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SUNSCREEN : A REVIEW

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ABSTRACT:

Now-a-days sunscreens have gained tremendous demand. Although the major concerns affecting the human skin is the long-term exposure to ultra-violet radiations (UVR) causing photo-damage and skin cancers. Sun screening agents have shown beneficiary effects on the skin by reducing the exposure of UVR and its associated symptoms. Moreover, various constituents have been recognized to have sun protecting activity, their safety and efficacy is still a concern. The United States Food and Drugs Administration (USFDA) and European Guidelines (EU) guidelines have made the sun protecting factor (SPF) and other such indices compulsory on the labels of such formulas to guide the consumers for better selection. The various ranges of radiations and skin types influence the mechanism of photoreaction as well as the choice of the formulation. Apart from existing agents, certain novel sun-screening agents and technologies are now available to provide better protection to human beings.

KEYWORDS: Ultra-Violet Radiations, Sunscreens, sun protecting factor, photoprotection

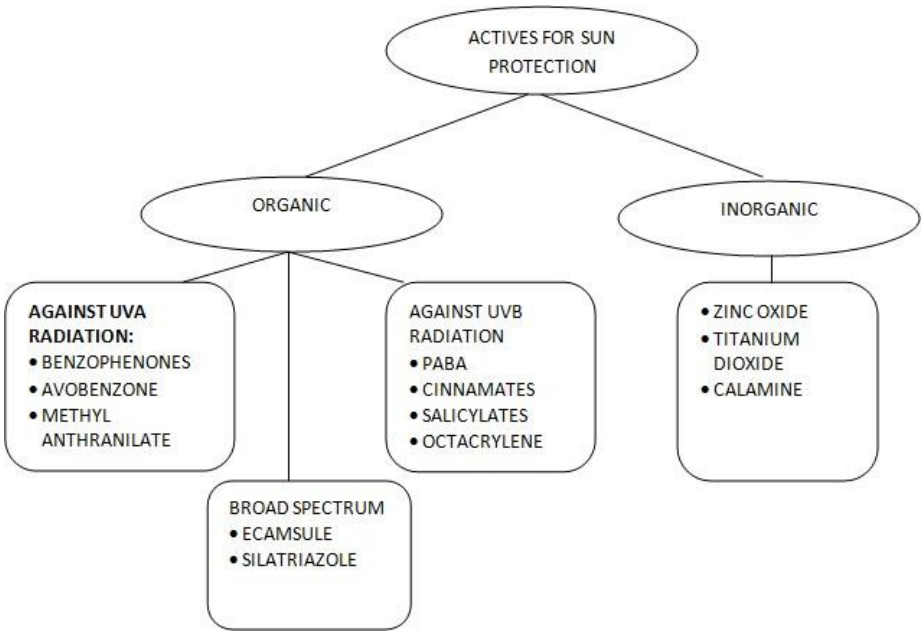
INTRODUCTION

Sunscreens are those agents which act by preventing and blocking the damaging effects of ultraviolet (UV) radiation of sunlight. Sunscreen, also known as suncream, sunblock or suntan lotion, is a lotion, spray, gel, foam, stick or other topical product that absorbs or reflects some of the sun's ultraviolet radiation and thus helps protect against sunburn [1,2]. Early civilizations used a variety of plant products to help protect the skin from sun damage. For example, ancient Greeks[3] used olive oil for this purpose, and ancient Egyptians used extracts of rice, jasmine, and lupine plants whose products are still used in skin care today. Zinc oxide paste has also been popular for skin protection for thousands of years. Among the nomadic sea-going Sama-Bajau people of the Philippines, Malaysia, and Indonesia, a common type of sun protection was a paste called borak or burak, which was made from water weeds, rice and spices[4]. It was used most commonly by women to protect the face and exposed skin areas from the harsh tropical

sun at sea[5,6]. In Myanmar, Thanaka, a yellow-white cosmetic paste made of ground bark, is traditionally used for sun protection. Norman Paul discovered the correlation between sun exposure and the development of skin cancer already in 1918[7]. A few years later, Karl Eilham Hausser and Wilhelm Vahle found that ultraviolet rays between 280 nm and 315 nm cause sunburn and concluded that the human skin could be protected by filtering out of those wavelengths. This influenced research concerning new organic sunscreen products with the aim to avoid the UVB effects on the human skin. Nonetheless, UVA rays were considered as harmless for a longer time. In 1936, Eugene Schueller, the founder of "L'Oréal", invented the first sunscreen, marketing one of his first formulations as "Ambre Solair". Two years later, Franz Greiter created the glacier crème ("Gletscher Crème"), after having been sunburnt while climbing in the Alps. This was the beginning of the sunscreen product "Piz Buin". In 1940, Benjamin Green developed a petroleum-based red jelly ("Red-Vet-Pet"), which was used by soldiers during World War II. He improved his formulation and so the "Coppertone suntan cream" arose in 1944. Later in 1962, Franz Greiter established the concept of sun protection factor (SPF). He created a method for measuring the effectiveness of a sunscreen product in terms of preventing sunburn. In 1977, Isaac Willis detected that UVA exposure causes ultrastructural changes of the skin, which leads to skin ageing. This better understanding of the effects of UVA and UVB rays, as well as changing consumer behavior, led to a change in the composition of UV filters in sunscreen products. In 1980, "Coppertone" was distributed as the first UVA/UVB sunscreen product.

CLASSIFICATION OF SUNSCREEN

The last FDA sunscreen monograph was issued in 1999, with a list of 16 approved sunscreen agents. It recommends that sunscreens be classified as organic and inorganic, replacing the previously used terms "chemical" and "physical", respectively. There are three commonly used nomenclatures for sunscreen agents in the world [8,9]. These are the International Nomenclature Cosmetic Ingredient (INCI) name, US adopted name (USAN), and trade name. Taking avobenzone (USAN) as an example, the INCI name for avobenzone is butylmethoxydibenzoylmethane, while Parsol 1789 is one of its many trade names.



A. ORGANIC SUNSCREENS

Organic UV filters are active ingredients that absorb UV radiation within a particular range of wavelengths, depending on their chemical structure. Once the UV filter absorbs energy, it moves from a low-energy ground state to a high-energy excited state. From this excited state, any of the following three processes may occur [10,11], depending on the ability of the filter to process the energy it has absorbed:

i. Photostable filter: This type of filter dissipates its absorbed energy to the environment as heat energy, and returns to the ground state. It is subsequently fully capable of absorbing UV energy again.

ii. Photo unstable filter: The filter undergoes a change in its chemical structure, or is degraded after absorbing UV energy. It is not capable of absorbing UV energy ag

iii. Photoreactive filter: In its excited state, the filter interacts with surrounding molecules including other ingredients of the sunscreen, oxygen, and skin proteins and lipids. This leads to the production of reactive species, which may have unwanted biological effects.

Organic sunscreens are further divided into UVB and UVA filters:

1. **UVB filters**

   a. PABA derivatives –Padimate O

   b. Cinnamates – Octinoxate, Cinoxate

c. Salicylates – Octisalate, Homosalate, Trolamine salicylate

d. Octocrylene e. Ensulizole

2. UVA filters

a. Benzophenones (UVB and UVA2 absorbers) – Oxybenzone, Sulisobenzone,Dioxybenzone

b. Avobenzone or Parsol 1789 (UVA1 absorber)

c. Meradimate (UVA2 absorber)

3. Newer generation broad spectrum (UVA + UVB) filters

Ecamsule (Mexoryl SX), Silatriazole (Mexoryl XL), Bemotrizinol (Tinosorb S), Bisoctrizole (Tinosorb M) Ecamsule is primarily a UVA filter, the patent for which is held by L'Oréal (sunscreens containing ecamsule are exclusive to L'Oréal and its brands). Tinosorb M is the first of a new class of UV filters that combine the properties of both UV conventional filters (organic and inorganic) – it scatters, reflects and absorbs UV light. Apart from Ecamsule, these filters are not yet US FDA approved, but are being used in other countries, such as the European Union and Canada.

A. INORGANIC SUNSCREENS

1. Zinc oxide

2. Titanium dioxide

3. Others - iron oxide, red veterinary petrolatum, kaolin, calamine, ichthammol, talc

Inorganic agents function by reflecting, scattering or absorbing UV radiation. Their opaque nature and "whitening effect" are an inherent disadvantage, which may be minimized by the use of micronized or ultrafine particles[12,13].

Ideal properties of sunscreens [14]

- There are various characteristics which are required by the sunscreens to categorize as the ideal sunscreen. Since these agents are both complex organic and inorganic in nature, the biodegradability of these molecules needs to be noted as it may pose a threat to the environment in which it is synthesized and formulated.
- An ideal sunscreen must absorb the rays causing sunburn, typically in the range of 2900-3300 Å and be stable in the presence of sunlight to which it is expected to show its efficacy.
- If the molecule is not stable and gets degraded, the by-product should have an absorption capacity of 2900-3300 Å.

- The decomposed products should not be toxic and irritating.
- It should be neutral in nature and should not be affected by the presence of an acid or a base and also should have a good solubility in the ointment base in which it is formulated and should not be easily washed away with water or during perspiration.
- A non-volatile agent will be ideal so that evaporation does not take place during application.

Although all the ideal characteristics cannot be obtained from a single agent, a combination of sunscreen agents are used together to formulate a sunscreen formulation.

UV RADIATION

UV radiation is part of the natural energy produced by the sun. On the electromagnetic spectrum, UV light has shorter wavelengths than visible light, so your eyes can‟t see UV, but your skin can feel it. Tanning beds also emit UV radiation[15].

Two types of UV light are proven to contribute to the risk for skin cancer:

- **Ultraviolet A (UVA):**
    - It has a longer wavelength (320-400nm).
    - Not directly absorbed by biological targets.
    - Penetrates deeper than UVB.
    - Affects connective tissue by producing reactive oxygen species; produces profound immunosuppression.
    - Responsible for tanning, photoaging [16], photocarcinogenesis, exogenous photosensitization and many idiopathic photodermatoses (including polymorphous light eruption).
- **Ultraviolet B (UVB):**
    - It has a shorter wavelength (290-320nm).
    - Responsible for the most severe damage
    - Direct impact on cell DNA and proteins
    - Acute damage – sunburn
    - Long-term damage – cancer [17]

Solar UV radiation is approximately 95-98% UVA and 2-5% UVB. UVC is completely absorbed by stratospheric ozone that also attenuates UVB. A given solar UVR spectrum varies with the solar zenith angle (the angle between an imaginary perpendicular line and a line from its base to the sun), which is dependent on time of day, season, and

latitude. The highest UVB content is found when the sun is directly overhead with the shortest path (e.g., noon, at the equator, at high altitude).

EFFECTS OF UV EXPOSURE ON THE SKIN

Ultraviolet (UV) radiation causes both beneficial and undesirable effects on the skin. The purpose of sun protection is to minimize unwanted effects without affecting the beneficial ones. The effects may present acutely while others develop over prolonged period. They include tanning, sunburns, photoaging and skin cancer [16,17]. Tanning refers to the delayed pigmentation of the skin which is considered desirable in many cultures.

The practice of cosmetic tanning has gained prominence among young Caucasians with the trend has been increasing with advancements in technologies that make it possible to produce artificial UV light.

The WHO has raised the alarm over this practice as it predisposes to skin cancer in the long term[18]. Sunburns refers to dermal erythema arising due to dilatation of superficial blood vessels is a common occurrence following exposure to UV rays. Extreme exposure causes the skin to become painful and edematous with or without blistering . The most common forms of skin cancer are; basal cell carcinoma, squamous cell carcinoma, and cutaneous malignant melanoma. The first two are grouped together as non-melanomas and are associated with higher morbidity and cause more extensive aesthetic changes on the skin while higher mortality occurs in the malignant melanoma [18,19] .

Exposure to UV radiation is considered to be a significant etiological factor for most forms of cancer. Photoaging which includes irreversible changes to the skin has been associated with chronic exposure to the sun.

USE OF SUNSCREENS FOR PROTECTION AGAINST ULTRAVIOLET-INDUCED SKIN DAMAGE

- With the advancements in the medical field as well as science in general that came about in the 20th century, it was demonstrated that the UV section of light contributes significantly towards skin damage[20].
- Studies in laboratory rodents enabled greater understanding of UV-induced immune depression, carcinogenesis, photodamage and photoaging.
- Animals irradiated with UV demonstrated lesser hypersensitivity, and they failed to reject organ implants, unlike the controls which were not irradiated indicating a reduction in the immunological capacities of the irradiated animals.

- Scientists also observed that the incidence of melanoma was higher in populations where sunbathing is common. More intensive studies confirmed that those who used sunscreens on a routine basis suffered skin damage to a much lesser extent.
- Widespread research has further characterized the causes of skin cancers, and the numerous cancer agencies have included UV rays as one of the significant human carcinogens.
- Public awareness campaigns have since led to greater acceptance and usage of sunscreens.
- Initial efforts were developed to produce anti UVA products specifically; recently most sunscreens formulations contain both anti-UVA and anti UVB agents.

MECHANISM OF PHOTOPROTECTION

Sunscreens act by preventing and minimizing the damaging effects of the ultraviolet sun rays following exposure to the sun [21,22]. Sunscreens have been demonstrated to increase the tolerance of the skin to UV exposure. They primarily work through two mechanisms as detailed below.

- Scattering and reflection of UV energy
- Absorption of the UV energy

Scattering and reflection of UV energy :

Scattering and reflection of UV energy from the skin surface. Mineral based (Inorganic sunscreens work primarily through this mechanism. They provide a coating that blocks sun rays from penetrating through the skin [23,24].

Absorption of the UV energy:

Absorption of the UV energy by converting it to heat energy thus reducing its harmful effects and reduce the depth through which it can penetrate the skin. Organic sunscreens work primarily through this mechanism[25].

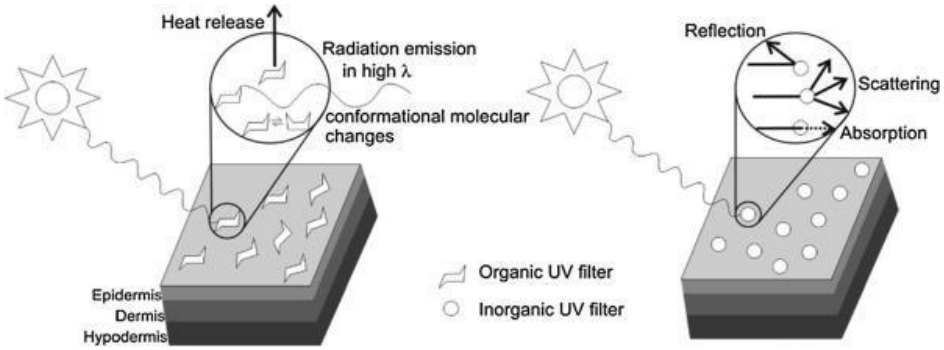


Figure 1: Mechanism of action of organic and inorganic sunscreen

Formulation of sunscreen product

- Formulation of sunscreen involves four critical steps:
  - selection of the target product design
  - choice of active ingredients
  - selection of product vehicle
  - product optimization
- The primary objective of the formulation expert is to develop a product that forms a continuous film on the skin. Penetration of the organic ingredients into the skin should be minimized.
- Organic sunscreens [26,27] are formulated as lotions and light ointments. On application, they form a thin film on the skin surface that affords UV protection. Other formulations include oils, gels, emulsions, mousses (fluid emulsions), aerosols, sticks, and powders.
- Inorganic sunscreens are more difficult to formulate due to their particulate nature. Traditionally, they were formulated as creams that were sticky, oily and unpleasant to use. Nanomization has allowed spray formulations that form a translucent layer on the skin that affords protection while maintaining the aesthetics of the product.
- Currently no nanomized spray formulations of sunscreens have been approved for registration owing to safety concerns as these nanoparticles may be inhaled and therefore cause system toxicities.
- Inorganic sunscreens [28,29] are formulated as pastes, emulsions, sprays, and ointments. Particle engineering approaches including micronization and nanomization of the particles are done to increase the aesthetic value of the products.
- The safety and convenience of the user guide the formulation approach. Any substance with potential skin irritancy and potential allergens must be avoided. Like other skin products, formulation requires the inclusion of adhering agents to promote skin adsorption as well as an appropriate vehicle into which the active substance is dispersed.
- Patents play an essential role in the development process, and careful consideration must be taken before embarking on product development .
- Among the challenges and concerns associated with topical sunscreens formulations involve the photostability of organic filters, broadening the effectiveness spectrum and parameters, incorporating active ingredients, improving cosmetic and sensory aspects, individualizing vehicles.

- The ideal sunscreen formulation should take into consideration aspects including efficiency for the intended use, the scope of protection spectrum (UVA and UVB), safety and tolerability for topical use, stability, no staining of clothes, adequate cosmetics, pleasant fragrance, resistance to water, spread-ability, high extinction coefficient, and affordable cost.
- Sunscreen formulations include the main sunscreen agents, excipients specific to the formulation type including an appropriate solvent or vehicle systems. The contents selection is determined by the intended use and the physicochemical nature of the ingredients.
- Purified water used in product formulation is prepared through reverse osmosis and other established methods of purifying water for industrial use.
- The most common sunscreen actives; titanium dioxide, zinc oxide, avobenzone, benzophenone 8, octocrylene, and oxybenzone are used. To vary the amount of sun protection, the level of the active ingredient is adjusted.
- Lademan and group established synergy between organic and organic sunscreens and demonstrated superior efficacy of products comprising of the two compared to those containing only organic or inorganic sunscreens.
- The FDA prescribes the maximum allowable concentration of each ingredient as well as the impurity content. It is common to find sunscreen being co-formulated with other skin products for value addition.
- A rationally designed and developed product enhances the compliance of the users while affording the necessary protection against the ultraviolet-induced skin damage.

Different type of formulation

- **Emulsion Sunscreen[30]**
  - An emulsion is termed a lotion or cream depending on its viscosity, respectively, below 50,000 and in the range of 150,000–500,000 centipoises, providing almost unlimited versatility . It is normally produced from two unmixable liquid phases (oiland water), namely “water-in-oil (W/O)” and “oil-in-water (O/W)” emulsions
  - Moreover, multiple emulsions (O/W/O and W/O/W), containing both O/W and W/O phases in a stable system, show an effective application in recent sun protection technology .

- Therein, water accounts for the largest proportion, while active ingredients contribute a little amount in an emulsion product. Thus, emulsion sunscreens are cost-effective vehicles .
- These formulations possess the ability to spread more easily on the skin and disperse from bottles . Further, this formula shows great effectiveness in strategies to achieve high SPF, create a uniform, thick and nontransparent sunscreen film when applied on the skin, and minimize undesirable interaction among active sunscreen ingredients .
- In other words, emulsion sunscreens also provide an elegant medium that can give the skin a smooth and silky feeling without greasy shine . However, these are extremely difficult to stabilize, especially at high temperatures.

- **Gel Sunscreen** [31]
  - Sunscreen gel seems to represent an ideal vehicle from an aesthetic perspective due to its purity and elegance. It is categorized into four main forms, namely aqueous, hydroalcoholic, microemulsion, and oil anhydrous formulations .
  - The aqueous gel must be composed of water and solubilizers (e.g., nonionic surfactants, organic agents, and phosphate esters) at sufficient proportions to ensure the gel will be transparent at all temperatures. Therefore, it is easily washed away when exposed to water or sweat.
  - Although organic active molecules (e.g., octyldimethyl PABA or octyl p- methoxycinnamate) are primarily attributed to the formula, they are used in low doses due to their high levels of carcinogenicity . Interestingly, the high concentration of organic filters is primarily responsible for increasing the SPF value. Thus, the aqueous gel provides low SPF compared to other kinds of gel sunscreens.
  - The hydroalcoholic gels are formulated by alcohol (ethanol) in conjunction with water, which are important in reducing additional solutes because most lipophilic ingredients are readily miscible in alcohol .
  - This form can provide the desired cooling effect, which is especially refreshing when applied to the skin on summer days .
  - However, this formulation also shows some negative aspects, such as quickly being washed way in the water, causing facial or eye sting on certain individuals, and providing low SPF .
  - The microemulsion gels are composed of small particles, allowing them to appear smooth, thick, and evenly on the skin, thus delivering an elegant feel and high SPF.
  - Unfortunately, it is markedly expensive to achieve transparent microemulsions containing high-level emulsifiers (15–25%)

- Particularly, most emulsifiers are irritating components, so this emulsion system pose a risk to human health . In addition, high emulsification proportion results in reduced water-resistance of these sunscreen products.
- The oil anhydrous formula possesses many attributes similar to ointments. However, oil anhydrous products are clear, while the ointments are translucent . These products can be produced as a gel by combining mineral oil and special silica . However, they are not widely sold because they are difficult to produce and quite expensive.

Aerosol Sunscreen[32]

- In addition to lotions and creams, aerosol sunscreens are topically applied to protect skin disorders from harmful sunlight. These products can be easily spread onto the surface of skin, and distribute active ingredients to form a thin film on the skin.
- However, this application may result in the uneven spreading of sunscreen agents, corresponding to some high-coverage areas with an excessive amount of sunscreen and other areas with little coverage to protect the skin satisfactorily.
- Nevertheless, the aerosol products have not become as popular as other sunscreens due to some critical negative aspects. First, they are typically oil-based, making them quite expensive and often reducing their effectiveness. In addition, it is hard observed where the sunscreen has been applied. Caution must be taken to avoid accidentally spraying sunscreen into the eyes.

Sun Stick [32]

- The sun stick is undoubtedly one of the most convenient products due to its small size and light weight.
- The sun stick is produced by two main emulsion components, namely oil and oil- soluble components, through the incorporation of petrolatum and waxes. Thus, it tends to have a greasy feel on the skin, which is a common problem of most water-resistant sunscreens.
- However, this product has gained great attention due to its ability to cover a very small surface area during each application. It is also easy to carry and re-touch.
- This form is subdivided into three categories namely,
    - Transparent
    - Semi-transparent
    - Matte sunscreen

- The transparent formula contains only chemical UV filters, while semi-transparent is formulated mainly by chemical and mineral substances and matte is composed of only mineral sunscreen ingredients.

Sunscreen related indices

Practicing dermatologists [33] often encounter patients complaining of worsening pigmentation or recurrent polymorphous light eruption in spite of using sunscreens with "good sun protection factor (SPF)" or "SPF >50". It is important for both dermatologists and the public to be aware that a good SPF value will not protect the skin from the entire UV spectrum. In fact, in 2007, the FDA has proposed that the expansion of SPF be changed to "sunburn protection factor" to indicate that it is only an index of protection against sunburn or UVB-induced erythema, and hence does not necessarily imply UVA or broad spectrum protection.

Various indices have been formulated by in vitro and in vivo methods to assess the efficacy of sunscreens with respect to specific components of the UV spectrum. These are as follows:

1. **UVB sunburn protection factor (SPF**) = Minimal erythema dose (MED) of photoprotected skin MED of unprotected skin

   Grading system for SPF:

   • Low: SPF 2 – 15
   • Medium: SPF 15 – 30
   • High: SPF 30 - 50
   • Highest: SPF >50

2. UVA protection indices

a. Japanese standard (persistent pigment darkening; in vivo method):

UVA protection factor (UVA PF) = UVA dose that induces persistent pigment darkening 2 to 24 hrs after exposure in sunscreen protected skin /UVA dose that induces persistent pigment darkening 2 to 24 hrs after exposure in unprotected skin

b. Australian/New Zealand Standard (in vitro method):

8-µm layer of the product should not transmit more than 10% of radiation of 320 to 360 nm OR 20-µm layer of the product should not transmit more than 1% of radiation of 320 to 360 nm.

c. European Union guidelines:

UVA protection factor (persistent pigment darkening method) = 1/3 of SPF AND Critical wavelength = 370 nm d. Boots star rating system (used in the United Kingdom): In vitro measurement of the ratio of a product‟s UVA (320-400 nm) absorbance over its UVB (290-320 nm) absorbance is used to calculate its Boots star rating (Table 2). Products with better UVA absorbance have a higher Boots star rating.

3. Immune protection factor (IPF):

Ability of sunscreen products to prevent UV-induced immunosuppression. IPFis assessed by complex methods such as the ability of a sunscreen to inhibit either thesensitization or elicitation arm of contact or delayed-type hypersensitivity reactions to allergens such as dinitrochlorobenzene (DNCB) and nickel, respectively. IPF is considered to correlate better with the UVA-protectiveness of a sunscreen than with its SPF.

4. Clothing indices

UV protection factor (UPF) = the ratio of average effective UV radiation irradiance transmitted and calculated through air to the average effective UV radiation irradiance transmitted and calculated through fabric (indicates how much longer a person can stay in the sun when fabric covers the skin, erythema being the end-point).

Grading of UPF:

- good protection (UPF 15 to 24)
- very good protection (UPF 25 to 39)
- excellent protection (UPF 40 to 50+)
- Fabric SPF is similar to SPF, except that fabric is used to protect the skin while testing, instead of a sunscreen.

3. Sunglass standards

- Luminous transmittance = Amount of light transmitted through a sunglass lens (e.g. a lens with 20% luminous transmittance allows 20% of the light to pass through it)
- The Australian Standard (AS/NZS 1067:2003) classifies sunglasses and fashion spectacles based on the amount of UV radiation that passes through the lenses: Categories of lenses: 0 to 4

- Fashion spectacles (luminous transmittance 80-100%): providing some protection from UV radiation but no reduction in sunglare.
- Fashion spectacles: providing protection from UV radiation and limited reduction of sunglare - not suitable for driving at night.
- Sunglasses for general use: providing good protection from UV radiation and sunglare.
- Sunglasses providing extra protection from UV radiation and sunglare.
- Sunglasses providing a high level of protection from UV radiation and sunglare (luminous transmittance 3-8%) - must not be used when driving.
- UVB transmittance: 5 percent of luminous transmittance (e.g., for lenses with luminous transmittance of 20 percent, 99 percent of UVB should be blocked out).
- UVA transmittance: lens categories 0 to 2: < luminous transmittance, lens categories 3 and 4: 50% of luminous transmittance.
- Minimum vertical diameter for adult sunglasses = 28 mm
- Minimum vertical diameter for child sunglasses = 24 mm
- Some sunglasses may also be labeled with an eye protection factor (EPF) number, developed by the Australian Radiation Protection and Nuclear Safety Authority (ARPANSA) ranging from 1 to 10. Sunglasses labeled EPF of 9 or 10 transmit very little UV radiation.
- Other sunglasses may be labeled UV 400 (blocking 100% of UV) or state the amount of UV radiation blocked as a percentage such as 99.9% or 100%.
- The only way to assess the protection of sunglasses is to have the lenses measured, either by the manufacturer or by a properly equipped optician.
- Dark lenses do not automatically filter out more harmful UV radiation and blue light as compared to light lenses. Inadequate dark lenses are even more harmful than inadequate light lenses (or wearing no sunglasses at all) because they provoke the pupil to open wider. As result, more unfiltered radiation enters the eye.
- The only “visible” quality test for sunglasses is their fit. For the best protection, one must use wraparound, close fitting, large-lens sunglasses that help to reduce reflected UV radiation and glare that can pass around the edge of the sunglasses and reach the eyes.

Factors determining the efficacy of sunscreens

• Sun Protection Factor (SPF) [34]

SPF is a scientific measure. It gives an idea of how much lower the risk of skin damage is due to the use of a sunscreen. It focuses on the time it takes for UVB rays to get through a sunscreen and cause the skin to go red, compared with the time this takes when there is no sunscreen. SPF, or Sun Protection Factor, is a measure of how well a sunscreen will protect skin from UVB rays, the kind of radiation that causes sunburn, damages skin, and can contribute to skin cancer. The factor is calculated by dividing the sun radiation dose needed to cause skin reddening with the dose needed to cause reddening without sunscreen.

SPF = sunburn radiation dose with sunscreen / sunburn radiation dose without sunscreen

This calculation is based on the application of 2 milligrams (mg) of sunscreen for each square centimeter (cm) of skin surface. If it takes 15 times longer to burn the skin with a sunscreen on than it does with no sunscreen applied, the SPF is 15.

In theory, if, under certain UV conditions, it would take 10 minutes for unprotected skin to start going red, an SPF 30 sunscreen would prevent this for 300 minutes, or 5 hours, which is 30 times longer.

Other factors have an impact.

These include:

- weather conditions
- time of day
- skin type
- how the lotion is applied
- how much is used
- other environmental and individual factors

When we spend time in the sun, we are exposed to two potentially harmful types of ray: UVA and UVB.Sun protection factor (SPF) is a number, for example, SPF15. It indicates how much protection a product offers against UVB light.

A product with a higher SPF number will offer greater protection.

According to the FDA, the use of a sunscreen with an SPF of 15 or above, combined with other measures, such as wearing sunglasses and avoiding the midday sun, can help preventTrusted Source.

In some places, protection levels are expressed as follows:

- Low protection: SPF is below 15
- Medium protection: SPF is 15 to 29
- High protection: SPF is 30 to 49
- Very high protection: SPF is over 50

Most people, for example, only use 25 to 50 percent of the recommended amount.

In addition, the blocking effect wears off after a maximum of 2 hours. After this, the lotion will need to be reapplied. The protection offered by sunscreens of different SPFs is as follows:

- SPF 15 blocks about 93 percent of all UVB rays
- SPF 30 filters out 97percent
- SPF 50 is an almost complete UVB block, at 98 percent

These percentages show that no sunscreen blocks all UVB. It also shows that an apparently large increase in SPF will boost the blocking power by only a small percentage.

Terminologies associated with Sunscreens

- **In-vivo sunburn protection factor (SPF):**

The Sun Protection Factor can be defined, as proposed by the FDA in 1978, as the numerical ratio between the minimal erythemal dose (MED) of sunscreen-protected skin, applied in the amount of 2 mg/cm2 and the Minimal Erythemal dose of unprotected skin, a mathematical relation that can be represented by the equation: SPF=MED (protected skin)/MED (unprotected skin)

- **In vitro Sunburn Protection Factor (SPF in vitro):**

The absolute protection performance of a suncare product against erythemal effective UV radiation, calculated from the measured in vitro transmittance and weighted with the erythema action spectrum and with the “standard” output spectrum of a UV solar simulator used for SPF testing.

- **In-vitro UVA protection factor (UVAPF):**

The absolute UVA protection afforded by a suncare product, calculated from the measured in-vitro transmittance after irradiation and weighted with the PPD action spectrum and with the “standard” output spectrum of a UVA-filtered solar simulator.

- **In-vitro UVA protection factor before UV exposure UVAPF:**

The in-vitro UVA protection factor measured before sample UV exposure. It is derived from the transmittance curve of the unexposed sample, weighted with the PPD action spectrum and with the "standard" output spectrum of a UVA-filtered solar simulator, after adjustment to the labeled SPF.

- **PFA (Protection Factor UVA) or UVA-PF (UVA Protection Factor):**

The ratio of PPD of protected skin to PPD of unprotected skin.

Critical Wavelength Value (λc):

The critical wavelength λc value for the test product is defined as that wavelength where the area under the absorbance spectrum for the irradiated product (obtained using the method described above) from 290 nm to λc is 90% of the integral of the absorbance spectrum from 290 nm to 400 nm.

- **UVA-UVB Ratio:**

Absorption of a 1.3 mg/square cm film is measured between 290 nm and 400 nm. The ratio of areas under the curve between 290-320 (UVB region) is compared with the area under the curve between 320 nm and 400 nm.

- **Broad spectrum sunscreen:**

Critical wavelength > 370 nm and UVA protection factor > 4

- **Water-resistant sunscreen:**

Maintains the labeled SPF value after two sequential immersions in water for 20 min (40 min)

- **Very water-resistant sunscreen:**

Maintains the labeled SPF value after four sequential immersions in water for 20 min (80 min)

- **Critical wavelength:**

The wavelength below which 90% of the sunscreen‟s UV absorbency occurs.

NEW SUNSCREEN TECHNOLOGIES

- **SunSpheres**

SunSpheres are styrene/acrylate copolymers that do not absorb UV irradiation but enhance the effectiveness of the active sunscreen ingredients. The SunSphere polymer beads are filled with water,

which migrates out of the particle, leaving behind tiny airfilled spheres, which have a lower refractive index (1.0) than the dried sunscreen film (1.4-1.5).

As a result, scattering of UV radiation occurs, increasing the probability of contact with the active UV filters in the sunscreen. SunSpheres are also available in a powder form, and can boost SPF by 50 -70% making it possible to reduce the concentration of active ingredients.

- **Microencapsulation**

Active sunscreen ingredients are entrapped within a silica shell, as a result of which, allergic or irritant reactions to the active ingredient can be minimized, and incompatible sunscreen ingredients can be safely combined, without loss of efficacy.

- Regulatory bodies

Several guidelines have come into play due to the ever-increasing number of sunscreen agents in the recent past. These regulations are to maintain and monitor the quality along with safety and toxicity profile of the sunscreen molecules both in regards to the human and environmental aspects, the main aim being providing adequate protection against the harmful UVR.

- **USFDA guidelines**

Earlier, the FDA had specified rules for the molecules protecting the skin against the UVB radiations. When research and development took place for molecules protection against UV B, more rules and regulations were put forth for providing the completely monitored production and release of sunscreen molecules. When misguiding and false statements started prefacing the market, US FDA revised to more stringent guidelines thus preventing the use of claims such as “broad spectrum, water and sweat proof, water resistant“ without proper investigation and test reports. Therefore, products claiming broad spectrum has to provide adequate documents proving its effect against UVA and UV B radiations. A product indicating „water resistant“ on its label should provide its duration of action.

Any claim which suggests immediate sun protection or sun protection prevailing for longer than two hours should not be mentioned without directing reapplication. Supporting documents need to be provided to FDA for approval in case any statement which suggests any of the above claims.

Drug fact is an integral part of the product label. SPF value is of utmost importance for sunscreen agents as it decides the category of the sunscreen to be used for maximum and effective protection.

- **EU guidelines**

EU also provides a minimum level of protection against UVA in terms of SPF. PPD (in vivo) or COLIPA (in vitro) are the measures by which UVA protection is measured, and it must be at least one-third of the SPF (in vivo) value. As per the guidelines, products are divided into low, medium, high and very high according to the SPF of the products ranging from SPF 6 to SPF 50+. Star system is also employed for consumer understanding and ease which denotes that 1 has least sun protection and 5 has the ultra sun protection.

- **Indian guidelines**

There are only two combination approved products as per the Official website of Industrial Regulatory Agency due to lack of guidelines in the standardization of sunscreen agents and approved ingredient list. The products available are a combination of octinoxate + avobenzone + oxybenzone + octocrylene + zinc oxide lotion and cinoxate + avobenzone + oxybenzone + titanium oxide lotion. Several others sun screening agents are widely used such as camphor derivatives and UV broad spectrum active agent.

- **Other countries guidelines**

Other countries such as Japan, Australia and New Zealand have similar guidelines though some of the regulations may differ.

Challenges in formulating sunscreen agents

- Even though the main aim of formulating an effective sunscreen is to protect the naked skin against various effects of the sun rays, there are many challenges that regulate the effective use of sunscreen all over the world.
- These challenges may be due to the geographical location, lifestyle diversification, environmental safety concerns and also the regulatory authorities controlling and regulating the use of certain ingredients in the certain cosmetic product due to their adverse reactions.
- Due to these differences, cosmetic sunscreen products are always under the scrutiny of the regulatory bodies regarding their safe use and efficacy; and amidst of all these controversies, the demand for a better sunscreen is high as it not only protects the skin from acute skin damages but also from various high-risk damage like DNA damage resulting in premature ageing wrinkle and ultimately skin cancer.
- safety and efficacy of sunscreen agents are because of the fact that most of the sunscreen agents used in the market are synthetic chemical entities which may be toxic when applied to the skin as it gets absorbed into the deeper layers of the skin and cause several undesired side effects .

- The increased amount of use of sunscreen can also cause a reduction in the formation of vitamin D due to blockage of UVR penetrating the skin .
- Even though physical sunscreen agents like TiO2 and ZnO do not penetrate into the skin, the is evidence where these particles, both in nanoparticulate or non-nano-particulate form have to cause melanoma formation in mammalian cells .
- The solubility of such molecules remains to be yet another challenge during formulating a sunscreen product. Some agents are dissolved in the oil phase while some are dispersed in the aqueous phase.
- Aqueous based formulations give less water resistance, while oilbased formulations have higher water resistance and safety but aesthetic elegance is low because of the oily appearance.

Another challenge is the environmental safety and toxicity. As the sunscreen agents are washed off to the water bodies, the aquatic animals are the ones which are affected because of the accumulation of such toxic substances in the water.

Evaluation Methods [35,36]

In 1934, Friedrich Ellinger determined the minimal erythemal dose (MED) from protected and unprotected skin by evaluating the protective efficacy of sunscreens using mercury lamp radiation on both forearms and expressed a coefficient of protection that decreased in value to the extent that protection increased.

In 1956, Rudolf Schulze proposed “Schulze Factor” which been used for decades in European countries, as a reference in the evaluation of sunscreens. Schulze Factor is exposure time required for the induction of erythema on sunscreen protected and unprotected skin by incremental doses of sunlight like radiation emitted from lamps.

In 1974, Greiter introduced the term Sun Protection Factor (SPF) to “Schulze factor.” From then till now SPF is popular term in evaluation of sunscreens.

In 1978, the North-American regulatory agency (FDA) proposed the first normatization to determine the Sun Protection Factor (SPF).

Following are newly accepted and followed methods of evaluation of sunscreens:

- In-vitro methods
- In-vivo methods

In-Vitro Methods:

Many regulatory agencies, such as the US Food and Drug Administration (USFDA) and The European Cosmetic Toiletry and Perfumery Association (COLIPA), mandate in-vivo testing on human subjects, using an erythemal endpoint to determine the SPF of a topical sunscreen.

The in-vivo tests are costly and time-consuming and may not be practical for routine product evaluation. The UV-1000S is designed to make the evaluation of SPF a simple and routine analytical procedure performed within the formulation laboratory.

Although in-vivo testing is mandatory to make a product label claim for SPF, an investment in the UV-1000S will insure that only one in-vivo test will have to be performed for each particular formulation. The measurement of an in-vitro SPF can be performed by measuring the diffuse transmittance in the ultraviolet spectrum of a carefully prepared sample.

There are two objectives in a sample preparation method.

The first is to simulate the application conditions used for in-vivo testing, both the applied quantity and substrate interaction. This would produce a reliable in-vitro SPF value that would positively predict the result of a subsequent in-vivo test. The second objective is for the method to be consistent enough to generate reproducible results sample-to-sample for the same sunscreen formulation. The spectral transmittance of a sunscreen in the ultraviolet spectral range can be used to predict an in-vitro SPF value based on standard erythema and solar data.The Boot‟s Star and critical wavelength methods for categorizing the effectiveness of UVA absorbers are also performed from spectrophotometric data. Any pre-irradiation of samples to evaluate their photostability, needs to be performed with a controlled dose from a solar simulator.The flash lamp used in the UV-1000S does not expose samples to excessive light doses, keeping the spectrophotometric analysis independent of any photostability issues. The recommended amount of sunscreen to apply in both FDA and COLIPA in-vivo methodologies is 2 mg/cm2 or 2 μL/cm2. Most sunscreens have a specific gravity of almost unity.The area of applicant on is measured and then the corresponding amount of sunscreen is measured using a pipette (volume) or weighed by loss. The ideal substrate for in-vitro SPF needs to be fairly transparent to the ultraviolet and simulate the porosity and texture of human skin, the in-vivo substrate.

1. In-vitro SPF determination (absorbance measurement) by UV- Spectrophotometer

- Weigh 1 g of all samples, transfer to a 100 ml volumetric flask, dilute to volume with ethanol, followed by ultrasonication for 5 min and then filter through cotton, rejecting the first ten ml.

- Transfer a 5.0 ml aliquot to 50 ml volumetric flask and dilute to volume with ethanol. Then transfer a 5.0 ml aliquot to a 25 ml volumetric flask and complete the volume with ethanol.
- Measure the absorptions of samples in solution in the range of 290 to 450 nm with every 5 nm increment using 1 cm quartz cell, and ethanol as a blank. Calculate average of three determinations and calculate SPF .

2. In-vitro Determination of SPF by UV 2000S Ultraviolet Transmittance Analyzer

- The principle based on the sample transmittance measurement, where transmittance is defined as the ratio of the illumination passed through a sample to the illumination impaging on the sample.
- Procedure: Weigh 100 mg of the investigational sample and spread on the 56 cm2 area to obtain a sample even film thickness of 2 µl/ cm2 on Transpore Tape as suggested in the operation manual of the UV-2000S Ultraviolet Transmittance Analyzer for the sample preparation and application technique.33-34 Expose the prepared sample to Xenon flash lamp for determining the Sun Protection Factor.
- While this is not done as part of mandatory requirements, in vitro testing avoids the variations and ethical issues of testing human volunteers. These tests do not measure the prevention of tanning but quantify UVA protection in the UVAI spectrum. These are then converted to a UV protection factor. The issue is the composition of the testing slide (quartz or acrylic) that the surface roughness of the sunscreen being tested on the slide can affect measurements, and therefore in vitro testing has also not been adopted.

IN-VIVO METHODS:

- In-vivo methods Following are commonly used in-vivo methods for SPF determination. All three methods have somewhat similar procedure except their endpoints and expression of results.
- Procedure: Human volunteers are irradiated with a UVA light source (320÷400 nm) and skin changes, yielding in a immediate or persistent pigment darkening or eryhema or tanning are observed after desired time following irradiation has been stopped.
- Observations: Within 60 sec after each exposure (IPD test), and again approximately 2 h after exposures (PPD test) and 16-24 h after exposures (PFA), the irradiated sites were evaluated under bright “warm while” illumination (approximately 1000 Lux at 6000 K) for pigmentation response and erythema.

- IPD (Immediate Pigment Darkening) by Kaidbey and Barnes:36 where UVA protection factor from the ratio of the sunscreen protected minimal immediate pigment darkening dose to the un-protected minimal immediate pigment darkening dose within 60 sec after each exposure is determined. Endpoint for this method is pigmentation producing a grade ≥1 within 1 min after each UVA exposure.
- PPD (Persistent Pigment Darkening) by Chardon et al.:37 where UVA protection factor from the ratio of the sunscreen protected minimal immediate pigment darkening dose to the un-protected minimal persistent pigment darkening dose, evaluated approximately 2 h after UVA exposure is determined. Endpoint for this method is pigmentation producing a grade ≥ 1, 2 h following UVA exposure. The advantage of the PPD method, when comparing with IPD, is that the residual colour that has developed after exposure to the radiation is stabilized and allows more precise readings.
- PFA (Protection factor in UVA) by Cole et al:38 where UVA protection factor from the ratio of the sunscreen protected minimal response dose (eryhema or tanning) to the unprotected minimal response dose, approximately 24 h after UVA exposures is determined.
- PPF (Phototoxic Protection Factor) by Lowe et al:33 where ratio of sunscreen protected minimal phototoxic dose, measured 72 h after UVA exposure. This method uses 8-methoxypsoralen to increase sensitivity of UV-light. Endpoint for this method is erythema or tanning producing a grade ≥ 1 within 16-24 hr after UVA exposure.

In the USA, sunscreens are considered “over the counter” (OTC) drugs and are considered under the FDA‟s Final Rule 2011 and the Sunscreens Innovation Act 2014 .

The FDA demands sunscreens are tested in 10 human volunteers under a high- intensity UV lamp and reddening of skin is evaluated the next day. The FDA allows manufacturers to discard three out of 10 test subjects and the SPF value on the label is the amount of UV that caused a sunburn in the remaining seven subjects.

New developments in sunscreens

- New molecules with broad spectrum efficiency are being identified from various biological sources like herbs, minerals and various oils from fish, etc.
- These chemicals constituents are responsible for their activity against solar radiations because of their anti-oxidant property to deactivate the free radical generation.
- These agents have shown greater and better protection against the radiations when compared to the synthetic molecules as these are bio-degradable causing less harm to the health and the environment.

Herbal formulations

- Herbs have been in the dictionary of treating ailments from centuries. They have known to contain certain phytoconstituents which relieve many diseases without causing adverse reactions as compared to synthetic molecules.
- Many molecules from natural sources have shown good photo-protecting efficacy, like anti-oxidants, due to which formulations are being made from these sources.
- Turmeric, vitamin E and c, aloe-vera, quercetin are some of the molecules which have shown great efficacy against harmful UVR.

CONCLUSION:

Sunscreen lotion may absorb or reflects some of the ultraviolet radiations and protects against sunburn. All sunscreens are graded with a Sun Protection Factor number. Skin protection also achieved through some of the cosmetic ingredients used in the formulation. SPF tells how long you may be exposed to UVB light before you burn. Sunscreen lotions or gels consists of a delivery vehicle containing one or more sunscreen active ingredients. When applied to the skin, these sunscreen actives divert ultraviolet rays before they can hurt the underlying skin. However, a thorough study reveals that sunscreen formulations are quite complex, needs careful selection of sunscreen agent and vehicle components to control multiple performance and in use limitations. There is strong evidence that sunscreen is safe to use and, when applied correctly, reduces the risk of skin cancer.

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