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PHARMACEUTICAL APPLICATIONS OF PLANT-BASED DERIVATIVES IN SUNSCREEN: A SUSTAINABLE APPROACH TO SKIN PROTECTION

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ABSTRACT
The Sun, while essential for life, can cause significant harm through prolonged exposure, particularly due to UV radiation. This can lead to various skin problems, including accelerated aging, hyperpigmentation, loss of elasticity, and even skin cancer. This paper provides an overview of different types of sunscreens, their history and classifications as per their mechanism of action.
Protecting the skin from sun damage is vital, and sunscreen is one of the most effective prevention methods. With the growing influence of social media highlighting its importance, most people now recognize the need for daily sunscreen use. Available worldwide, sunscreens offer a wide variety of formulations to suit individual needs. The following section will explore potential phytoconstituents that can be incorporated into sunscreen products as an alternative to synthetic filters.
KEYWORDS: *Sunscreen, UV A, UV B, UV C, skin cancer, Sun Protection Factor, Physical sunscreen, Chemical sunscreen, Systemic sunscreen, Sustainable, Plant-based derivatives, Ozone layer, Lignin, Rosmarinic Acid, Eucheuma cottonii, Hylocereus polyrhizus, L-Ergothioneine, Moringa oleifera, Padina australis, Pterocarpus marsupium, Rutin succinate, Salicornia europaea, Sargassum glaucescens, Scytonemin, Sorbates, Strychnos af. darienensis, Fucoxanthin*

1) INTRODUCTION
Sunscreens, also known as sunblocks or sun protectors, are designed to shield our skin from UV radiation. There are three main types: ultraviolet A (UVA) at 350 nm, ultraviolet B (UVB) at 300 nm, and ultraviolet C (UVC) at 250 nm. [25] Exposure to these rays can cause skin burns, premature aging, discoloration, and even tumor formation over time.

2) HISTORY
The first sunscreen was formulated by 2 German scientists Hausser and Vahel in 1928 and contained the main active ingredients such as benzyl salicylate and benzyl cinnamate. [16] In later years sunscreen was formulated by an Australian chemist H.A. Milton Blake (1932) with the UV filters as "salol" (phenyl salicylate) having a concentration of 10%. Its UV protection capacity was later tested by the University of Adelaide and was manufactured and sold commercially by Blake company - Hamilton Laboratories.

3) SUN PROTECTION FACTOR
Sunscreens feature a sun protection factor (SPF) rating, which indicates their effectiveness against sunburn. For instance, SPF 15 means only 1/15th of solar radiation reaches the skin. A minimum SPF of 30 is recommended for effective protection, and sunscreen should be applied at a rate of 2 mg per square centimeter of skin.

While SPF indicates protection against UVB rays, it doesn't guarantee the same for UVA rays. Therefore, choose a broad-spectrum sunscreen to ensure adequate protection against both types of UV radiation.

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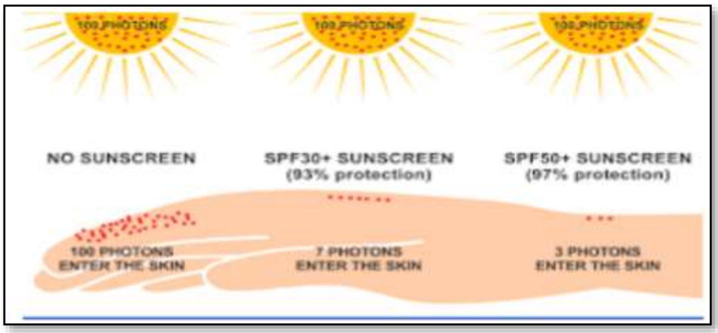

4) CLASSIFICATION OF SUNSCREEN

Based on the mechanism of action, sunscreens are broadly classified into three categories namely; [18]

4.1 Physical Sunscreens -They scatter or reflect UV radiation owing to the large particle size [11] Some inorganic filters are as follows:

i. ZnO
It is one of the most used broad-spectrum metal oxide filters due to its ability to absorb and then reflect the UVB and UVA rays [16] [17].

ii. TiO_2
It is also a broad-spectrum filter that protects from UVA and UVB radiations [3]. It exists in either amorphous or crystalline form. The crystalline form can be of three different types: anatase, rutile, and brookite, which have different permeability [7].

iii. Calamine
iv. Kaolin
v. Talc

4.2 Chemical sunscreens (Containing Organic Filters)

They can absorb UV radiation however, it can, in turn, lead to the generation of free radicals, and therefore there is concern regarding the utilization of synthetic chemical filters. [11] [6]

These compounds can be more precisely categorized by their chemical structure.

i. 4-aminobenzoates
ii. Cinnamates
iii. Salicylate esters
iv. Anthranilates
v. Dibenzoylmethanes

4.3. Systemic Sunscreen -These sunscreens accumulate in the skin after getting absorbed and thus offer protection against UV rays. They are not meant for daily use and therefore do not predominate in the market. These include;

i. Ascorbic acid
ii. Tocopherol
iii. Aspirin
iv. Selenium
v. Retinol
vi. Corticosteroids

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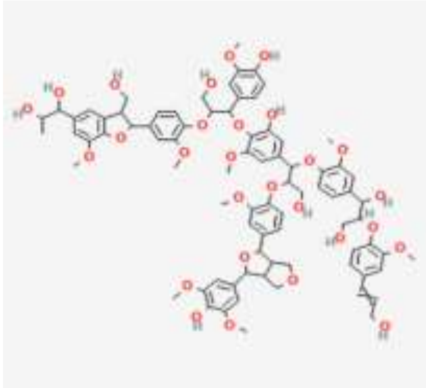
5) SUSTAINABLE APPROACH:

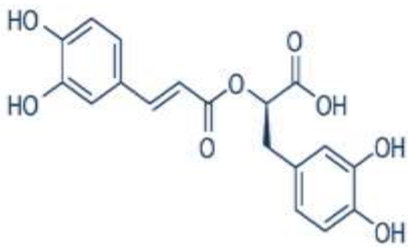
5.1) Lignin



Lignin is a promising alternative UV filter which can also be an effective tint. While acetylation brightens its pigment, it can lower SPF values. Many formulations use iron oxides for UV protection, but technical lignins like kraft and cat lignin possess structures that provide better UVA and UVB protection. [18]

Formulations often include antioxidants to combat free radical damage, which causes aging and inflammation. Lignin's phenolic group stabilizes antioxidant activity, while ortho substitutions, like methoxy groups, further enhance this effect. [17]

5.2) Rosmarinic Acid



It effectively slows down vitamin depletion which in turn decreases oxidation. The phenolic acid contained within it mitigates cellular damage resulting from UV B-induced oxidation by elevating glutathione levels and reducing lipid peroxidation in HepG2 liver cells. Furthermore, it exhibits antioxidant activity that is 3.2 times greater than that of ascorbic acid. [8] Rosmarinic acid alone offers limited UV protection, but when combined with inorganic filters like titanium oxide and zinc oxide, its effectiveness increases. Additionally, its antioxidant properties help prevent free radical damage to the skin.

5.3) *Eucheuma cottonii*

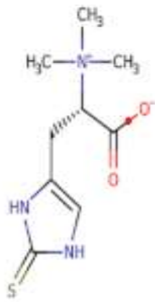
Eucheuma cottonii is a seaweed found in various colors—red, brown, and green—and is commonly farmed in tropical seas. It is a rich source of K-carrageenan, phlorotannins, and flavonoids, demonstrating antioxidant properties that protect against UV-induced free radicals. [2]

5.4) *Hylocereus polyrhizus*

Hylocereus polyrhizus(Red-fleshed dragon fruit) is a vine cactus species. It has purple-red color and high antioxidant content. The peel extract (HPPE) contains bioactive compounds such as ferulic acid, chlorogenic acid, and gallic acid, along with high levels of catechin and vanillin. [23]

High-Performance Liquid Chromatography (HPLC) has identified rutin, which helps inhibit reactive oxygen species (ROS) that can damage cells by stabilizing free radicals.[4] HPPE also contains riboflavin (vitamin B), which aids in recycling glutathione and acts as an important antioxidant, protecting the body from free radical damage and promoting skin cell turnover. [4]

5.5) L-Ergothioneine



Ergothioneine is mainly found in Mushroom varieties. It is observed that photoaged skin can be due to mutations in the mitochondria genome i.e., deletion of large no. of (4977 bp) which is known as "common deletion (CD). When UV rays interact with cells it goes and breaks single and double strands of DNA causing CD, but when tested with EGT there were no CD phenomena seen which helped in concluding that EGT helps in reducing the photo-aging of an individual. [9] Tripeptide glutathione (GSH) which is an abundant intracellular non-protein thiol helps in maintaining redox reactions in cells by interacting with ROS, and RNS. [19] ETG helps in increasing glutathione levels which decrease in the body when exposed to radiation. [2]

5.6) *Moringa Oleifera*

Moringa oleifera, from the *Moringaceae* family is widely known as the "drumstick tree." Studies have proven that *M. oleifera* have antimicrobial, anti-inflammatory, antioxidant, antimicrobial, hypoglycemic activities etc. [6]
M. oleifera leaf extracts, characterized by HPLC, contain the following key chemical constituents;

i. Ellagic acid
ii. Chlorogenic acid
iii. Ferulic acid
iv. Rutin
v. Quercetin

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While the leaf extract has primarily been tested in vitro, it appears to possess considerable potential in sunscreen formulations, owing to the variety of beneficial chemical constituents it contains. [6]

5.7) *Padina Australis*

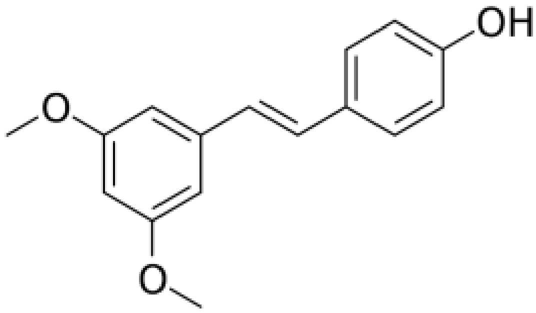
Antioxidants are effective against photolytic damage. *Padina australis*, a brown alga found in Malaysian waters, contains high levels of phenolic compounds and flavonoids, which can be extracted using ethanol or water. Liquid chromatography-mass spectrometry (LCMS) has shown that ethanol extracts have significantly more concentration of these compounds. [4]

Phenolic compounds can act as endogenous antioxidants by donating electrons. Additionally, the carotenoid fucoxanthin may provide UV protection, improving cell survival and reducing intracellular reactive oxygen species (ROS). [4] Thus, it is a promising source of antioxidants and UV protectants.

5.8) *Pterocarpus Marsupium*

Pterostilbene is a potent stilbenoid classified within the phytoalexin group, and it is extracted from *Pterocarpus marsupium*. This compound plays a crucial role in the plant's defense mechanisms. [6]

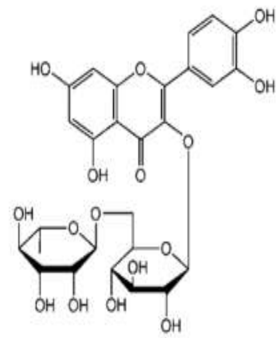
It shows its antioxidant activity by reductions in ROS (reactive oxygen species) production which is triggered by hydrogen peroxide as well as UV A radiation. It exhibits free radical scavenging activity that is dose-dependent; specifically, a higher dose in the formulation leads to increased activity. Additionally, it supports the DNA repair mechanism by activating the Nrf2/ARE pathway through PI3K-dependent mechanisms. [5]



5.9) Rutin succinate

Rutin succinate (MS) protects against UV damage by scavenging free radicals linked to photoaging and carcinogenesis. Combining sunscreen filters with MS increases SPF values and helps prevent peroxide radical formation, which can degrade these filters, enhancing their stability. [9]

The sunscreen containing Rutin achieved the highest SPF, indicating that Rutin effectively enhances filter stability and extends the product's shelf life. [9]



5.10) *Salicornia europaea*

Salicornia europaea or Glasswort is a halophytic plant. It possesses diverse biological properties like anti-inflammatory antioxidant, antihyperlipidemic, etc. [10] The following results were obtained after conducting tests to study its protective effects;

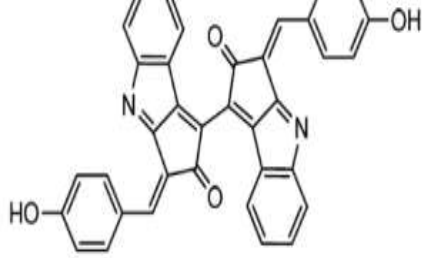
1. Applying water-soluble Salicornia extract improves skin texture.
2. UVB radiation disrupts the structure of keratinocytes, but the extract helps prevent these changes.
3. It corrects the misorientation of mitotic division in keratinocytes, balancing asymmetric and symmetric divisions.
4. Treatment with the extract enhances skin stratification after UVB exposure, though its exact mechanism of action remains to be fully explored. [10]

5.11) *Sargassum Glaucescens*

Sargassum glaucescens is a marine brown alga that belongs to the family *Sargassaceae*. [11]

Marine algae are rich in metabolites which could be used for reducing oxidative stress and preventing skin aging. These metabolites are mycosporine-like amino acids (MAAs), sulphated polysaccharides, polysaccharides, and polyphenols. [26]

Sargassum is also rich in omega (ω)-3 fatty acids involving eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). [20] These compounds help in sun protection by reducing ROS. [11]



5.12) Scytonemin

Scytonema is a cyanobacterial, lipid-soluble metabolite that is found in an extracellular sheath of the organism. [24] This hydrophobic pigment consists of a dimeric molecule with phenol and indole subunits, which protect cellular structures by reducing reactive oxygen species (ROS) and minimizing DNA lesions from oxidative damage. This protective role is essential for cellular integrity and health, and the molecule also has anti-inflammatory and anti-proliferative properties. [24]

5.13) Sorbates

Sorbates are preservatives that prevent microbial contamination without changing color, odor, taste, or flavor, with potassium sorbate being the most common alternative to parabens.

UV radiation can lead to sunlight-induced melanoma, resulting in cyclobutane pyrimidine dimers (CPD) that may cause carcinogenic mutations. This risk can be reduced using melanin-based triple state quenchers (TSQ), such as sorbates TSQ, which absorb UV energy and dissipate it as heat, thereby enhancing UV protection. [12]

5.14) *Strychnos Af. Darienensis*

Strychnos af. darienensis, found in Peru, is part of a genus known for its toxic compounds but also contains valuable secondary metabolites like indole alkaloids, phenolic acids, lignans, and flavonoids with potential medicinal benefits. [16]

Flavonoids, such as luteolin and strychnobiflavone, have anti-aging effects on skin fibroblasts by reducing ROS production and protecting cells from UV radiation, even reversing UVB-induced damage. [13]

5.15) Fucoxanthin (Innovation by Incorporating Into SLN)

Fucoxanthin is a natural carotenoid obtained from seaweeds. [22] It has a typical dark yellowish or reddish color and contains a plethora of properties including anti-inflammatory, anti-oxidant, radio-protective, etc. [15]
New drug delivery systems (NDDS), such as Nanostructured Lipid Carriers (NLCs) and Solid Lipid Nanoparticles (SLNs) have core sizes of 10 to 1000 nm. [21] SLNs are particularly effective as drug delivery agents for various reasons:

a) High drug-loading capacity
b) Controlled and target-specific release of phytoconstituents which minimizes side effects. [14]
c) stability during storage, resisting physical and chemical stresses without forming toxic byproducts.

6.CONCLUSION

Natural alternatives are becoming increasingly popular, resulting in a rise in commercial sunscreens containing herbal extracts. Many herbs have proven photoprotective properties, with potential for discovering more.

However, developing organic and environmentally friendly sunscreens faces challenges. Evaluating the effectiveness of herbal extracts through Sun Protection Factor (SPF) can be complex, requiring extensive in vivo and in vitro study data, which is often hard to obtain. To date, no country has officially approved any botanical compound as a UV filter for sunscreen.

Although many herbal candidates may not match the SPF values of synthetic options, their unique properties continue to generate interest in the sunscreen market.

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