatter UV rays away from the skin's surface. When these microparticles are evenly spread across the epidermis (the upper layer of the skin), they increase the optical path of photons. This extended path increases the absorption of photons, leading to higher Sun Protection Factor (SPF) ratings and ultimately enhancing the sunscreen's efficacy in shielding against UV radiation.

- **Organic Sunscreen**

Organic sunscreens have long been the cornerstone of sunscreen formulations, and while inorganic sunscreens are growing in popularity, organic varieties still dominate the market. These sunscreens are typically classified into groups such as anthranilates, benzophenones, camphors, cinnamates, dibenzoylmethanes, p-aminobenzoates, or salicylates. These aromatic compounds work by absorbing specific segments of the UV radiation spectrum, converting it into less energetic wavelengths like heat or light, or facilitating photochemical reactions such as cis-trans or keto-enol isomerization.In the United States, there are currently 23 organic sunscreen agents approved for over-the-counter (OTC) sunscreen products, including red petrolatum. However, only nine of these are commonly used, while the rest are rarely, if ever,found in today's sunscreen formulations. Among the nine frequently used agents, five are predominant in sunscreen products worldwide. Organic sunscreens are often combined becauseno single agent, at permitted levels set by the U.S. FDA, can achieve high Sun Protection Factor

(SPF) ratings alone. Combining different organic sunscreens can broaden the absorption spectrum, enhancing overall UV protection.The choice of specific combinations of organic sunscreens depends on the intended use of the sunscreen product, whether for recreational or daily photoprotection, and desired attributes such as waterproof or sweat-proof properties. Recently, there has been a growing trend towards combining organic and inorganic sunscreens in formulations, reflecting ongoing advancements in sunscreen technology and consumer preferences for enhanced UV protection.

- **Dibenzoylmethane Derivatives**:

- High absorption capacity in the UV-A region.
- Susceptible to decomposition upon sunlight exposure, reducing sun protection efficacyduring UV exposure.
- Photofragmentation can occur, leading to the formation of free radicals that maydamage the skin.

- **Benzophenone Derivatives**:

  - Absorb or dissipate Ultraviolet radiation, particularly UV-A.
  - Matsumoto et al., 2003 reported cytotoxic effects associated with these derivatives.

- **Para-Aminobenzoic Acid (PABA) and its Derivatives**:

  - Absorb UV-B radiation effectively.
  - Soluble in 70% alcohol at concentrations of 2-5%, allowing penetration into deeperdermal layers and longer retention in the skin.
  - Can cause photoallergic reactions in some individuals.

- **Salicylate Derivatives**:

  - Weak absorbers of UV-B radiation.
  - Used primarily to minimize the photodegradation of other photoprotectants.

- **Benzotriazoles (e.g., Mexoryl SX)**:

  - Mexoryl SX is a photostable broad-spectrum filter known for its effective sunprotection.
  - Helps reduce photoaging and photosensitivity reactions.
  - Mexoryl SX is a trademark of L'Oréal.

➢ **Studies with Organic Sunscreen**

Para-aminobenzoic acid (PABA) was patented in 1943 and served as the primary organic sunscreen active for many years. Its derivatives, such as 2-ethylhexyl-o- dimethylaminobenzoate (Padimate O) and amyl p-dimethylaminobenzoate (Padimate A), weredeveloped and widely used during the 1960s and 1970s. However, due to concerns over photorelated toxicity, these PABA derivatives are now rarely used in sunscreens. Despite theirdiminished use, PABA has been extensively studied.Early research, such as that by Hodges etal., demonstrated that PABA exhibited increased bacterial cytotoxicity after exposure to ultraviolet radiation (UVR). Subsequent studies found that PABA can sensitize the formation of cyclobutane dimers in DNA of both bacterial and mammalian cells upon UV exposure. Furthermore, PABA was shown to form adducts with thymine and thymidine after UV irradiation. These findings extended to aqueous solutions containing bacterial plasmid DNA, suggesting potential adverse effects.Studies also implicated PABA derivatives like Padimate O in mutagenic behavior under sunlight or solar-simulated radiation (SSR). Research by McHugh and Knowland indicated that irradiated Padimate O generated DNA strand breaks andlesions, which could be mitigated by free radical scavengers. This effect was likely linked to the generation of singlet oxygen during irradiation.Collectively, these studies suggest that PABA and its derivatives, including Padimate O, may pose risks under conditions of intended use with sunlight exposure. The data underscore the importance of rigorous testing and evaluation of sunscreen ingredients to ensure safety and efficacy in protecting against UV radiation-induced damage.

- **Inorganic Sunscreen**

During the past decade, inorganic sunscreens have seen increasing use in both beach and daily photoprotection products. This trend is driven by their perceived safety and effectiveness, particularly in blocking UVA rays, and concerns over potential adverse effects associated withorganic sunscreens. Inorganic sunscreens, such as titanium dioxide (TiO_2) and zinc oxide (ZnO), are generally considered harmless pigments that do not penetrate the skin and are less affected by light energy compared to organic alternatives.Titanium dioxide and zinc oxide areboth odorless white powders with distinct appearance and

attenuation spectra. They are used in microfine powders in sunscreen formulations, with an average particle size of approximately
0.20 microns or less and a well-controlled distribution. These microfine powders are not fundamentally new in terms of particle size but represent a refinement of existing particle sizedistributions. Unlike traditional pigment grades, microfine powders do not contain smaller particles; instead, they optimize the lower end of the particle size distribution through specialized manufacturing.Each particulate has an optimal size for scattering visible light, which is typically ideal for use as a white or colored pigment. However, for sunscreen applications, it is desirable to reduce the average particle size below the optimal light-scatteringsize to allow visible light transmission, making the sunscreen virtually invisible on the skin. This characteristic has driven the development of microfine grades of metal oxides now widelyused in sunscreen and daily skin care products.In sunscreen preparations, zinc oxide and titanium dioxide are often coated with materials such as silicones, fatty acids, or oxides of aluminum, silicon, or zirconium. These coatings, originally developed by the paint industry, help disperse particles more evenly, reducing agglomeration when applied as a thin film. Propercoating enhances compatibility between the particles and the dispersion medium, improving product aesthetics and reducing manufacturing costs. Moreover, coatings can potentiallyreduce any photoreactivity of the metal oxides, further enhancing their safety profile in sunscreen formulations.

Nano Lipid Carrier (NLC): Nano lipid carriers (NLCs) are specialized formulations where drugs or active ingredients are encapsulated within a mixture of solid and liquid lipids. Unlike Solid Lipid Nanoparticles (SLNs), NLCs are designed to prevent the formation of crystals, which can limit drug release and stability. Rania et al. developed an NLC formulation loaded with oxybenzone, which was then formulated into a gel. Their study demonstrated a remarkableincrease—six to eight times—in both Sun Protection Factor (SPF) and protection against erythemal UVA radiation compared to formulations using free oxybenzone. This significant enhancement in sunscreen efficacy is attributed to the improved solubility and controlled release of oxybenzone within the NLC structure. Importantly, NLCs also show a lower potential for skin irritation compared to conventional sunscreen products, making them a promising advancement in sunscreen technology for safer and more effective UV protection.

Nano-capsules: Nano-capsules are tiny hollow spheres, each with a diameter less than 200 nm,making them nanoparticles. They have the unique ability to be filled with either polar or non- polar solvents. Alvarez et al. conducted research where they developed nano-capsules containing Octyl methoxycinnamate (OMC) using biodegradable polymers. Their study demonstrated that these OMC-loaded nano-capsules offer superior protection against UVA- induced erythema compared to traditional gel formulations. This improvement is attributed tothe nano-capsules' ability to provide controlled release of OMC, ensuring prolonged and effective defense against UVA radiation. Additionally, the use of biodegradable polymers enhances stability and skin penetration of OMC, potentially reducing skin irritation andimproving overall sunscreen performance. This makes nano-capsules a promising technology for enhancing the efficacy and safety of sunscreen products.

Nanoparticles: Nanoparticles are extremely small particles, typically ranging in size from 1 to 100 nanometers, which gives them unique properties due to their one-dimensional structure. Marcela et al. developed a novel sunscreen formulation by encapsulating zinc oxide nanoparticles and octocrylene within polystyrene-co-methyl methacrylate (PMMA/PS) nanoparticles using mini-emulsion polymerization. These PMMA nanoparticles were then incorporated into a gel formulation. The study reported that the gel containing PMMAnanoparticles achieved a Sun Protection Factor (SPF) greater than 30. This indicates that the sunscreen formulation effectively protects against both UVA and UVB radiation, highlightingthe potential of nanoparticles in enhancing sunscreen efficacy. Utilizing PMMA/PS nanoparticles in sunscreen formulations represents a promising approach to provide high SPFprotection while maintaining product stability and skin compatibility.

Nanosuspension: Nanosuspensions are colloidal dispersions with particle sizes below 1 µm, stabilized by surfactants. Villalobos et al. developed a nanosuspension consisting of carnaubawax and titanium dioxide, distributed into both aqueous and lipid phases. Their study found that the Sun Protection Factor (SPF) value of the titanium dioxide nanosuspension dispersed inthe lipid phase was higher compared to the aqueous phase. This suggests that incorporating titanium dioxide into lipid-based nanosuspensions enhances its effectiveness in protecting against UV radiation. The use of nanosuspensions allows for improved dispersion and stabilityof active ingredients like titanium dioxide, potentially leading to more efficient sunscreen formulations with enhanced SPF values for better sun protection.

- **Studies with Inorganic Sunscreen**

Although metal oxides like titanium dioxide (TiO2) and zinc oxide (ZnO) have been used in consumer products for years and are generally considered inert, recent photocatalytic applications of TiO2 have prompted a reevaluation of their effects in sunscreens. TiO2, a semiconductor, can absorb light and generate free radicals under certain conditions. With a band gap of 3 eV, TiO2 can be excited by UV radiation at wavelengths below 380 nm, makingit susceptible to excitation by UVB and UVA in sunlight. When TiO2 is photoexcited, an electron is promoted from the valence band to the conduction band, leaving a positively charged hole that can react with absorbed species, potentially forming hydroxyl radicals in anaqueous environment. This photocatalytic property has been used experimentally to degrade organic materials and purify water. Concerns have arisen that photoreactive pigments in sunscreens could degrade organic UV filters in the formulation. Studies using commercially representative sunscreens with both organic and inorganic filters showed that coated microfineZnO and TiO2 were photoprotective for organic sunscreens like octyl methoxycinnamate andavobenzone. Even uncoated microfine ZnO demonstrated similar protective effects. These findings indicate that in finished formulations, these metal oxides do not degrade adjacent organic molecules but actually enhance their stability.

NATURAL SUNSCREEN

Natural products, produced by living organisms as secondary metabolites, are found in natureand exhibit various beneficial properties. Organisms exposed to UV radiation have developed numerous photoadaptive mechanisms, including antioxidant and UV-absorbing properties. These natural products can effectively protect against UV-induced damage, making them valuable components in skincare and sunscreen formulations. Their ability to neutralize free radicals and absorb UV radiation helps mitigate the harmful effects of sunlight on the skin.

Table No.1

Natural Sunscreen, Biological Source	Geographical Source	Part of plant
Aloe Vera, Aloe barbadensis (41)	East and South Africa (42)	Leaves (43)
Rambutan, Nephelium lappaceum (44)	Southeast Asia like Malaysia, Indonesia, Thailand (45)	Peel of fruit (46)
Propolis, Apis mellifera (47)	Europe, North America, non-topical regions of Asia (48)	Resins obtained from different parts of plants (49)
Black Tea, Camelia sinensis (50)	Asia, Africa, South America (51)	Leaves (52)
Curcumin, Curcuma longa (53)	India, China, Pakistan, East Indies (54)	Rhizomes (55)
Pomegranate, Punica granatum (56)	Mediterranean basin, America, Australia, South Africa, Asia (57)	Fruits, peel(58)
Grape, Vitis vinifera (59)	South America (60)	Seeds (61)
Tomato, Solanum lycopersicum (62)	Central Asia, Mediterranean Basin(63)	Fruit (64)
Ginkgo, Ginkgo biloba (65)	China, Japan (66)	Leaves (67)
Avocado, Persea americana(68)	Mexico, South Africa, Brazil (69)	Seeds (70)

Sources of Natural Sunscreen products:

List of Natural products which are used in preparation of Sunscreen formulation and are listedin Table 1:

Merits of Natural Sunscreen over Synthetic Sunscreen:

- Natural sunscreens are increasingly used instead of synthetic sunscreens like oxybenzone and octinoxate in places like Hawaii, Key West, and the US Virgin Islands because synthetic sunscreens cause bleaching of coral reefs.

- Synthetic sunscreens can negatively affect human skin by inducing Reactive OxygenSpecies (ROS). Natural antioxidants such as alpha carotene, ascorbic acid, andflavones can donate electrons and halt the free radical chain reaction, providing a safer alternative.
- Natural sunscreens protect the skin from premature aging, keeping it smooth andenergetic.
- Natural sunscreens are generally cheaper and more readily available than synthetic sunscreens.
- They are compatible with all skin types, making them a versatile option for sunprotection.

SUNSCREEN EFFICACY

Sunscreens represent unique products because, if applied properly, their efficacy is guaranteed based on their ability to prevent sunburn, which has traditionally been the primarycriterion for their evaluation. However, as discussed in this paper, this singular criterion is nolonger sufficient for evaluating sunscreen products in the future. The need for broad-spectrumUVB and UVA photoprotection products has become apparent. Unlike any other over-the- counter drug, the final sunscreen product is tested for efficacy before being distributed to consumers. The methods used to evaluate the efficacy of sunscreens will be briefly consideredto ensure they meet the new standards for comprehensive UV protection.

SPF: A measure of protection against UVB

There is no question regarding the efficacy of sunscreens in preventing sunburn. Sunscreens are specifically designed and evaluated for this purpose. The Sun Protection Factor (SPF) ofa sunscreen is defined as the ratio of sun exposure that the skin can tolerate before burning orminimal erythema becomes apparent, with and without sunscreen protection. Essentially, SPFmeasures the protection factor against sunburn. Since the action spectrum for UVR-induced sunburn is similar to that for certain types of DNA damage, it has often been inferred that protection against sunburn also equates to protection against DNA damage and other relatedoutcomes. However, it is now understood that each biological response has a unique action spectrum. Even when different responses share similar action spectra, the threshold or dose- response to UVR, particularly in the case of UVA efficacy, can differ significantly.

Measures of UVA efficacy

When the SPF system originated, it was commonly accepted that the action spectrum for UVR-related skin changes or damage was similar to that for erythema in human skin. For example, the action spectrum for non-melanoma skin cancer (NMSC) in rodents is similar tothat for erythema in human skin. However, we now know that the action spectra for other endpoints, such as photoaging and possibly melanoma, are not the same as erythema. BecauseSPF utilizes erythema as the endpoint and UVA is only mildly erythrogenic, it is clear that SPF alone does not adequately describe a sunscreen’s protective profile. In practical terms, itis possible to have an SPF 15 sunscreen that blocks only a limited amount of UVAII (320- 340 nm) and virtually no UVAI (340-400 nm). The ideal test for UVA photoprotection shoulduse a biological event mediated by these wavelengths as an endpoint. Unfortunately, to date,no representative surrogate for UVA events has been universally agreed upon. Several in vivotests have been proposed but not widely adopted. For example, immediate pigment darkening,8-methoxypsoralen (8-MOP) phototoxic protection, and UVA erythema protection have beenstudied, each with critical concerns, such as exaggerated protection factors in 8-MOP-sensitized skin or lack of UV-dose reciprocity for UVA-induced erythema.Similarly, in vitrotests have been described, most based on spectrophotometric measurements. One such test, the critical wavelength (CW), has been proposed to evaluate sunscreens for their UVA absorption, based on methods outlined by Diffey. In this method, the transmission through asubstrate, both with and without the sunscreen, is measured wavelength-by-wavelength usinga light source with a continuous output over the terrestrial UVR spectrum. The attenuation spectrum of the sunscreen is then determined. Importantly, prior to attenuation testing, the sunscreen can be subjected to a preirradiation step, thus testing for any photoinstability of theproduct. The CW is the wavelength at which 90% of the total area under the attenuation spectrum from 290 to 400 nm is obtained. This procedure provides a qualitative means to assess the UVA attenuation of a sunscreen product.

SUNSCREEN SAFETY

It is important to distinguish between long-term safety concerns and short-term adverse reactions. Sensitivities, both photoinduced and non-photoinduced, to organic sunscreens are well documented but seemingly rare events. Although these reactions likely impact compliance, they do not represent the long-term toxicity issues discussed in this paper. Typically, the toxicological evaluation of any chemical where human exposure is likely includes short-term in vitro studies believed to be predictive of long-term or delayed toxicity.This is evident in the carcinogenic risk assessment of chemicals, where bacterial mutation assays have become a mainstay. For sunscreens, the assessment of mutagenic potential presents a unique challenge due to their specific function of absorbing UVR. As such, short-term in vitro approaches measuring various endpoints, often including UVR exposure, have been conducted with sunscreens. These studies generally focus on cytotoxicity or genotoxicity, such as bacterial mutagenicity and mammalian cell clastogenicity, including concurrent UVR exposure.Photogenotoxicity testing of a chemical is evaluated against resultsobtained with a positive control, 8-MOP, the only demonstrated human photocarcinogen. However, assessing any compound using these in vitro tests remains tenuous. Nonetheless, numerous studies have examined the acute interaction between UVR and chemicals for bothorganic and physical sunscreens. These studies aim to identify the effects sunscreens have onUVR-induced damage, whether genetic or cytotoxic, and by inference, UVR-induced skin carcinogenesis. Although this strategy is still in its infancy, it currently appears to have littleimpact on human safety assessment.

RESULT AND DISCUSSION

Several observations regarding the examined studies can be made. This systematic review aims to evaluate the effectiveness of sunscreen in preventing melanoma, non-melanoma skincancer (basal cell carcinoma, squamous cell carcinoma), and precancerous skin lesions. The effectiveness of sunscreen is regulated by a multifactorial model. It depends not only on its SPF, UV spectral absorption, and active ingredients but also on the amount applied, the typeof sunscreen formulation, coverage of sun-exposed areas, frequency of reapplication, sun elevation, and other factors. The guidelines from the FDA and the International Organizationfor Standardization agree that the amount of sunscreen applied for testing SPF should be 2 mg/cm^2. This is the amount of sunscreen necessary to achieve the labeled SPF rating. However, applying the recommended quantity of sunscreen does not guarantee properprotection against UV radiation. Effective sunscreen application and adequate body coverageafter application are crucial for full protection. The sunscreen should remain stable during UV exposure on the superficial part of the skin to create a protective film.

In the included studies, only one case in the sunscreen group involved participants being trained to apply 2 mg/cm^2 on exposed areas 20–30 minutes before leaving the shade. In all other studies, participants followed a self-application routine, applying a layer to all exposedsites every morning or according to their usual routine, with sunscreen application merely suggested in most cases. Reapplication of sunscreen every two hours or after activities such as working, swimming, playing, or exercising outdoors is mandatory to ensure complete protection throughout the exposure time. Sun-protective behaviors and sunscreen applicationpatterns are fundamental and should not be excluded from a study. All the factors mentionedabove should be considered to obtain results that accurately reflect the real effect of sunscreen action rather than merely the expression of intrinsic risks. Skin cancer incidence increases with decreasing latitude due to greater UV energy exposure. Additionally, ambient factors such as ozone layer depletion play a role. The ozone layer, a region of the Earth's stratosphere,absorbs some of the sun's UV radiation; its depletion leads to regions being overexposed to UV radiation. Ozone depletion is most evident in polar regions, and studies have shown a close correlation between increased skin cancer incidence in Caucasians living near these regions.

Only one study provided specific information about where participants used sunscreen, suchas within Norway or other locations, during vacations, in low or high latitude areas, and whichsunscreen they used on those occasions. It is important to consider that trials conducted in subtropical areas often involve mainly unintentional sun exposure, as the population in theseregions is generally well aware of the hazards of sun exposure.

CONCLUSION

In the current socio-economic scenario, there is a significant increase in skin cancer cases per year, accompanied by constant pressure to reduce the costs related to medical treatments (directcosts), extra-medical expenses, and intangible human costs. In the health system, assessing these costs is essential for concentrating resources effectively. The most apparent acute benefitof currently available sunscreens is the prevention of sunburn from UVR exposure. This effecthas been suggested to be both a benefit and a potential concern. The obvious benefit is the prevention of sunburn, which may reduce the risk of nonmelanoma and perhaps melanoma skincancers, as the severity and frequency of sunburns have been associated with NMSC formation. This systematic review aims to be a scientific tool that uses a reproducible and transparent approach to evaluate the results of individual studies, making them available to health care decision-makers.

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