

A Summarized Review of Formulation, *in Vitro* Evaluation of Sunscreen

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Abstract:- The efficacy and safety of sunscreens are diminished when their agents permeate the skin, resulting in systemic circulation and unidentified negative effects. The filters in sunscreens must remain on the skin's surface with minimal penetration through the dermis in order to preserve their safety and efficacy. Sunscreen should always be worn, even in the event that filters manage to get through. Damage like as erythema, the production of free radicals, aging of the skin, and skin cancer brought on by UV radiation. Research is being done to limit skin penetration, assess sun protection factor (SPF), and improve formulation properties and stability in order to target potential negative effects caused by topical absorption of sunscreens. *In vitro* or *in vivo* investigations are used in current assays to determine sunscreen penetration since they mimic the physiological conditions of use. This review's objectives are to reexamine data on sunscreen skin penetration over the last ten years and identify variables that may increase skin penetration or boost sunscreen efficacy. Sunburn is caused by ultraviolet B radiation, but ultraviolet A may be more damaging to the skin. Sunscreens should ideally block both wavebands. A sunscreen's sun protection factor is mostly determined by how well it blocks ultraviolet B. The efficiency of preventing ultraviolet A is not measured. Sunscreens may be organic or inorganic chemicals. If metal oxide sunscreens are made into nanoparticles, their cosmetic acceptance might increase. It doesn't seem that absorbing organic sunscreens and nanoparticles has any appreciable systemic effects. Frequent use of sunscreen prevents melanoma, squamous cell carcinoma, and actinic keratosis from developing.

Keywords:- Sunscreen, Sun Protection Factor, Permeation, Sunburn.

I. INTRODUCTION

Sunscreen is widely being used as a photo-protective agent to defend against UV rays. A sunscreen preparation is described as a mixture that prevents sunburn in the targeted region when applied topically. Sunscreens are used to supplement the body's defences against UV radiation from the sun, which is damaging. Its capacity to absorb, reflect, or deflect solar radiation determines how it functions. The calculation of a sunscreen's sun protection factor (SPF) involves comparing the duration required to cause sunburn on

skin protected by sunscreen with the duration required to cause sunburn on skin that is not covered by sunscreen.^[1] The efficacy of sunscreens to prevent UV-induced sunburns and their chemopreventive properties determine how effective they are.^[2] A wide range of specifications must be met by the perfect sunscreen composition. It must filter or absorb the sunburn-causing photons, which are in the 2900–3300 Angstrom range. In the presence of light, air, and moisture, it should be stable; if it breaks down under these circumstances, the breakdown products should absorb similarly to the original compound in the 2900–3300 Angstrom range. It is desirable for the chemical and its breakdown products to be nontoxic and nonirritating under use conditions. It should be almost neutral to ensure that the presence of either base or acid on the skin does not have any negative consequences. It should be poorly soluble in water to avoid being quickly removed by perspiration and well soluble in the ointment base or vehicle in which it is to be prepared. In order to prevent evaporation during use, it should be comparatively nonvolatile. It shouldn't be absorbed through the skin quickly.^[3]

Sunscreens were first created to shield users from sunburn caused by prolonged sun exposure. These products had minimal effect on ultraviolet A (UVA) radiation, but were intended to prevent ultraviolet B (UVB) rays, which are responsible for sunburn. It is now established that ultraviolet A radiation damages cells located beneath the epidermis, potentially resulting in early ageing of the skin and certain forms of skin cancer. Nowadays, sunscreens are available that block both wavebands. Nowadays, a lot of individuals use sunscreens on a daily basis. They are also found in many "anti-ageing" moisturising creams, lipsticks, and other cosmetics.^[4]

The skin's barrier against the damaging effects of direct UV radiation is a sunscreen, which is a photoprotective agent against UV radiation. Currently being developed are broad-spectrum sunscreens that gradually lessen the negative effects of direct UV light.^[5] Phytoconstituents are becoming more and more popular as necessary ingredients in cosmetic formulations because they are natural, have antimutagenic, anticarcinogenic, and nontoxic effects, and can significantly inhibit the intricate process of carcinogenesis. Synthetic photoprotective agents have the potential to be toxic and carcinogenic. Natural herbal ingredients used in cosmetics soothe skin more effectively, especially hypoallergenic

skin^[6] contains natural elements that may effectively protect the skin against UVA and UVB rays, air temperature fluctuations, pollution, hyperpigmentation, and ageing. It can also revitalise the skin, because bioactive chemicals are harmless, have no negative side effects, don't include any harmful synthetic compounds that could endanger human health, and are environmentally sustainable, their application in cosmetic formulations has grown recently.^[7] Furthermore, bioactive substances have a wide range of pharmacological characteristics. These include being naturally occurring preservatives and antioxidants, hypoallergenic in comparison to synthetic products, and environmentally begin.^[8]

II. DISEASES CAUSED BY UV – RAYS

A. Sunburn

- Sun exposure can cause various types of skin damage, including sunburn and sun poisoning. Treatment may be necessary for the mild to severe symptoms.
- If you have blisters, hives or rash, fever and chills, nausea, thirst, headache, pain and tingling, or visual issues, sunburn may be sun poisoning.^[18]
- Midday and the hours right before and after (between 10 AM and 4 PM) are when UV rays are most powerful.^[19]
- Hot, red, and sensitive skin are the initial signs of sunburn; it also hurts to touch or press the skin and causes dehydration. A few days later, the skin may peel, blister, and swell.^[20]
- Home remedies for mild sunburns include applying damp cloths or compresses to relieve pain, taking a tepid bath without soap, patting the skin dry gently, applying soothing creams or lotions, using over-the-counter pain relievers like Tylenol, and moisturising the skin.^[21]
- Skin cancer (malignant melanoma, basal cell carcinoma, squamous cell carcinoma) and persistent skin damage can result from sunburn.^[22]
- Those with fair skin and those with specific pigment abnormalities are more vulnerable to sunburn.^[23]
- There are several illnesses and ailments that increase the risk of sunburn, including as vitiligo, xeroderma pigmentosum, lupus, albinism, and porphyria.^[24]
- Certain drugs may make you more susceptible to sunburn (photosensitivity).^[25]
- Severe sunburn is the cause of sun poisoning, which manifests as fever, chills, nausea, disorientation, fast breathing, quick pulse, dehydration, and shock.^[26]

B. Mechanism of Photoaging and Chronological Skin Aging

Variable epidermal thickness, dermal elastosis, reduced/fragmented collagen, elevated matrix-degrading metalloproteinases, inflammatory infiltrates, and vascular ectasia are all signs of photodamaged skin. The fact that ROS destabilise other molecules and start chain reactions that quickly deteriorate biomolecules such as telomere shortening and degeneration, mitochondrial damage, membrane degradation, and oxidation of structural and enzymatic proteins—makes them especially dangerous. Collagen and elastin are the extracellular matrix's structural proteins. Angiogenesis and metastasis are facilitated by the breakdown and remodelling of collagen and elastin fibres, and the damaged proteins in these tissues act as extra photooxidative stress sensors. Collagen fragments accumulate over time and as a result of prolonged UV exposure, which compromises the mechanical and functional characteristics of the skin extracellular matrix. Skin surface texture and skin resilience are linked to elastic fibres, such as oxytalan fibres in the papillary dermis, and the production of elastic fibres by fibroblasts is promoted by elevated expression of fibulin-5. Fibulin-5 is an early marker of photoaged skin, and its induction is thus a damage-repair mechanism.^[27]

C. Mechanism of UV Induced Immunosuppression

The UV rays suppresses the immune system in several ways.^[28]

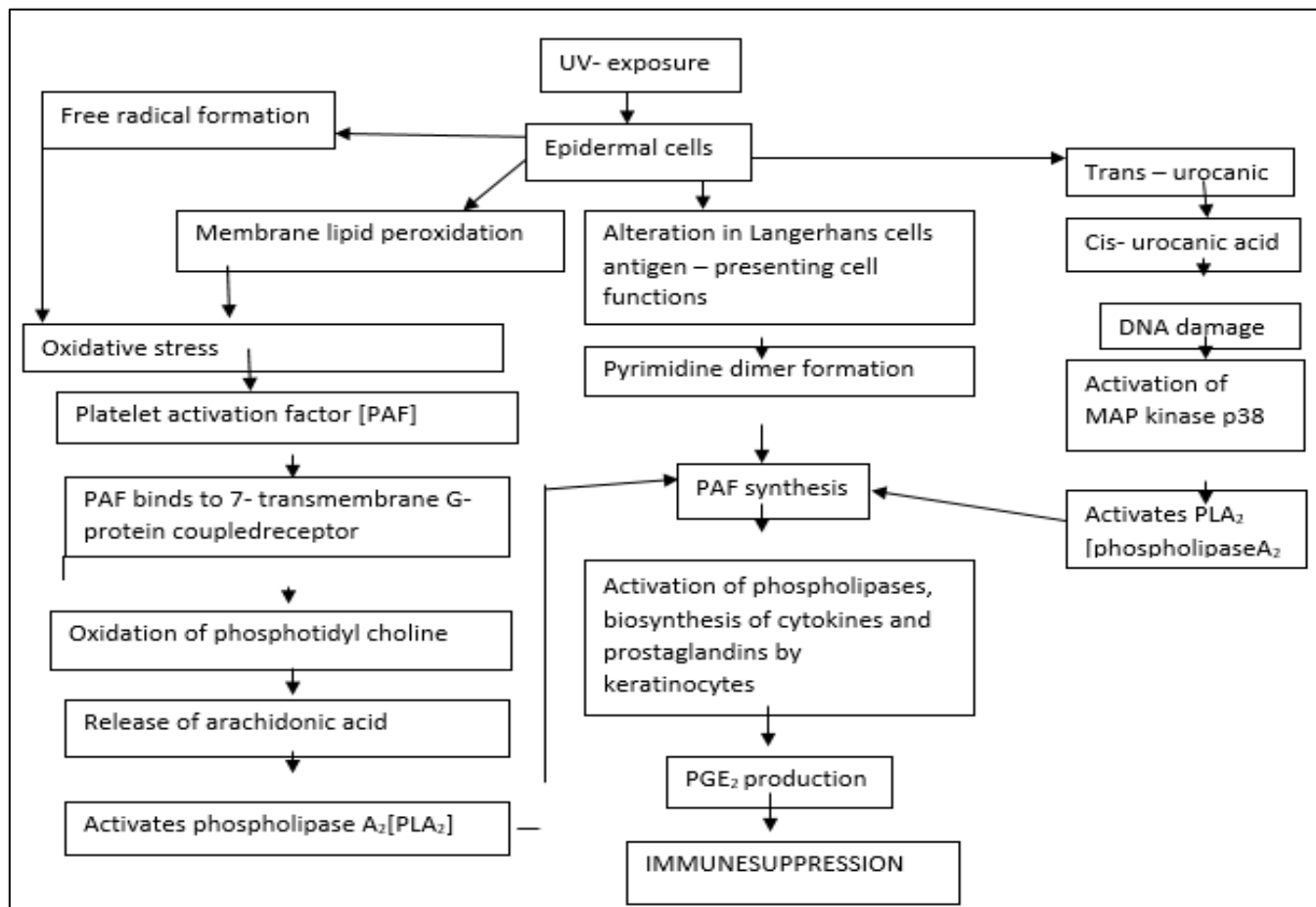


Fig 1: Mechanism of UV Induced Immunosuppression

D. UVB Response in Melanoma

Skin infiltration by neutrophils and macrophages is brought on by UVB radiation. The promotion of macrophage recruitment into the skin is facilitated by the upregulation of CCR2 and ATF2 in melanocytes. This, in turn, triggers the synthesis of CCL2, MMP-9, and IFN- γ in macrophages. Melanocytes and macrophages engage in a positive feedback loop via which melanocytes upregulate CCL8, a CCR2 ligand, and encourage further macrophage recruitment. This is facilitated by IFN- γ signalling from macrophages. The influx of neutrophils and macrophages triggers an inflammatory response that advances angiogenesis, melanoma cell invasion, survival, and metastasis. Moreover, UVB independently controls MC1R signalling and melanin synthesis. UVB-induced induction of pigmentation genes and consequent rise in melanin synthesis boosts NER and cell survival but reduces proliferation and, eventually, melanomagenesis. UVB-induced signalling via MC1R initiates the DNA damage response. In order to trigger NER, signalling via α MSH and MC1R phosphorylates ATM and ATR, increases XPC, and encourages the recruitment of XPA. To lessen oxidative stress in melanocytes and melanoma, α MSH also activates genes related to the response to oxidative stress. Additionally, XPC and XPA are activated to cause NER by UVB-induced IL-23 expression. Melanin synthesis, MC1R signalling, and IL-23 signalling can all

prevent UVB-induced melanomagenesis. Activating Transcription Factor 2 (ATF2), α -Melanocyte-Stimulating Hormone (α MSH), Ataxia Telangiectasia and Rad3-related (ATR), Xeroderma Pigmentosum Group C (XPC), type II Interferon (IFN- γ), Interleukin-23 (IL-23), Nucleotide Excision Repair (NER), Melanocortin 1 Receptor (MC1R), Ataxia Telangiectasia Mutated gene (ATM), Ataxia Telangiectasia and Rad3-related (ATR); Xeroderma Pigmentosum group A (XPA).^[29]

III. CLASSIFICATION OF SUNSCREEN

A. Sunscreen Classically Divided into Physical or Chemical Sunscreens:-

➤ Chemical Sunscreen

Chemical sunscreens absorb UV photons through the skin, transform them into heat, and then expel the heat from the body. Physical blockers are inorganic substances that absorb, scatter, or reflect UV radiation. Physical UV absorbers, such as zinc oxide and titanium dioxide, are thought to be extremely effective UVR protectors. Combinations of ZnO and TiO₂ are especially useful because they can filter UVA and UVB rays, offering greater UVR protection than is possible with single components.^[30] Their size is less than 100 nm, and they are utilised as nanoparticles

in sunscreens. Because these mineral particles are much less noticeable after application, their smaller size promotes the cosmetic acceptability by consumers.

ZnO's UVA-UVB absorption curve is broad, but TiO₂ offers superior UVB protection. Because inorganic filters can not absorb into the skin, the hazards to human health associated with them are generally very low. Nevertheless, inhalation exposure poses a concern, which is why spray sunscreen products containing nanoparticles are advised to be avoided.^[31] While UV-B rays produce sunburn, UV-A rays play a major role in skin cancer and rapid ageing of the skin. Because of this, many medical professionals strongly advise using sunscreen to reduce or perhaps completely eliminate the damaging effects of UV rays on our skin, bearing in mind that exposure to UV radiation is linked to around 90% of all cases of skin cancer. It is recommended to protect against UVB and UVA radiation. Broad-spectrum protection is typically achieved by combining chemical sunscreens that absorb UV rays with physical inorganic sunscreens that reflect UV rays. As part of an overall sun protection programme, the proper application of sunscreens should be paired with avoiding the midday sun and donning protective clothes and sunglasses.^[32] Unfortunately, false information about the toxicity, safety, and severe side effects of the active chemicals now utilised in sunscreens is spreading through the media and the Internet, discouraging people from wearing sunscreens.^[33] Chemical sunscreens are carbonyl-conjugated organic molecules that are typically aromatic. The amount of UV protection that chemical sunscreens provide can be used to categorise them. According to well-known studies, persistent pigment darkening (PPD) is a stable end point that is induced by all UVA wavelengths and is unaffected by fluence rate; in other words, it is a trustworthy endogenous UVA dosimeter in the skin.^[34]

➤ *Problems Associated with Chemical Sunscreens Are:*

- Needs around 20 minutes to take effect after application.
- Chemical sunscreens can cause erythema, edoema, and irritation as a result of the multiple ingredients combined to provide broad spectrum UVA and UVB protection, which can be particularly bothersome for people with dry skin and a compromised moisture barrier.
- Sensitive skin types are more susceptible to irritation the higher the SPF (such as formulas with an SPF of 50 or more).
- Reapplication is necessary more frequently because the protection it provides is depleted more quickly in direct UV radiation.
- Enhanced risk of redness in skin types susceptible to rosacea, as it converts UV radiation into heat, exacerbating flushing.
- May clog pores in skin types with oily pigmentation.^[35]

➤ *Physical Sunscreen*

It has become clear in recent years how important it is to wear appropriate UVA protection.

Standards used in the US and Europe to evaluate sunscreen products' UVA protection differ. According to US Food and Drug Administration rules for broad-spectrum status, the majority of tested sunscreens provided appropriate UVA protection; however, nearly half of the sunscreens tested failed to meet EU standards. Oxybenzone, meradimate, avobenzene, and tetraphthalidine dicamphor sulfonic acid are the components of UVA sunscreen. Broad spectrum is a term designed to mean protection from both UVA and UVB.^[36,37]

➤ *Problems Associated with Physical Sunscreens are:*

- Certain sunscreen formulae are unsuitable for medium-to-dark skin tones due to their high opacity, which leaves a white film on the skin and renders the topical treatment unappealing from a cosmetic stand point.
- May not be as protective if not applied liberally and precisely, as UV light has the ability to pass through the molecules of sunscreen and penetrate the skin.
- Easily rubs, sweats, and rinses off, necessitating more frequent reapplication when needed outside.

Few studies, have been done on the use of Polymeric Nanoparticles (NPs) of the chemical and physical constituents included in (titanium dioxide, zinc oxide, octyl methoxycinnamate, oxybenzone, octocrylene, and luteolinon) to increase the effectiveness of sun protection. It is necessary for UV-absorbing chemicals to build up in the top layers of skin to ensure water resistance and a thick layer of light absorption. Antioxidants may be added to food to further benefit by scavenging free radicals. In this regard, the potential action of natural polyphenols as antioxidants and photoprotectans makes them appealing.^[38]

IV. MATERIAL AND METHOD

A. *Material:*

➤ *NaCl*

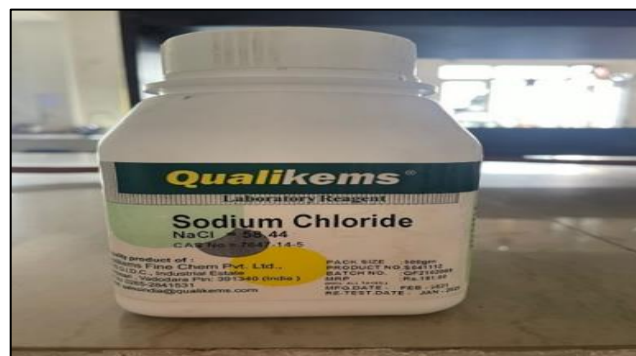


Fig 2: NaCl

Table salt's chemical name is sodium chloride. It is mostly utilised as a thickening, emulsifying, or texturizing agent in skincare products. Sodium chloride is frequently used in exfoliating scrubs and some washing products to produce a mildly abrasive impact for skin exfoliation. While sodium chloride is usually thought to be safe to use in skincare products, people with sensitive or broken skin should take caution when using products that include it as it may cause discomfort.

- *The Advantages of NaCl are*
Exfloation, texture and consistency, cleansing.^[39]

➤ *Paraffin Liquid*

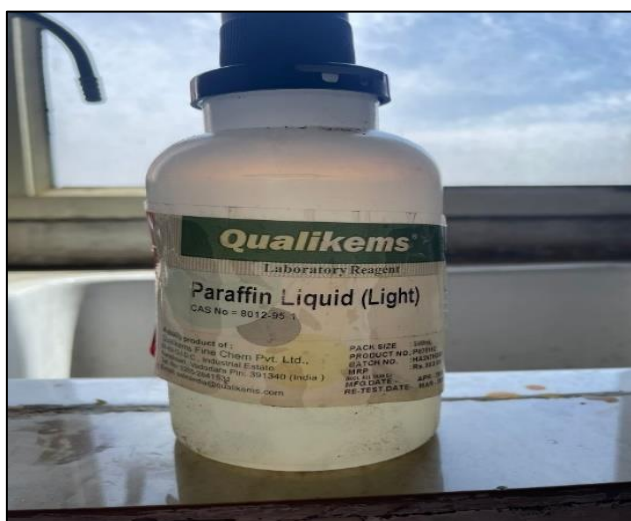


Fig 3: Paraffin Liquid

Liquid Paraffin is a prescription medicine used in the treatment of dry skin. This relieves dryness and leaves the skin soft and hydrated.^[40]

➤ *Borax*

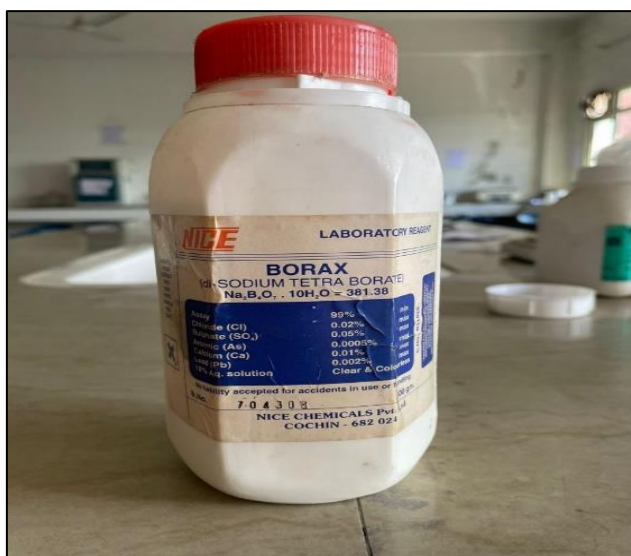


Fig 4: Borax

Borax helps a number of products act to inhibit microbial growth on and in the skin as well. Also, the Borax present in cosmetics, especially in lotions and creams, softens the water phase of the product, thereby enabling its contrasting oil and water components to bind well together.^[41]

➤ *Triethanolamine*

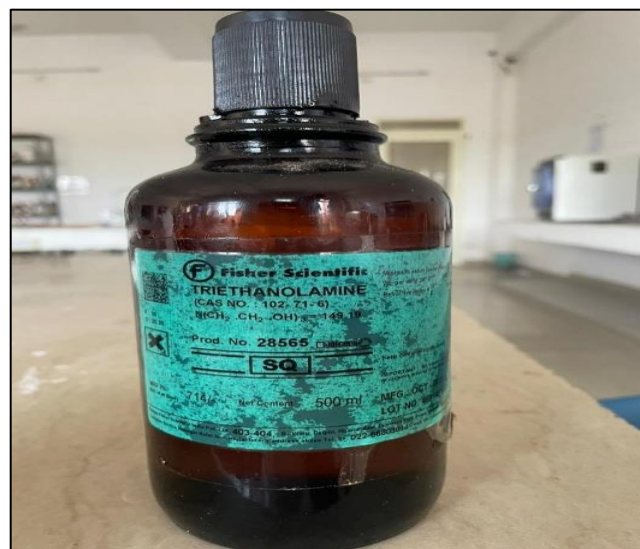


Fig 5: Triethanolamine

It is a tertiary amino compound, it has a role as a buffer and a surfactant. It act as a stabilizer in creams and also act as a thickening agent.^[42]

➤ *Zinc Oxide*

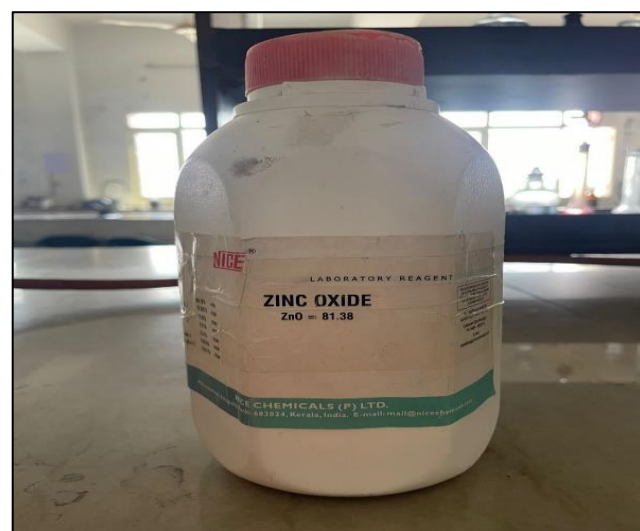


Fig 6: Zinc Oxide

Zinc oxide is a great physical sunscreen because it applies a thin coating to our skin that reflects UVA and UVB radiation without penetrating. Zinc oxide gives you broad spectrum protection from UVA, meaning your skin is getting the best sun protection possible.^[43]

➤ *Glycerin*

Glycerin is commonly used with occlusives, another type of moisturizing agent, to trap the moisture it draws into the skin.^[44]

➤ *Bees Wax*

Beeswax has excellent compatibility with oils, it is a little sticky, which can increase the movement resistance between organic sunscreen agents, thus reducing the precipitation and aggregation and making them evenly distributed.^[45]

B. Method

It is an oil-in-water type emulsion product.

C. Preparation of Oil Phase

- Add 3gm of bees wax in 4ml of paraffin liquid and heat them on waterbath at 62°C to 65°C.
- After melting of beeswax add 2gm of zinc oxide and 0.5gm of methylparaben in it.
- Stir them properly.^[46]



Fig 7: Oil Phase

D. Preparation of Water Phase

- Take 2% solution of NaCl, add 3ml of glycerin, 2ml of triethanolamine, and 2gm of borax.
- Heat all of them and stir properly.

Now slowly add the oil phase in water phase at a temperature between 65°C to 80°C with a continuous stirring.^[47] Then add perfume for the fragrance.

Table 1: List of Chemicals

Sr.no.	Chemicals	Quantity taken
1	Beeswax	3gm
2	Paraffin liquid	4ml
3	Zinc oxide	2gm
4	Methylparaben	0.5gm
5	Sodium chloride	2%
6	Glycerin	3ml
7	Borax	2gm
8	Triethanolamine	2ml
9	Mogra	q.s

V. RESULTS

➤ *Performed Various Evaluation Parameters that are Written Below:*

- **Appearance :-** we were able to determine the cream’s appearance by looking at its colour, opacity.
- **Homogeneity :-** The examination was conducted via manual hand contact.
- **p^H :-** The p^H of the sunscreen should be measured in the p^H meter after is calibration.^[48]

Table 2: Determination of p^H

Sr.no.	Sunscreen	p ^H
1.	F1	6.05
2.	F2	6.91
3.	F3	7.21

➤ *Spreadability:*

The spreadability of sunscreens determined their therapeutic efficiency. The appropriate amount of sunscreen was applied between two slides, and under specified load directions, and the two sides took the time in seconds to slide off. Spreadability was defined as the amount of time it took to separate two slides in less time.^[49]

The formula for calculating it is:

$$S = M \times L / t$$

Where, M = weight tied to the upper slide

L = length of glass slide

T = time taken to separate the slide

Table 3: Spreadability test

Sr.no.	Sunscreen	Spreadability(%)
1.	F1	98±0.9
2.	F2	98±0.7
3.	F3	96±0.8

➤ *Viscosity*

It should be measured in a viscometer at 10 rpm. Using a 1/10 dilution of the cream in distilled water.^[50]

Table 4: Determination of Viscosity

Sr.no.	Sunscreen	Viscosity (cps)
1.	F1	181.0
2.	F2	178.0
3.	F3	180.5

➤ *Sun Protection Factor (SPF)*

The sun protection factor of a sunscreen is determined by a highly regulated clinical test using lamps that stimulate solar radiation on human volunteers. It measures the time taken for a minimal erythema to appear when sunscreen is applied compared to the minimal erythmal dose (MED) without sunscreen.

$$\text{SPF} = \frac{\text{MED with sunscreen}}{\text{MED without sunscreen}}$$

- SPF 15 protects against 93% of UVB rays.
- SPF 30 protects against 97% of UVB rays.
- SPF 50 protects against 98% of UVB rays.
- SPF 100 protects against 100% of UVB rays.

So, this formulation of sunscreen gives about SPF 30 that means it gives 97% protection form UVB rays.^[51]



Fig 8: Determination of SPF

Odour :- The smell of formulation was checked by applying preparation on hand and feel the fragrance.^[52]

VI. DISCUSSION

The Most apparent acute benefit of currently available sunscreen is the prevention of sunburn from UVR exposure. This effect has been suggested to be both a benefit and a potential concern. The obvious benefit is the prevention of sun burn that may reduce the risk of non-melanoma and perhaps melanoma skin cancers because severity and frequency of sun burn. The study attempted to develop sunscreen cream using zinc oxide and examined their efficacy for preventing sun burn. The purposed UV spectrophotometric method is simple, rapid uses low-cost reagent and can be used for determination of SPF values in many cosmetic formulation. It can perform both during production process, on final product.

The result showed strong-to-moderate absorption of UV radiation along the whole range and this ability may be due to the presence of zinc oxide.

VII. CONCLUSION

The study attempted to develop sunscreen using zinc oxide and examined their efficacy for preventing sunburn. One might say that the current study will hopefully result in better sunburn treatments. Sunburns are caused by exposure to UV light. By altering the composition, the formulations F1, F2, and F3 were created, and their SPF and physical-chemical characteristics were assessed.

The Study showed that Formulation was found to be more stable with high SPF value, proving a better sunscreen. The use of sunscreen is an important component to sun protection. Regular and appropriate use is associate with a decreased risk of various skin complication and cancers as result of radiation exposure. Thus it can be concluded that there is great market potential for sunscreen chemicals either synthetic or natural or in combination due to awareness of protection from hazardous UVA as well as UVB rays.

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