Formulation Development and Evaluation of Sunscreen

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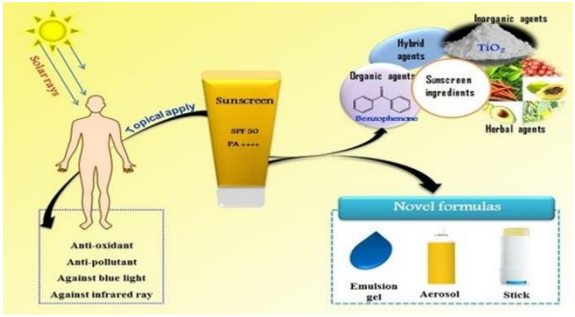
Abstract **- Ultraviolet radiation has been demonstrated to cause skin disorders, including sunburn and relative symptoms of prolonged exposure. It has been reported that sunscreens have beneficial effects in reducing the incidence of skin disorders (sunburn, skin aging, and immunosuppressant) through their ability to absorb, reflect, and scatter UV. Many commercial products have recently been manufactured from not only usual organic and inorganic UV filters, but also hybrid and botanical ingredients using typical formulations (emulsion, gel, aerosol, and stick). Particularly, these products have been supplemented with several preeminent properties to protect against the negative effects of not only UVB, but also UVA. However, the use of sunscreen has faced many challenges, including inducing photo allergic dermatitis, environment pollution, and deficiency of vitamin D production. Therefore, consumers should efficiently apply suitable products to improve sun protection. As well as to avoid the side effects of sunscreen.**

Index Terms **- sunscreen; organic, inorganic, hybrid, botanical agent, emulsion, gel, aerosol, stick formulations, antioxidants, anti-pollutants, defence-blue light and –IR. 1**



INTRODUCTION

Skin is the largest and outer part of the body, which is directly exposed to sun may leads to photo damage of skin which is most sensitive. The major effect of solar radiation is caused by the ultraviolet region of the electromagnetic spectrum. It may cause effects to the eye, skin, and Immune system. Extend exposure of UV radiations may initiate the production of reactive oxygen species, may causes oxidative injury and impairment of the antioxidant system. These may lead to impair the metabolic pathways of the skin, which leads to photo aging, erythematic, edema, sunburn, lines and wrinkles, photosensitivity, immunosuppressant, DNA damage and skin cancer in most severe conditions. These sunscreens are incorporated in many cosmetic formulations like creams, lotion and moisturizer and other skin care products. The main use of sunscreen is to preserve the skin against UVA and UVB rays and to spread the moisture content of skin and its own natural oils, which may be lost during the expose to solar radiation. The sunscreen should be safeguard, chemically inert, non-irritating, nontoxic and photo stable. The skin's natural sunscreens such as squalane, proteins, absorbing lipids and nucleotides have been used from many years.3

Sunlight reaching the surface of the earth contains:
Visible rays, Ultra-violet rays, Infra-red rays
UV Rays (particularly wavelength below 320 mμ) are responsible for most of the therapeutic as well as noxious effects that we attribute to sun light. The UV Spectrum is broken in to three parts:

1. Very high energy (UVC)
2. High energy (UVB)
3. Low energy (UVA)

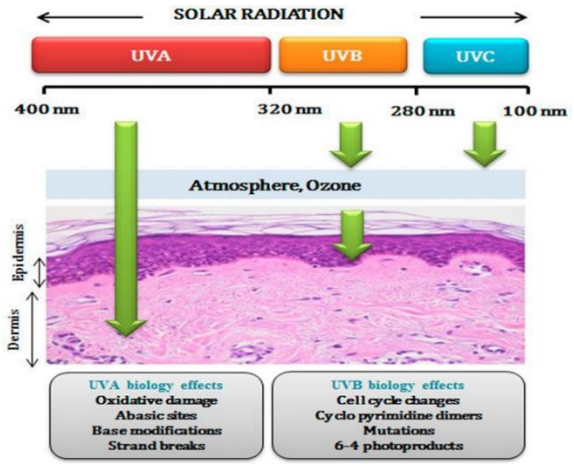
Ultraviolet is categorized in three ranges:

1. UVA is radiation in the 320-400 nm range
2. UVB is radiation in the 290-320 nm range
3. UVC is radiation in the 100-290 nm range

Whereas Visible and IR radiations do not harm to the skin.
Very high energy radiation (UVC) is currently blocked by ozone layer.
High energy radiation (UVB) does the more immediate damage.

But Lower energy radiation (UVA) can penetrate deeper into the skin, leading to long term damage.

Radiation type	Characteristic Wavelength	Effects of human skin	Visible human eye?
UVC	200-290nm (short –wave UV)	DNA damage	NO
UVB	290-320nm (mid-range UV)	Sunburn DNA damage skin cancer	NO
UVA	320-400nm (Long-wave UV)	Tanning skin aging DNA damage skin cancer	NO
Visible	400-800nm	None currently known	YES
IR	800-120,000nm	Heat sensation (high IR)	NO



Hence, addition of other sunscreen agent along with physical sunscreen is better option to enhance the level of protection. Physical (titanium dioxide, zinc oxide) and chemical (octyl methoxycinnamate, oxybenzone, octocrylene, and luteolinon) ingredients can be incorporated into sunscreens in the form of nanoparticles (NPs), which reportedly can optimize material delivery into the outer skin layers.7-9There are few reports available on the application of NPs of physical and chemical sunscreen ingredients (titanium dioxide, zinc oxide, octyl methoxycinnamate, oxybenzone, octocrylene, and luteolinon) to improve sun protection efficacy. UV-absorbing agents must accumulate within the upper skin layers in order to provide a dense light-absorbing layer and guarantee water resistance. Skin penetration of four different types of rutile titanium dioxide was assessed using the skin of micro pigs. TiO2 was able to penetrate into the vacant hair follicles.12-16 Physical UV absorbers like titanium dioxide and zinc oxide have been considered as highly protective agents against UVR. ZnO and TiO2 combinations are particularly valuable because of their ability to filter both UVA and UVB radiations, providing broader UVR protection than that observed with individual component.10, 11.

SELECTION OF SUNSCREEN BASED ON SKIN TYPES

Wash your face with the help of a gentle cleanser. This will ensure that the makeup, pollutants and other dirt are removed. Wait for an hour and make sure that you do not touch your face. Your skin should return to its natural state which will help determine the type of your skin. Take a tissue paper and dab your face. The area consisting of your forehead and nose must be the place where you concentrate. This is where you should wipe with the help of a tissue. So, what's your skin type?

There are 4 types of skin explained below.

Normal Skin: If your skin shows no oil or no flaking and it feels smooth and supple, then hooray! You have a normal skin type.

Oily Skin: If there is lots of grease on the tissue paper, then you have an oily skin type. It is common that you might have a shine and large pores.

Dry Skin: If the tissue paper is accompanied by lots of flakes and dead skin, then your skin is dry. You need to consider moisturizing your skin.

Combination: Any combination of the above-mentioned skin types is a combination skin type. This is very common and most of you might as well have this skin type. Your skin is generally oily in the forehead and nose area and dry elsewhere.

Which SPF is the Best for You According to Your Skin Type?

You can see that SPF 50 does not offer significantly more protection than SPF 15. The SPF 50 might offer you a little more protection but not too much as well. If your skin type is normal, we would recommend that you use SPF 30 sunscreen. For a dry skin type, a sunscreen with a moisturizer is advisable. If you have oily skin type, we recommend that you use an SPF 50 Sunscreen. SPF 15 Sunscreen works best for combination skin type or dark skin tone. You can also

customize your options by choosing SPF 20, 25, etc. and use these options based on your experience.

SUNSCREEN REGULATIONS

US-FDA method:
The FDA proposal measures in-vitro UV transmittance through a sunscreen film using the critical wavelength method. Sunscreen products offering primarily UVB protection would have a critical wavelength less than 320nm, whereas those providing both UVB and UVA protection would have critical wavelengths between 320 and 400nm. FDA requires that sunscreen products have a critical wavelength of at least 370nm to be labeled as providing 'broad spectrum'UVA and UVB protection.

UK method of boot star rating:
The UK method, called as Boots star rating system, also measures the UV transmittance through a sunscreen film. The substrate for measurement is abraded PMMA plates. The ratio between the mean UVA and UVB absorbance measured before and after irradiation of the sunscreen products is calculated.

European countries:
COLIPA guidelines are mainly to the liquid and emulsion type sun protection products.

Australia:
Australian standard (AS) method uses spectrophotometer for measurements of the solar radiation transmitted by a sunscreen product to yield a percentage of UVA radiation absorbed by the product. According to this test, a product is designated as a long wave protector only if it transmits less than 10% of the incoming UV radiation between 320 and 360 nm
International Organization for Standardization (ISO):
It is an independent, non-governmental international organization in Geneva with a membership of 162 national standards bodies.

There are different methods of ISO for sunscreens:
ISO 24443:2012
ISO 24442-2011
ISO 24444-2010
India:
Indian being Asian population comes under Type–IV skin pattern which burns minimally and tans easily. Freckles are rare but still use of sunscreen is necessary to avoid tan. Indian regulations date from the Indian Drug and Cosmetic Act (1940) as amended from time to time considers sunscreens as cosmetics. Bureau of Indian Standards (BIS), a participating member of the ISO, sets the relevant cosmetic product standards.

China:
Sunscreens are regulated under the Hygienic Standard for Cosmetics 2007. Currently sunscreens can only be labeled up to SPF 30+.The product must be labeled in Chinese language and have a Chinese name. Water resistance norms should be followed if labeled.6

SUNSCREEN FORMULATIONS

1. EMULSION FORMULATION
2. GEL FORMULATION
3. AEROSAL FORMULATION
4. SUN STICK FORMULATION

1.Emulsion formulation
An emulsion is termed a lotion or creams depending on its viscosity, respectively, below 50,000 and in the range of 150,000–500,000 centipoises, providing almost unlimited versatility.17 it is normally produced from two unmixable liquid phases, namely "water-in-oil" and "oil-in-water" emulsions18. These formulations possess the ability to spread more easily on the skin and disperse from bottles18. 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 temperatures17.

2.GEL SUNSCREEN
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, hydro alcoholic, micro emulsion, and oil anhydrous formulations17. 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 temperature. Therefore, it is easily washed away when exposed to water or sweat1719. The hydro alcoholic 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. The micro emulsion 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 17, 20.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 21 However, they are not widely sold because they are difficult to produce and quite expensive

3.AEROSOL SUNSCREEN

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 22.

4.SUN STICK

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 waxes17. This form is subdivided into three categories, namely transparent, semi-transparent, and matte sunscreen 23. 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 23.

SUNSCREEN EVALUATION

In vivo Evaluation of Sunscreens

MED is a measure of the amount of energy per unit area (J·cm−2) required to cause minimal erythematic. Validation of SPF in vivo is made through an artificial source of UVR on human subjects. In Europe, the SPF is accepted if determined in at least 10 subjects 33. In vivo evaluation of SPF has several drawbacks. First of all, this evaluation method is expensive in terms of money and time. Moreover, it raises several ethical issues concerning the potential damage to skin volunteers. Finally, it evaluates only the erythematic which is caused by UVB and UVA-II, therefore the protection against the remaining UVA spectrum of UVR is not represented in the SPF value. The importance of adequate UVA protection is apparent with improved understanding that UVA may induce damages to cellular DNA via oxygen radical species as UVA energy interacts with endogenous photosensitizes 34. In vivo evaluation of sunscreen's UVA protection requires high doses of UVA, thus being troublesome for economical and ethical issues. Three methods have been proposed for in vivo UVA protection evaluation: IPD (Immediate Pigment Darkening), PPD (Persistent Pigment Darkening), and UVA-PF (UVA Protection Factor). IPD and PPD are based, respectively, on immediate (seconds) or persistent (2–24 hours) pigmentation changes of the skin caused by UVA irradiation.

IN-VITRO EVALUATION OF SUNSCREEN:

An in vitro SPF test method would be advantageous if it could generate results faster and cheaper. Furthermore, it could avoid the ethical concerns associated with in vivo testing. Several in vitro techniques have been developed, but at present there is no broadly accepted method. In vitro approaches generally consist of a film of sunscreen applied to an artificial test substrate and a spectrophotometer which analyzes the amount of UVR passing through the film of product. Vitro-Skin (IMS Inc.) is a synthetic skin substrate that must be used following an exact hydration procedure35. That Vitro-Skin gives very good performances for sunscreen tests, even if the use of this material presents many disadvantages, notably a relatively high cost per sample, the need to hydrate the substrate starting the day before testing, a relatively short lifetime of the hydrated sample. Biologically derived substrates, like excised stratum corneum and excised human epidermis, have also been used but the outcome of the tests using these products was generally not reproducible 36. In a recent investigation 39 we have correlated the correspondence between in vitro SPF data and values reported by the manufacturers. At present the FDA is not replacing the in vivo SPF test with an in vitro SPF test 37, since one of the limitations of an in vitro test is the lack of data on the performance characteristics of in vitro test substrates, such as quartz or artificial skin. FDA, in the 2007 rule 38, stated that data failed to show that a substrate could effectively simulate the complex features of human skin. In the new 2011 rule 37 FDA decided to confirm the exclusion of an in vitro test, due to the lack of new data to validate in vitro tests.

NOVEL PROPERTIES OF COMMERCIAL SUN PROTECTION PRODUCTS

1.SUNSCREEN WITH ANTIOXIDANTS AND ANTI-AGING

Beneficial effects of natural agents, many sunscreens have been produced by combining one or more natural ingredients (e.g., extracts and nutrient compositions) and conventional ingredients (e.g., TiO2, ZnO, and benzoate derivatives). Particularly, these products have been found to be safe and are able to overcome undesirable effects by reducing the utilization of inorganic and organic compounds 24.

2.SUNSCREEN COMBINED WITH DNA REPAIR ENZYMES

There is no denying the fact that UV radiation can penetrate deep into the skin and damage cells where skin cancer originates 25.

DNA Repair Enzymes	Proposal mechanisms and proven effects
Topical T4 End nuclease	Enhancing DNA repair by eliminating cyclobutene pyrimidine dimmers (CPDs) Reducing of precancerous and cancerous in high-risk individual.
Photolysis	Using energy from blue light to quickly repair damaged DNA by catalyzing electron transfer reactions, resulting in the splitting of cyclobutene rings.
8-Oxoguanine glycosidase	Identifying and initiating repairing photo lesion (8-oxo-7,8 dihydroguanine) caused by ROS Reducing of UVB-induced tumor progression in mice.

Table: 2

3. SUNSCREEN AGAINST ENVIRONMENTAL POLLUTANTS

UV rays, pollutants, such as particulate matter (PM), polyaromatic hydrocarbons, sulphur oxides (SO2), and nitrogen oxides (NOx), can negatively affect skin. It has been indicated that these pollutants can induce inflammation, hyper pigmentation, and collagen breakdown, leading to skin dryness, dark spots, loss of firmness, uneven skin tone, aggravation of acne, and wrinkle formation 26.

4. SUNSCREEN AGAINST BLUE LIGHT

Blue light (380–500 nm) is derived from sunlight or electronic devices such as Smartphone's, tablets, and computers 27. Due to its high energy, it is useful on photodynamic therapy when using a combination of photosynthesizing drug and a high-intensity light source to treat cancer28, 29. When blue light enters deep into the skin, it can cause deleterious effects all skin layers by generating ROS and weakening the epidermal barrier, thereby damaging the extracellular matrix and accelerating aging 23,30.

5. SUNSCREEN AGAINST THERMAL IR

IR rays, accounting 54.3% of total solar radiation reaching the Earth, have also been proposed to be deleterious to human skin.31, 32 Regarding its ability to penetrate the epidermis, dermis, and subcutaneous tissues, this radiation can be a detrimental factor that damages collagen content of the skin through the creation of ROS radicals and increased MMP-1 and MMP-9 activity in the same manner of UV rays 31, 32. The results showed that the infrared protection factor (IPF) in protected skin was greater than that of unprotected skin.

APPLICATIONS

The dose used in FDA sunscreen testing is 2 mg/cm2 of exposed skin.2 Some studies have shown that people commonly apply only 1/4 to 1/2 of the amount recommended for achieving the rated sun protection factor (SPF), and in consequence the effective SPF should be downgraded to a 4th root or a square root of the advertised value, respectively.4 A later study found a significant exponential relation between SPF and the amount of sunscreen applied, and the results are closer to linearity than expected by theory.5

VARIOUS EXAMPLES OF SUNSCREEN PREPARATION

Which are mentioned below?

Class	Sources	Mode of action of photo protection
Flavonoids Apigenin(5,7,4'-trihydroxyflavone) is a widely distributed plant flavones	Cereal grains and aromatic herbs (parsley, rosemary, thyme), fruits (apples, cherries, grapes), vegetables (beans, broccoli, celery, leeks, onions, barley, tomatoes) and beverages (tea, wine)	Inhibits UV mediated induction of ornithine decarboxylase activity, down-regulates COX-2 expression in macrophages

Chrysin(5,7-dihydroxyflavone), an analog of apigenin, is a natural flavones	Propolis and honey	Inhibits UV mediated induction of ROS
Quercetin (3,5,7,3',4'-pentahydroxyflavone, is one of the most potent antioxidant compounds	Fruits and vegetables (apples, grapes, tomatoes etc…) bevearges (tea, redwines), olive oil.	Protects skin's antioxidant systems (glutathione peroxidase, glutathione reductase, catalase and superoxide dismutase activities), prevention of UVC radiation-induced liposome per oxidation SPF of quercetin matches to homosalate, a synthetic sunscreen agent.
Silymarin is a standardized extract of flavonolignan diastereoisomers silibinin A and silibinin B in a roughly 1:1 ratio, the diastereoisomers isosilibinin A and isosilibinin B, silicristin, and silidianin	Seeds of the milk thistle	Inhibition of UVB-induced oxidative stress, inflammation and suppression of immune system
Genistein (4',5,7-trihydroxyisoflavone	Soybean isoflavone	Through enhancement of antioxidant enzyme activities and scavenging of oxygen free radicals, specific inhibitor of protein tyrosine kinase, and phytoestrogen
Isoflavones like daidzein, genistein, and glycitein	Byproduct of soybean (*Glycine max* L) oil processing and also present in Red clover (*Trifolium pratense* L.)	Able to inhibit UVB induced keratinocyte death, release of hydrogen peroxide (H2O2), and UVB induced MAPK phosphorylation
Tannins Catechins including (−) epicatechin (EC), (−) epicatechin-3-gallate (ECG), (−) epigallocatechin (EGC), (−) epigallocatechin-3-gallate (EGCG), (+) catechin, and (+) gallocatechin (GC)	Green tea, pomegranate, Amla	Reduces DNA damage and erythematic formation due to protection of DNA repair enzymes from inactivation by ROS and due to UVB absorption ability of green tea polyphenolic.
Anthocyanidins Anthocyanidins mixtures	Colored (range from yellow to purple (except green) fruits, flowers and berries, vegetables, cereal grains, (e.g. Pomegranate (*Punica granatum*)	Inhibits the adverse effects of UVB exposure including translocation of transcription factors NF- kB and AP-1, over expression of the pro-inflammatory cytokine IL-8, cleavage of procaspase-3 (a key step in apoptotic pathway), and DNA fragmentation
Cyanidin 3-glycosides	Citrus species	Protects skin via transcriptional mechanisms of NF-κB and MAPK signaling
Pelargonidin	Strawberries and other berries	Blocks collagen destruction and inflammatory responses via transcriptional mechanisms of NF-κB and MAPK signaling
Carotenoids β-carotene, lycopenes	Tomatoes (*Solanum Lycopersicum*), Carrots (*Daucus carota*) and in many red-orange-colored fruits and vegetables	As a chain breaking antioxidant in a lipid per oxidation.

Table:3

6 ADVANCES IN SUNSCREENS

- Nano sunscreen
- Sun sport
- Sunscreen sprays
- Roll-on sunscreen
- Sunscreen for children.

CONCLUSION

It can be concluded that there is great market potential for sunscreen chemicals either synthetic / natural / in combination due to awareness of protection from

hazardous UVA as well as UVB rays. Photo stable , uniform UVA /UVB protective sunscreen product with high SPF can be minimum ideal requirement but natural chemicals like poly phenols (flavonoids,tannins),carotenoids , anthocynidins , few vitamins , fixed oils and volatile from vegetables, fruits, medicinal plant parts (leaves , flowers , fruits, berries), algae and lichens are more effective due to their long term beneficial effects especially against free radical generated skin damaging along with UV - rays blocking. These natural chemicals incorporated sunscreens might provide cost effective, truly broad spectrum sunscreen products with anti-oxidant, wound healing, anti-inflammatory and many more skin protective effects .6

ACKNOWLEDGEMENT

The authors are thankful to prof.M.Sumakanth, the principal of RBVRR women's college of pharmacy, Hyderabad.

CONFLICT OF INTREST

The Authors declare no conflict of interest

ABBREVATION USED

UVA: Ultraviolet-A-radiation; UVB: Ultraviolet-B-radiation; Ultraviolet-C-radiation: UVC; SPF: Sunburn protective factor, ISO: International Organization Standardization DNA-Deoxyribonucleic acid. MED: minimal erythemal dose.

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