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PREVENTIVE ROLE OF SELECTED PLANT EXTRACTS AND PHYTOCOMPOUNDS AGAINST UV INDUCED DAMAGES–INSIGHTS FROM VARIOUS EXPERIMENTAL MODELS

JEGATHISWARY GANASAN[1,3], THIRUVENTHAN KARUNAKARAN[3], SIVAKUMAR MOHAN[1], WAN IRYANI WAN ISMAIL[1,2] AND RAMESHKUMAR SANTHANAM[1,2,4]*

[1]Faculty of Science and Marine Environment, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia. [2]Biological Security and Sustainability Research Group, Faculty of Science and Marine Environment, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia. [3]Centre for Drug Research, Universiti Sains Malaysia, 11800 Pulau Pinang, Penang, Malaysia. [4]School of Bio Sciences and Technology, Vellore Institute of Technology, 632014 Vellore, Tamil Nadu, India.

**Corresponding author: ramesh@umt.edu.my, rameshcra@gmail.com*
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Abstract: Plants and their derivatives are increasingly recognised for their potential to mitigate Ultraviolet (UV)-induced damage. Despite this, comprehensive reviews are limited, addressing advancements, contradictions, and research gaps in plant derivatives—including extracts, fractions, and phytocompounds. This review evaluates recent and reliable data on plant-based solutions to prevent or minimise UV-induced damage across various experimental models. A systematic literature search was conducted using PubMed, ScienceDirect, Google Scholar, Wiley, and Springer for studies published from 2010 to 2024. Keywords included "UV radiation", "skin cancer", "photoprotection", "photoaging", "photodamage", "phytochemicals", "sunscreen", and "wrinkling". Studies focusing on plant extracts, fractions, and phytocompounds targeting UV-induced damage were prioritised. UV radiation triggers inflammation, DNA damage, dysregulation of cell signalling pathways, and tumour progression. Phytofractions rich in flavonoids, polyphenols, polysaccharides, and terpenoids counteract these effects. Notably, fruit extracts effectively protect against UV damage by targeting specific biomarkers *in vitro* and *in vivo*. Pre-treatment with fruit extracts before UV exposure offers comparable photoprotective properties to post-exposure treatment. This review provides a comprehensive overview of recent research on plant derivatives in UV protection, offering valuable insights for researchers and industry professionals.

Keywords: UV radiation, photoprotection, phytocompound, plant extract, sustainability.

Introduction

The earth would be uninhabitable without the sun. Plants utilise solar rays for photosynthesis while animals and humans rely on them for various purposes. The sun emits various electromagnetic wavelengths, including Ultraviolet (UV), visible, and infrared light. Among these, UV wavelengths have garnered significant attention compared to other forms of solar radiation (Svobodová & Vostálová, 2010). Heliotherapy or artificial UV rays can effectively treat various skin conditions, including vitiligo, psoriasis, atopic dermatitis, and localised scleroderma. Furthermore, UV radiation, independent of vitamin D production has been shown to alleviate symptoms of multiple sclerosis (Lucas *et al*., 2015).

Despite these benefits, excessive sun exposure poses risks to human health, affecting the immune system, eyes, and skin (Gallay *et al*., 2019). Short-wavelength UV rays, although containing greater energy compared to visible light and infrared radiation are particularly hazardous (Dupont *et al*., 2013). Chronic and acute skin damage, including skin cancer, associated with sun exposure is increasingly recognised (Godic *et al*., 2014; Mohan *et al*., 2024). Malignant melanoma, Basal Cell Carcinoma (BCC), and Squamous

Cell Carcinoma (SCC) are among the most prevalent forms of skin cancer linked to UV radiation exposure (D'Orazio *et al*., 2013; Lee *et al*., 2020). Moreover, alarming global statistics underscore the urgency of addressing UV-induced damage, with 2020 reporting 57,043 melanoma-related deaths and 63,731 fatalities attributed to non-melanoma skin cancer (Sung *et al*., 2021). Excessive sun exposure impacts human health and contributes to environmental pollution and ecosystem damage.

The prevalence of photocarcinogenesis has increased due to limited skin defence capabilities, changing lifestyles, and ozone depletion (Kahremany *et al*., 2022). UV exposure has surged, primarily driven by outdoor recreation and cosmetic tanning desires rather than occupational needs. Despite progress in ozone layer preservation, sufficient ozone-depleting substances persist, leading to annual ozone depletion (World Meteorological Organisation, 2021). This depletion intensifies UV penetration onto earth's surface, exacerbating its detrimental effects on human health. UV radiation, ubiquitous in the environment, contributes to various skin conditions and diseases, including photoaging, inflammation, and skin cancer.

Current sunscreen products are vital in mitigating UV-induced damage and protecting human health (Rabinovich & Kazlouskaya, 2018; Bhattacharjee *et al*., 2021). However, traditional sunscreens often contain chemical filters such as oxybenzone, octinoxate, and homosalate, which can harm marine life and ecosystems, contributing to environmental pollution. Additionally, the efficacy of some sunscreen ingredients, like octocrylene and avobenzone, in blocking harmful UV radiation is debated, raising concerns about their long-term environmental impact and effectiveness in preventing skin damage. Therefore, there is a growing need for innovative, environmental friendly sunscreen formulations that provide effective UV protection while minimising adverse environmental effects (Santhanam *et al*., 2022). Over the past decade, secondary metabolites from plants capable of absorbing UV radiation have garnered increased research interest for their potential to prevent and mitigate UV-induced damage (Petruk *et al*., 2018; Mansuri *et al*., 2021; Verma *et al*., 2023). While numerous reviews have highlighted promising plant derivatives, contemporary review papers addressing advances, contradictions, and research gaps in potential plant derivatives against UV-induced damage remain scarce. Inconsistent outcomes across research studies may stem from variations in experimental models and methodologies, underscoring the need for a further mechanistic understanding of bioactive chemicals' potential to counteract UV damage. Additional reviews are necessary to bridge the gap between laboratory discoveries and practical applications in cosmetics and medications.

Therefore, this review aims to present the most recent and reliable data on plant extracts, fractions, and phytocompounds targeting UV-induced damage across various experimental models. It discusses their modes of action in preventing or treating UV-induced damage. It offers valuable insights for researchers and scientists in discovering and developing novel plant derivatives with low-cost, high-efficacy UV prevention, and minimisation activities. Additionally, it provides valuable insights for the pharmaceutical and cosmetics industries by summarising emerging trends and approaches that require further exploration and future clinical trials.

Methodology

A comprehensive and systematic approach was employed to achieve the objectives outlined in this review. We systematically searched English-language sources published between 2010 and 2024 using academic search engines such as Google Scholar, Wiley, and Springer. Keywords related to UV radiation, skin cancer, photoprotection, photoaging, photodamage, phytochemicals, sunscreen, and wrinkling were used to retrieve relevant articles, reviews, reports, and books. Initially, 400 articles were collected during the search process. The selection criteria

prioritised studies focusing on plant extracts, fractions, and phytocompounds targeting UV-induced damages in various experimental models, including studies conducted in cell cultures, animal models, and human clinical trials. Note that exclusion criteria included non-English publications, studies unrelated to UV-induced damage, and those lacking sufficient data on the phytochemical composition or bioactivity of the plant derivatives. After applying the inclusion and exclusion criteria, 181 articles remained and were further studied. Consequently, these articles were categorised into three subcategories: Phytofractions (21 articles), phytocompounds (38 articles), and fruit extracts (20 articles), all specifically examined for their effects against UV-induced damage. Through a rigorous screening process, the most recent and reliable data were selected for inclusion, ensuring a comprehensive analysis of this field's current state of research.

Results and Discussion

Ultraviolet Radiation and Biological Damage

According to electrophysical parameters, UV energy is classified as UVA, UVB, and UVC, with UVC having the shortest wavelength (100 nm to 280 nm) and the most energy, UVA having the longest wavelength (315 nm to 400 nm) and the least energy, UVB falling in the middle with a wavelength of 280 nm to 315 nm. The intricate interplay of UV radiation with molecules, cells, and tissues underscores its wide-ranging impact (Pfeifer & Besaratinia, 2012; D'Orazio *et al*., 2013; U.S. Food and Drug Administration, 2020). The quantity of UV radiation at the ground level and the proportion of UVA to UVB are influenced by several factors, including cloud cover, latitude, season, and time of day (Schuch *et al*., 2013). Nevertheless, the sun primarily emits UVA, with only about 5% of terrestrial UVB rays (Pfeifer & Besaratinia, 2012; Mohiuddin, 2019). UVB radiation is absorbed by the outer layer of the skin, known as the epidermis, and blocked by the stratum corneum by up to 70%. In contrast, UVA radiation passes through the dermo-epidermal junction and extends deeper into the papillary dermis (Ryšavá *et al*., 2021), as illustrated in Figure 1.

Mechanisms of Ultraviolet Radiation A-induced Damage

UV rays cause a wide range of harmful mechanisms. Ultraviolet A (UVA) is divided into two subtypes, UVA1 and UVA2, distinguished by wavelengths ranging from 340 nm to 400 nm and 315 nm to 340 nm, respectively. Although UVA penetration is considerable, its immediate damage has traditionally been regarded as less visible than that caused by UVB. Exposure

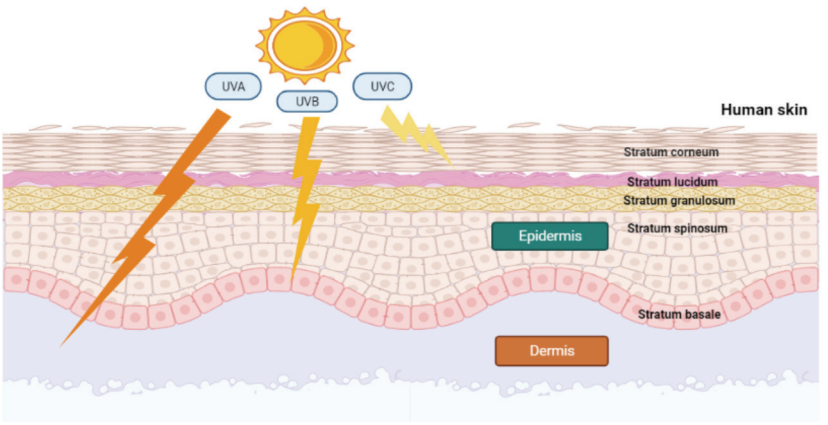

Figure 1: Solar radiation absorption by human skin depends on wavelength. UVA wavelengths reach the dermis layer while UVB reaches the epidermis layer, including basal cells. Meanwhile, UVC is absorbed by the stratum corneum, the epidermis's outermost layer (created using Biorender software)

to high levels of UVA causes a quick and short-lived tan primarily through the photo-oxidation of pre-existing melanin rather than by producing new pigments. However, this increased pigmentation provides only marginal photoprotection benefits (O'Leary *et al*., 2014). Given that UVA irradiation frequently comes from tanning beds, this type of tanning is ineffective at providing adequate defence against sunlight (Dupont *et al*., 2013).

Current understanding shows that previously thought to be relatively benign, UVA primarily catalyses the formation of Reactive Nitrogen Species (RNS) and Reactive Oxygen Species (ROS) through interactions with intrinsic chromophores or photosensitisers. Notably, these interactions involve various compounds such as Nicotinamide Adenine Dinucleotide (NADH), Nicotinamide Adenine Dinucleotide Phosphate (NADPH), quinones, nucleic acid bases, heme, aromatic amino acids, flavins, eumelanin, porphyrins, 7-dehydrocholesterol, carotenoids, and urocanic acid (Baeyens *et al*., 2023; Bastos *et al*., 2023).

The resultant ROS include Hydrogen Peroxide (H_2O_2), Singlet Oxygen ($^1O_2$), Hydroxyl Radical ($OH^{\cdot}$), Ozone (O_3), and Superoxide Radical ($O_2^{\cdot -}$), whereas RNS encompass Nitrogen Dioxide (NO_2), Peroxynitrite Anion ($OONO^-$), and Nitrogen Oxide (NO). These species can oxidise biological components, producing oxidised products such as protein carbonyls and lipid hydroperoxides, which have been linked to skin problems. Cysteine thiols are similarly targeted by ROS and RNS, leading to oxidative changes and the generation of Reactive Sulfur Species (RSS). Natural antioxidants in the body, particularly ketones often counteract the damage caused by free radicals. These antioxidants mitigate damage by donating electrons to unstable molecules via intramolecular hydrogen bonding. However, excessive free radical production can lead to cellular oxidative stress, potentially causing damage to enzymes, nucleic acids, proteins, and lipids (Petruk *et al*., 2018).

ROS and RNS cause a range of Deoxyribonucleic Acid (DNA) lesions, including cross-linking, single-strand breaks, and mismatched DNA bases. Among these, the guanine base has the lowest ionisation potential, making it especially prone to oxidation. As a result, the primary oxidative product, 8-oxo-7,8-dihydroguanine (8-oxoG), emerges as a critical outcome (Svobodová *et al*., 2012). This oxidative injury, catalysed by UVA, indirectly increases the risk of skin malignancies through the progression of DNA lesions, which are key initiators of photocarcinogenesis. Notably, UVA's carcinogenic potency is less than UVB's, making the dose-response relationship difficult to establish (Pfeifer & Besaratinia, 2012). The core concept is that UV causes oxidative injuries and prolonged UV exposure and unrepaired lesions lead to oxidative stress, resulting in oxidative damage to the human body. This oxidative damage significantly contributes to accelerated skin ageing, manifesting as wrinkles, fine lines, loss of skin elasticity, and hyperpigmentation. This underscores the importance of protecting the skin from UVA exposure (Mansuri *et al*., 2021).

Furthermore, UVA demonstrates immunosuppressive properties and may promote skin tumour development in the spectral range of 360 nm to 380 nm (Dupont *et al*., 2013). Research highlighting the human action spectrum's maxima at both UVA (370 nm) and UVB (300 nm) wavelengths has shown that sunlight at 370 nm delivers 100 times more UV energy than sunlight at 300 nm, underscoring the potency of long-wave UVA in causing immunosuppression after consistent sun exposure (Bens, 2014). This is supported by UVA being responsible for approximately 75% of solar-induced immunosuppression. Additionally, UVA impairs cellular energy and adenosine triphosphate normalisation, with nicotinamide emerging as a UVA immunosuppressive inhibitor. By initiating the alternative complement pathway, UVA further modulates the development of abnormal memory T-cells, adding to its complex immunological impacts (Halliday *et al*., 2011).

In summary, UVA's effects extend beyond DNA damage to include immune suppression, which hampers the body's ability to counteract radiation-induced damage and amplifies the complexity of its role in UV-related skin pathologies.

UVA radiation is associated with various skin disorders and diseases due to its deep penetration and ability to induce oxidative stress. Other than that, it plays a significant role in their exacerbation. Chronic UVA exposure accelerates photoaging, leading to wrinkles, skin elasticity loss, and hyperpigmentation due to collagen breakdown (Pfeifer *et al*., 2020). UVA also contributes to skin cancers, including melanoma, BCC, and SCC, through oxidative DNA damage and immune system impairment. Photosensitivity disorders triggered by UVA include Polymorphous Light Eruption (PMLE) and Chronic Actinic Dermatitis (CAD), which present as itchy red papules and eczematous lesions, respectively (Merin *et al*., 2022). Solar urticaria, a rare condition causing hives upon UVA exposure, results from an allergic-type skin reaction (Harris *et al*., 2023). Additionally, melasma, characterised by dark facial patches, and lupus erythematosus, an autoimmune disease are exacerbated by UVA, highlighting the radiation's role in both skin and systemic disorders (Bernerd *et al*., 2022).

Mechanisms of Ultraviolet Radiation B-induced Damage

UVB rays are a form of the electromagnetic UV spectrum partially inhibited by ozone. In prior work, UVB was discovered to react with the Aryl hydrocarbon Receptor (AhR), resulting in the generation of a tryptophan-derived photoproduct (FICZ-6-formylindolo[3,2-b] carbazole) (Abel & Haarmann-Stemmann, 2010). AhR is a transcription factor for ligands present in numerous skin cells such as melanocytes, fibroblasts, keratinocytes, and Langerhans cells (Dupont *et al*., 2013). A cytosolic multiprotein complex binds inactivated AhR. When interacting, however, the complex detaches and AhR is transferred to the nucleus, where the expression of genes with the Xenobiotic Responsive Element (XRE) is triggered. These genes affect the proteins that cause oxidation, inflammation, pigmentation, immunosuppression, premature ageing, and skin cancer (Abel & Haarmann-Stemmann, 2010). In this context, the free amino acid tryptophan may be used as a chromophore to absorb UVB radiation in the skin cell cytosol. Therefore, AhR contributes to UVB-induced tanning and skin inflammation (Esser *et al*., 2013; Vogeley *et al*., 2019).

Moreover, UVB with high energy passes through the epidermal layer and reaches the basal cells in the upper dermal, where chromophores interact, resulting in ROS production, activating growth factors of the cell surface, NADPH oxidase, and cytokine receptors (Dupont *et al*., 2013; Cavinato & Jansen-Dürr, 2017; Petruk *et al*., 2018). This results in signal transduction within the cell via tyrosine phosphorylation and the corresponding adaptor proteins on receptors. Nuclear factor-kappa B (NF-κB) as well as activator protein 1 (AP-1) are activated, both of which are involved in the gene transcription of proinflammatory cytokines and matrix-degrading enzymes, respectively (Komatsu *et al*., 2017; Petruk *et al*., 2018). Therefore, various signalling pathways are triggered, resulting in lower production of collagen and upregulation of Matrix-Metalloproteases (MMPs), causing connective tissue degradation, cell build-up, production, and build-up of senescence-associated secretory phenotype components as well as elastic fibre degradation (Cavinato *et al*., 2016; Cavinato & Jansen-Dürr, 2017). These events cause the morphological development of skin wrinkles with epidermal thickening, followed by dryness, hyperpigmentation, and complexion loss, which are the primary features of photo-aged skin (Cavinato *et al*., 2017; Komatsu *et al*., 2017).

Unlike UVA, UVB is absorbed directly into DNA, notably through the heterocyclic aromatic bases, and absorbs chromophores with a maximum absorption wavelength of 260 nm to 280 nm. UVB exposure induces two type of

mutagenic lesions: Pyrimidine-(6–4)-pyrimidone photoproducts (6-4PPs) and Cyclobutane Pyrimidine Dimers (CPDs), which occur between adjacent pyrimidine bases on the same DNA strand (Svobodová *et al*., 2012). CPDs form three times as frequently as 6-4PPs. When exposed to UVB and UVA rays, 6-4PPs are transformed into Dewar valence isomers, which are only slightly photoactive but can be reversed following exposure to short UV wavelengths (Farivar, 2019). The Nucleotide Excision Repair (NER) mechanism is primarily responsible for the repair of 6-4PPs and CPDs. As depicted in Figure 2, NER failure or overburdening of the reparability is responsible for the build-up of skin cell mutations and represents a major phase in the initiation of photocarcinogenesis (Svobodová *et al*., 2012). In detail, Figure 2 elucidates that UVB induces DNA damage by increasing ROS formation, which then disrupts DNA strand bonds. Mismatching of DNA bases will form 6-4PPs or CPDs, leading to DNA lesions. Consequently, unrepaired DNA lesions or prolonged UVB exposure will result in SCC or BCC.

In general, Base Excision Repair (BER) and NER mechanisms will fix dimerised base-containing DNA lesions like UV photoproducts. Cockayne syndrome and Xeroderma Pigmentosum (XP) are two rare human genetic illnesses characterised by a lack of NER. UV-hypersensitive cells are determined in the cells of those who are afflicted. XP patients had an increased risk of all types of skin cancer, indicating that pyrimidine dimers promote both melanoma and non-melanoma cancers (Pfeifer & Besaratinia, 2012). Aside from the harm of UVB irradiation, delayed tanning is a skin protective strategy against UVB exposure involving melanin formation and primarily intends to mitigate sunburn (Mohiuddin, 2019). Regrettably, it appears ineffective in preventing photocarcinogenesis (Miyamura *et al*., 2011).

Mechanisms of Ultraviolet Radiation C-induced Damage

UVC, the high-energy rays are absorbed by stratospheric oxygen, which is then degraded and recombined to generate Ozone (O_3). The resulting O_3 molecules can operate as a screen, absorbing most of the sun's UVB photons (Pfeifer & Besaratinia, 2012). Concerns have been raised since the 1970s regarding stratospheric ozone layer depletion as a cause of increased UV exposure. In that era, some articles stated that human activities such as chlorofluorocarbons could affect ozone layers by releasing inert chemicals into the atmosphere (Dupont *et al*., 2013). The ozone layer continues to degrade. However, the Antarctic ozone hole, which recently set a new record in 2020, closed in late December following the rapid emergence from mid-August due to the natural climate (World Meteorological Organisation, 2021).

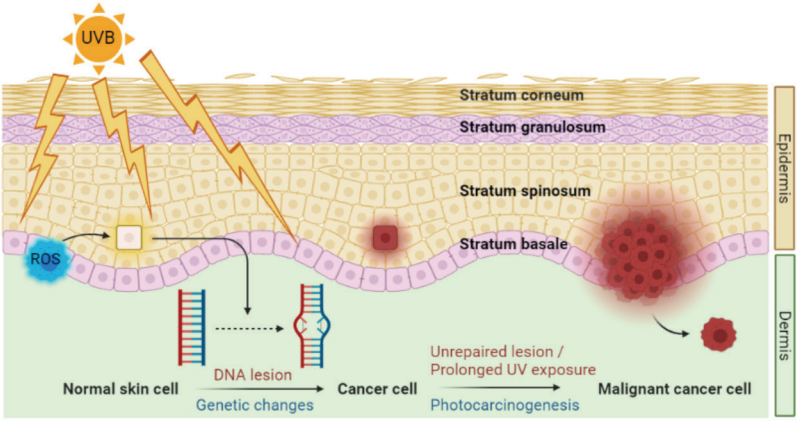

Figure 2: Initiation of UVB-induced photocarcinogenesis due to unrepaired DNA lesions and prolonged UV exposure (created using Biorender software)

The closure of the ozone hole is a positive development, yet, as indicated in the previous decade, another menace to the ozone layer, in the manner of climate change and greenhouse gases, lies in the future (Baldwin & Lenton, 2020; Aslam *et al*., 2021). Dr. Oksana Tarasova, who claimed that even after healing the ozone hole, there are still sufficient ozone-depleting chemicals in the atmosphere to induce yearly ozone depletion has also backed up the prior statement (World Meteorological Organisation, 2021; Tarasova *et al*., 2023). Therefore, it is obvious that ozone depletion leads to increased UV penetration on the earth's surfaces, causing more severe damage to human health. This underscores the need for continued research and vigilance in monitoring the ozone layer, as the ongoing issue and the importance of staying informed cannot be overstated.

Note that ozone effectively blocks UVC. However, human exposure is still possible through artificial sources like sunlamps and lasers. In laboratory studies, it is absorbed by the stratum corneum (Warren & Casey, 2019). Germicidal lamps emitting UVC at 254 nm effectively sterilise unicellular organisms (Yamano *et al*., 2020). The recent surge in COVID-19 cases has led to a growing consideration of UVC lamps for disinfection purposes in our society. However, this increased use poses a potential danger unless strict guidelines are followed (U.S. Food and Drug Administration, 2021). UVC exposure can lead to severe skin burns, erythema, and eye damage, such as photokeratitis (Yamano *et al*., 2020). Due to its short penetration depth, UVC radiation carries a low risk of photocarcinogenesis, cataracts, or permanent vision loss (U.S. Food and Drug Administration, 2020). The most serious impacts of UVC include skin carcinogenicity in animal models and humans due to genotoxicity (Sliney, 2013). UVC bands correspond to the protein, RNA, and DNA absorption spectrums and can cause DNA damage via 6-4PPs and CPDs, leading to indirect or direct DNA strand breakage, mutations, and neoplastic transformation as previously stated (Pfeifer & Besaratinia, 2012; Cortat *et al*., 2013; Widel *et al*., 2014; Schuch *et al*., 2017).

Potential Natural Extracts, Fractions, and Phytocompounds Against UV-induced Damage

Given the rising prevalence of skin cancer and the difficulties of treating metastatic cancer, new preventive and treatment interventions for skin cancer and other UV-induced damages are required. Synthetic active chemical compounds such as benzophenone and Para-aminobenzoic Acid (PABA) derivatives are now utilised in sunscreens while imiquimod and 5-fluorouracil are used topically to treat skin cancer (Bahner & Bordeaux, 2013; Bhattacharjee *et al*., 2021; Nahm *et al*., 2021). Many synthetic sunscreen compounds such as oxybenzone, nanoparticles such as Zinc Oxide (ZnO), Titanium Dioxide (TiO_2), Cerium Oxide (CeO_2), amino benzoic, and padimate O have adverse effects. It includes contact allergies, organ toxicity, endocrine disruption, photoallergies, reproductive toxicity, hormonal disruption, skin irritations, and even cancer (Shusterove & Romero, 2020). Furthermore, recent data shows that a male melanoma patient treated with a combination of 5-fluorouracil, imiquimod, and tretinoin had cutaneous adverse effects, including mild oozing, crowning, erythema, and burning in treatment regions (Nahm *et al*., 2021).

Skin cancer management and treatment typically involve a combination of surgical, topical, and systemic therapies. Surgical options include excision, Mohs surgery, and cryotherapy, which are highly effective for localised skin cancers. Topical treatments such as imiquimod and 5-fluorouracil are used for superficial BCC and SCC by promoting an immune response or inhibiting DNA synthesis in cancer cells (National Cancer Institute (US), 2024). Photodynamic Therapy (PDT) is another topical treatment that involves applying a photosensitising agent to the skin, which is then activated by light to destroy cancer cells. For advanced or metastatic skin cancer, systemic treatments like targeted therapy and immunotherapy have shown significant promise.

Targeted therapies such as V-Raf Murine Sarcoma Viral Oncogene Homolog B (BRAF) and Mitogen-Activated Extracellular Signal-Regulated Kinase (MEK) inhibitors are used for melanoma with specific genetic mutations. Immunotherapy, including checkpoint inhibitors like pembrolizumab and nivolumab helps to boost the body's immune system to attack cancer cells. These treatments have revolutionised the management of advanced melanoma, improving survival rates significantly (Gruber & Zito, 2023).

Plant-based products, in contrast, have fewer negative effects on the skin than synthetic products since they are non-irritants and non-toxic (Bhattacharjee *et al*., 2021). Therefore, the new trend towards using herbal products is growing rapidly, beyond providing ideal solar protection against dangerous UV irradiation (Rabinovich & Kazlouskaya, 2018). Plants are inevitably subjected to UV radiation and adapt to the changing environmental surroundings (Takshak & Agrawal, 2019). These adaptations emerge as altered physiological aspects, plant morphology, and biochemical and genetic modifications that allow promising chemicals to be synthesised as a protective mechanism (Cheynier *et al*., 2013; Kapoor *et al*., 2020).

These phytoconstituents with antioxidant and anti-cancer properties act as UV ray adsorbents (Verma *et al*., 2023). Hence, plant extracts, phytofractions, and natural compounds, including polyphenols, peptides, and polysaccharides are being explored to produce plant-based UV prevention and minimisation agents using various experimental models. Hence, common and extensively studied natural compounds that play a medicinal role in UV-induced damage have been selected to be discussed in this review. These natural compounds were chosen based on the following criteria: Extensive research and scientific evidence supporting their efficacy and safety; strong antioxidant and photoprotective properties; well-elucidated mechanisms of action against UV-induced damage; and demonstrated efficacy *in vitro* and *in vivo* models.

Flavonoids

Flavonoids' structure and range allow them to be separated into six subclasses: Anthocyanins, isoflavones, flavan-3-ols, flavanones, flavonols, and flavones (Hui *et al*., 2013). Various flavonoids have been tested to find their medicinal roles against UV irradiation such as genistein, delphinidin, malvidin, cyanidin, baicalin, juglanin, and fisetin. For instance, in hairless mouse skin, cyanidin-3-glucoside (C3G) at concentrations of 250 μM and 500 μM reduced UVB-mediated oxidative damage and inflammation through modulating the MAP kinase and NF-κB signalling pathways (Pratheeshkumar *et al*., 2014). Genistein, a soybean isoflavone has anti-cancer and anti-ageing properties (Cavinato *et al*., 2017). In this study, genistein (10 mg/kg) protects hairless mice from UVB-mediated lipid peroxidation but not catalase inhibition. Genistein helps protect the skin and increases cell proliferation by lowering p53 expression and apoptosis. It also has anti-nitrosative effects and decreases UVB-induced Peroxynitrate Anion ($ONOO^-$) formation (Terra *et al*., 2015).

Delphinidin, an anthocyanidin pigment, lends blue colour to various flowers and fruits and is an antioxidant (Cavinato *et al*., 2017). Pre- and post-irradiation of Human keratinocyte Cell lines (HaCaT) with delphinidin was shown to reverse the detrimental effects of UVB treatment on metabolic activity and cell elastic modulus. The regenerating benefits of delphinidin may be related to its antioxidant and inhibitory effects on MMP activity (Sobiepanek *et al*., 2016). In short, a wide variety of flavonoid compounds have the potential to prevent UV-induced damage due to their antioxidant property. The Structure-Activity Relationships (SARs) of flavonoids are influenced by several key features: Hydroxyl groups on the B-ring enhance antioxidant activity, the C-2-C-3 double bond in flavones and flavonols improves UV absorption and stability, and glycosylation affects solubility and bioavailability, as exemplified by C3G's efficacy in mitigating UV-induced oxidative damage (Panche *et al*., 2016).

Glycosides

Glycosides, including the subclasses of phenolic glycosides, coumarin glycosides, and flavonoid glycosides like hesperidin are widely explored better to understand the protective mechanism of action against UV exposure (Santhanam *et al*., 2018). Previous research has shown pre-treatment of HaCaT cells with salidroside (20 µg/mL or 40 µg/mL), a phenylethanoid glycoside, reduced UVB-mediated cytoplasmic ROS levels, restored nuclear factor erythroid 2-related factor 2 (Nrf2) transcription activity, and boosted gene and protein expression of antioxidants NAD(P)H-quinone oxidoreductase and heme oxygenase 1 (HO-1). The study also found that dosing guinea pigs with 0.1% w/w salidroside reduced epidermal thickening, apoptosis, and sunburn (Yuan *et al*., 2017). Another study found that salidroside administration (1 µM - 10 µM) reduced UVB-mediated expression of senescence-associated proteins p16, p21, and p53 and inhibited cell cycle arrest. Moreover, salidroside protected cells from UVB-induced MMP-1, tumour necrosis factor-alpha (TNF-α), and interleukin 6 (IL-6) production (Mao *et al*., 2015). Overall, this data points to salidroside's potential as a UVB-induced senescence preventive compound.

The latest study investigated the mitigative effect of two novel phenolic glycosides from juvenile watermelon (*Citrullus lanatus*), which are citrulluside T and citrulluside H, on UVB-mediated damage in human dermal fibroblasts (NHDFs) at a dosage of 100 µm. Citrulluside H and T inhibited MMP-3 and MMP-1 expression, which are known to cause wrinkles. Notably, citrulluside H and T suppressed UVB-mediated MAPK/AP-1 and NF-κB activity, as well as inhibited ROS and MMP production (Itoh *et al*., 2021). Taken together, glycosides, particularly phenolic glycosides like salidroside and new compounds like citrulluside H and T have shown promise in protecting the skin from UV damage. They lower ROS levels, boost antioxidant activity, protect the skin, and inhibit inflammatory responses. For glycosides, the SARs involve the sugar moiety and the aglycone structure. Note that the type and position of the sugar group influence solubility and stability while the aglycone's structure determines biological activity (Kytidou *et al*., 2020). These findings highlight the potential of glycosides as natural components for UV damage prevention and skin protection.

Polysaccharides

Researchers developed an anti-UVB cell clone of *Bupleurum scorzonerifolium* with higher polysaccharide levels than normal callus (Li *et al*., 2011). This polysaccharide reduced ROS and lipid peroxidation in HaCaT cells by increasing superoxide dismutase activity, a vital enzyme for maintaining the prooxidant/antioxidant equilibrium and regulating cells and tissues. It also protects against UVB-mediated DNA damage (Dai *et al*., 2011). Besides, innate polysaccharides from wolfberry (*Lycium barbarum*) possess significant antioxidative, anti-inflammatory, anti-cancer as well as anti-ageing effects by increasing endogenous defence mechanisms (Xiao *et al*., 2013; Yang *et al*., 2014; Li *et al*., 2017). Pre-treatment of HaCaT cells with 300 µg/mL *Lycium barbarum* polysaccharides elevated the expression of Nrf-2-dependent Antioxidant Response Element (ARE) target genes and reduced ROS production. Moreover, reductions in p38 MAPK activation, caspase-3 activation, and MMP-9 expression were also observed (Li *et al*., 2017).

Another interesting study found that low-molecular-weight pectin hydrolysates from the orange peel that underwent bio-conversion reduced UVB-induced apoptosis and enhanced cell proliferation in HaCaT cells at a 0.5% w/v concentration (Kwon *et al*., 2016). Expanding on the photoprotective properties of polysaccharides, researchers discovered that *Astragalus membranaceus* Polysaccharide (AP) successfully protects HaCaT cells from UVA-induced photodamage. This is accomplished by lowering UVA-induced intracellular ROS generation, maintaining Mitochondrial Membrane Potential (MMP), and positively modulating ATP concentration (Li *et al*., 2020).

Additionally, *Dendrobium nobile* Lindl. Polysaccharides (DNPs) were studied to investigate the protective effects against UVA-induced photoaging in human foreskin fibroblasts (HFF-1 cells). UVA exposure has been shown to decrease cell viability, elevate ROS and lipid peroxidation levels, and decrease the activity of antioxidant enzymes such as Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GSH-Px). On the other hand, pre-treatment with DNPs at different doses (0.06 mg/ml, 0.18 mg/ml, 0.54 mg/ml) significantly counteracted these UVA-induced effects.

DNPs effectively reduced UVA-induced photoaging by inhibiting the JNK/c-Fos/c-Jun pathway and suppressing MMP-1, MMP-2, MMP-3, MMP-9, and SA-β-Gal expression (Li *et al*., 2022). In addition to its protective effects against UVA radiation, DNPs have also demonstrated photoprotective properties against UVB-induced damage. The study expanded its focus to investigate their ability to reduce UVB-induced damage in HaCaT cells (Long *et al*., 2023). UVB radiation caused a decline in cell viability, with substantial cytotoxicity found at levels more than 30 mJ/cm^2. On the contrary, pre-treatment with DNPs at concentrations less than 800 µg/mL for 24 hours had no cytotoxic effects. They notably treat HaCaT cells with 200 µg/mL DNPs prior to UVB exposure, increasing cell viability significantly. This is accomplished by DNPs scavenging ROS, regulating the MAPK pathway, and preventing apoptosis (Long *et al*., 2023).

Overall, DNPs appear to have photoprotective potential. These findings are consistent with the previous studies, emphasising polysaccharides' capacity to reduce UV-induced damage by increasing cell viability and proliferation. The SARs for polysaccharides include molecular weight and sugar composition. Higher molecular weight polysaccharides such as those from *B. scorzonerifolium* show greater ROS scavenging abilities. The type of sugar units and their linkages impact the polysaccharides' efficacy in modulating oxidative stress and cellular responses, as seen with *L. barbarum* polysaccharides. In conclusion, polysaccharides derived from various botanical sources exhibit significant photoprotective ability against UVA and UVB radiation, making them promising candidates for skincare and anti-ageing therapies. Their ability to reduce ROS, alter signalling pathways, and increase cell viability highlights their importance in protecting the skin from UV-induced damage.

Phenolic Acids

Phenolic acids such as gallic acid, the main compound in plant extracts, including *Galla chinensis* and *Vitis vinifera* seeds are effective against UVB-induced damage in hairless mice, photoaging and oxidative stress in keratinocytes, respectively (Sun *et al*., 2015; Decean *et al*., 2016). Furthermore, Caffeic Acid (CA) decreased skin oedema, epidermal layer thickening, and hyperplasia in Swiss albino mice in both acute (10 days) and chronic (30 weeks) UVB-mediated inflammation and photo carcinogenesis studies. CA also reduced the expression of inflammatory proteins such as IL-6, TNF-α, NF-κB, and cyclooxygenase-2 (COX-2) while increasing peroxisome proliferator-activated receptor gamma (PPARγ) protein expression.

In this investigation, topical CA (1%) was found to be considerably more effective than intraperitoneal administration, 15 mg/kg body weight (Balupillai *et al*., 2015). Caffeic acid's anti-inflammatory and anti-photocarcinogenic actions against long-term UVB exposure revealed that IL-10, nuclear signal transducer and activator of transcription 3 (STAT-3), and Janus kinase 1 (JAK-1) expression were suppressed. The anti-photocarcinogenic effect of 15 mg/kg body weight CA Swiss albino mice is also explained by reduced cyclin-D1 expression and increased thrombospondin 1 (TSP-1) protein expression (Balupillai *et al*., 2016). Other than that, Ferulic Acid (FA) decreased UVA-induced MMP-1 production *via* increasing Glutathione (GSH) levels and catalase mRNA expression in HaCaT cells (Pluemsamran *et al*., 2012).

Similarly, FA suppressed MMP-9 and MMP-2 synthesis in female nude mice exposed to UVB via translational protein phosphorylation. Surprisingly, this study is not due to a decrease in Raptor protein expression, which is essential for mTOR-mediated phosphorylation of 4E-BP1 and p70S6K (Staniforth *et al*., 2012). Notably, reversing UVB-induced inflammatory and apoptotic signalling pathways may explain why SCC was prevented in Swiss albino mice (Ambothi *et al*., 2015). The SARs of phenolic acids are characterised by hydroxyl and carboxyl groups. Note that multiple hydroxyl groups enhance radical scavenging and reduce oxidative stress, as seen with caffeic acid. The carboxyl group in compounds like ferulic acid contributes to metal ion chelation and mitigation of UVB-induced damage. In summary, phenolic acids modulate UV-induced protein expression and consequent pathways to inhibit photodamage.

Terpenoids

Terpenoids, a modified class of terpenes are classified as sesquiterpenes, triterpenes, diterpenes, monoterpenes, and sesterpenes. Most terpenoids are bioactive and used to treat numerous disorders (Perveen, 2018). Lucidone from *Lindera erythrocarpa* protected HaCaT cells from UVA-induced cell death, lipid peroxidation, ROS production, and DNA damage by modulating the antioxidant genes. The effect of lucidone on HO-1, NAD(P)H quinone oxidoreductase 1 (NQO-1), γ-glutamate-cysteine ligase (γ-GCLC) transcriptional activation of Nrf2 is important in this matter.

Accordingly, lucidone protects against UVA by increasing intracellular antioxidant enzyme levels and antioxidant gene expression. Lucidone suppressed Bcl-2-associated X protein (Bax) expression, restored B-cell lymphoma 2 (Bcl-2) levels, and thereby prevented keratinocyte apoptosis (Hseu *et al*., 2015). Linalool, a monoterpene, prevented acute UVB-induced photo carcinogenesis and inflammation in Swiss albino mice via reducing TNF-α, NF-κB, and COX-2 upregulation, as well as modulating apoptotic pathways (Gunaseelan *et al*., 2016; Takshak & Agrawal, 2019). Linalool pre-administration inhibited the expression of proliferative markers, which explains the prevention of dysplasia formation as well as SCC and, as a result, lowered tumour incidence in mice skin (Gunaseelan *et al*., 2016). Terpenoid SARs depend on ring structures and functional groups. The type of ring structure affects stability and activity, with sesquiterpenes like lucidone showing strong antioxidant properties. Functional groups, such as hydroxyl and methoxy, influence the terpenoid's ability to interact with cellular targets and modulate oxidative stress. In brief, terpenoids are promising plant compounds to be employed as a broad-spectrum photoprotective agent as they are effective against UVA and UVB-mediated damages.

Figure 3 summarises the potential natural compounds evaluated in UV-induced damages using various experimental subjects. Keratinocytes, fibroblasts, mice, and guinea pigs are the experimental subjects used by researchers to investigate the role of phytocompounds stated in this review. The keratinocyte cell line is the most common *in vitro* model among researchers used to evaluate potential phytocompounds against UV-induced damage. In contrast, hairless mice are the most common *in vivo* model.

Other than these selected compounds, numerous potential compounds from varying classes are extracted from plant parts' fractions and studied widely against UV rays, as shown in Table 1. The chemical structures of the compounds listed in Table 1 are systematically illustrated and categorised by their respective chemical classes in Figure 4.

Euterpe oleracea Martius

The common name for the tree is *Euterpe oleracea* Martius is açai, which is a South American palm with purple-black berries that are widely consumed due to their antioxidant, antinociceptive, immunomodulatory, and anti-inflammatory properties (Holderness *et al*., 2011; Kang *et al*., 2012; Dias *et al*., 2015;

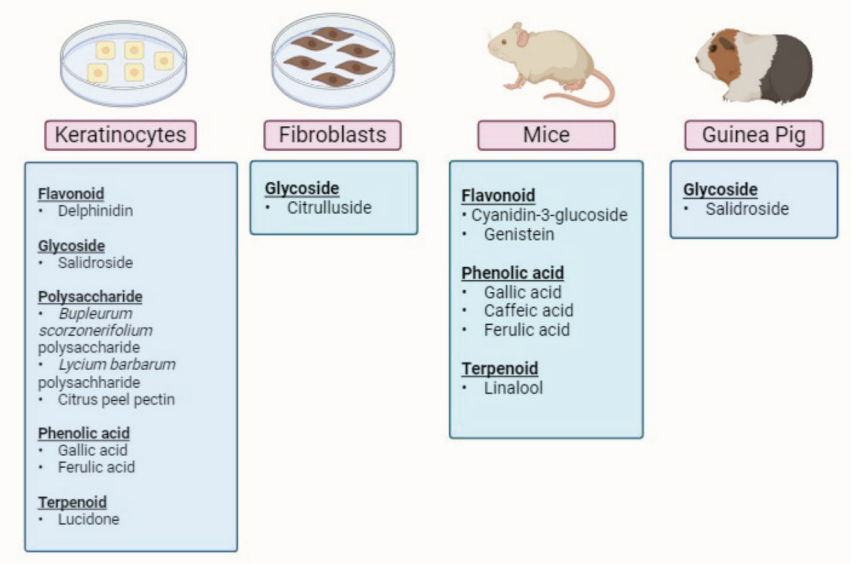

Figure 3: Summary of potential plant compounds investigated in UV-mediated damages using different experimental models (created using Biorender software)

Peixoto *et al*., 2016). This is attributed to açai's rich polyphenol content, especially flavones and anthocyanin (Rufino *et al*., 2011; Dos Santos *et al*., 2015; De Oliveira *et al*., 2021). The protective activities of hydrophilic extracts from açai berries against UVA were examined using immortalised fibroblasts (BALB/3T3 fibroblasts) at a dose of 10 mg/mL (Petruk *et al*., 2017). UVA exposure reduced GSH levels and increased lipid peroxidation and intracellular ROS in fibroblasts. Pre-treatment with açai extract, in contrast, avoided those negative effects as well as p38 phosphorylation, which mediates post-transcriptional processes (Wang *et al*., 2016). This study discovered that malvidin and cyanidin, flavonoids present in methanolic açai extract, significantly inhibited these molecular oxidative stress pathways. Consequently, this study indicated that açai extract can protect cells even after UVA damage, proving that it is not just a sunscreen effect (Petruk *et al*., 2017). Therefore, açai extract can be employed in both sunscreen formulations and pharmaceutical agents.

Emblica officinalis Gaertn

Amino acids, minerals, vitamin C, gallic acid, and a wide variety of flavones, alkaloids, and tannins are abundant in amla (*Emblica officinalis* Gaertn.) (Rojas Camargo *et al*., 2016). An intriguing *in vivo* investigation was conducted on UVB-irradiated HR-1 hairless mice to explore the photoaging effects of amla fruit extract and collagen peptide. In this investigation, 5% w/w Amla Extract (AE) was given orally with and without gelatin hydrolysate, which was an animal collagen peptide. As an outcome, AE and collagen peptide inhibited 8-hydroxy-2'-deoxyguanosine (8-OHdG) development, epidermal hyperplasia, as well as improved skin moisture and wrinkle development (Fujii *et al*., 2013).

In particular, DNA oxidative damage is defined by 8-OHdG, a DNA base-modified byproduct linked to UVB-mediated carcinogenesis (Brand *et al*., 2018). BER repairs these DNA lesions and failure of the mechanism can result in photocarcinogenesis (Zinovkina, 2018). AE was effective in

Table 1: Effects of potential phytofractions comprising bioactive compounds against UV-induced damages

Phytofraction	Compound	Classification	Experimental Model	UV Ray	Effects	Reference
Malvidin enriched fraction	Malvidin	Flavonoid	BALB/3T3 fibroblasts	UVA	• Reduction of ROS production • Counteract lipid peroxidation • Reduction of GSH depletion	(Petruk *et al.*, 2017)
Cyanidin enriched fraction	Cyanidin	Flavonoid	BALB/3T3 fibroblasts	UVA	• Attenuation of p38 and MAPKAPK phosphorylation • Reduction of intracellular ROS production • Counteract lipid peroxidation	(Petruk *et al.*, 2017)
Opuntia ficus-indica L. cladodes small molecular weight fraction (OSMF)	Eucomic acid Piscidic acids	Phenolic acid	Human keratinocyte cell line (HaCaT)	UVA	• Antioxidant activity • Modulation of apoptosis • Reduction of GSH depletion	(Petruk *et al.*, 2017)
Ethyl acetate fraction of *Eugenia hiemalis* leaves	Galloylarbutin	Phenolic glycoside	L929 fibroblasts	UVB	• Inhibition of ROS production • Counteract lipid peroxidation	(Iwanaga *et al.*, 2021)
Ethyl acetate fraction of *Nectandra hihua* leaves	Quercitrin Avicularin Juglalin Afzelin Astragalin	Flavonoid glycoside	L929 fibroblasts	UVB	• Inhibition of ROS production • Counteract lipid peroxidation	(Oliveira *et al.*, 2018)
Ethyl acetate fraction of okra	Rutin	Flavonoid glycoside	Human dermal fibroblasts (HDF)	UVB	• Inhibition of ROS production • Reduction of antioxidant depletion • Inhibition of DNA damage	(Patwardhan & Bhatt, 2016)
Ethyl acetate fraction of *Zanthoxylum rhetsa* bark extract	Hesperidin	Flavonoid	Human dermal fibroblasts (HDF)	UVB	• Inhibition of MMPs expression • Inhibition of pro-inflammatory cytokine production • Inhibition of protease activity	(Santhanam *et al.*, 2018)
Ethyl acetate fraction of *Senegalia polyphylla* leaves	Vitexin Isoquercetin	Flavonoid glycoside	L929 fibroblasts	UVA and UVB	• Reduction of glutathione depletion • Counteract lipid peroxidation • Reduction of plasma membrane disruption	(Dare *et al.*, 2021)

Tocotrienol-rich fraction (TRF) from non-GMO palm fruits	Tocotrienol	Vitamin E	Human keratinocyte cell line (HaCaT) and human subjects	UVB	• Reduction of intracellular ROS production • Reduction of IL-6, IL-8, and COX-2 overexpression • Mitigation of erythema and tanning	(Yap, 2018)
Ethyl acetate fraction from leaves of *Nectandra cuspidate*	Epicatechin Isovitexin Vitexin	Flavonoid Flavonoid glycoside	L929 fibroblasts and sex-matched hairless mice (HRS/J)	UVB	• Reduction of cell death • Reduction of ROS and lipid peroxidation • Reduction of GSH and catalase depletion • Mitigation of MMP-2 and MMP-9 activity and myeloperoxidase • Reduction of epidermal thickening and edema	(dos Anjos Oliveira Ferreira *et al*., 2020)
Aqueous fraction of *Phyllanthus orbicularis* whole plant extract	Quercetin Kaempferol Silymarin Gallic acid	Flavonoid Phenolic acid	Plasmid pCMUT (1762 bp)	UVB	• Inhibition of CPD formation on DNA • Inhibition of oxidised bases	(Tamayoa *et al*., 2018)
Flavonoid-enriched fraction of *Eugenia caryophylata* (clove) buds	Quercetin Kaempferol	Flavonoid	Human dermal fibroblast cells	UVB	• Reduction of endogenous enzymatic antioxidant depletion • Suppression of oxidative DNA damage • Inhibition of Nrf2 and HO-1 overexpression	(Patwardhan & Bhatt, 2015)
Chloroform fraction *Arrabidaea chica* leaves	Scutellarein Apigenin	Flavonoid	L929 fibroblasts	UVA and UVB	• Attenuation of intracellular ROS • Reduction of mitochondrial $O_2^{\bullet-}$ • Inhibition of lipid peroxidation	(Ribeiro *et al*., 2018; Siraichi *et al*., 2013)

Flavonoid-enriched fraction (FEF) of fennel seeds	Rutin	Flavonoid glycoside	Human dermal fibroblasts (HDF)	UVB	• Reduction of endogenous enzymatic antioxidant depletion • Inhibition of intracellular ROS generation • Prevention of apoptotic morphological changes	(Patwardhan & Bhatt, 2019)
Lycium barbarum fruits polysaccharide fraction	-	Polysaccharide	HRS/J female mice	UVA and UVB	• Counteract collagen fragmentation • Counteract epithelium thickening	(Neves *et al.*, 2021)
Anthocyanin-rich blackberry methanol fraction	Cyanidin Delphinidin	Flavonoid	C57Bl/6 mice keratinocytes	UVB	• Upregulation of catalase expression • Inhibition of ROS • Expression of antioxidant enzymes	(Murapa *et al.*, 2012)

Abbreviations: COX-2: Cyclooxygenase-2; CPD: Cyclobutane Pyrimidine Dimers; DNA: Deoxyribonucleic Acid; GSH: Glutathione; HO-1: Heme Oxygenase-1; IL-6: Interleukin 6; IL-8: Interleukin 8; MAPKAPK: Mitogen-Activated Protein Kinase-Activated Protein Kinase; MMPs: Matrix Metalloproteinases; Nrf2: Nuclear Factor Erythroid 2–Related Factor 2; p38: p38 Mitogen-Activated Protein Kinase; ROS: Reactive Oxygen Species; UVA: Ultraviolet A; UVB: Ultraviolet B.

suppressing oxidative damage and tumour progression in this study due to its high phenolic content, which included gallic acid, mucic acid, ellagic acid, and geraniin (Fujii *et al*., 2013). This elucidates the antioxidative effects of AE and collagen peptides on the skin of hairless mice. On the other hand, collagen peptide plays an essential role in preventing skin cells from wrinkling since collagen, particularly type I collagen, regulates skin hydration, maintains the structure of the extracellular matrix (ECM), and maintains elasticity (Reilly & Lozano, 2021). In conclusion, combined AE and collagen peptide administration exhibited significant protective effects against UVB-induced photoaging in hairless mice. This can be attributed to AE's antioxidative properties, particularly its high phenolic content and collagen peptide's role in skin hydration and elasticity.

Garcinia brasiliensis

Bacupari, *Garcinia brasiliensis* is a native species of Brazil's Amazon forest. Note that *Garcinia* fruit has anti-cancer characteristics (Martins *et al*., 2011). Its seed extracts, epicarp, and pericarp exhibit anti-inflammatory, antioxidant, as well as antinociceptive effects (Santa-Cecília *et al*., 2011; Paixão *et al*., 2023). *G. brasiliensis* Epicarp Extract (GbEE) was tested for photo chemopreventive and photoprotective activities *in vitro* (L929 fibroblasts) and *in vivo* (sex-matched hairless mice).

The fibroblasts indicated that the 10% and 20% GbEE solutions have photoprotective effects similar to commercial sunscreen with a Sunscreen Protection Factor (SPF) value of -15. At 10% GbEE formulation, GSH depletion decreased, cytokine release of IL-1β and TNF-α increased, and myeloperoxidase activity increased, which is an inflammatory process biomarker. Notably, pre-treatment with 10% GbEE topical formulation reduced IL-1β and TNF-α overexpression from 463% to 63% and 234% to 64%, respectively (Figueiredo *et al*., 2014). The extracts' chemical content, which is high in polyisoprenylated benzophenone derivatives, bioflavonoids, xanthones, and

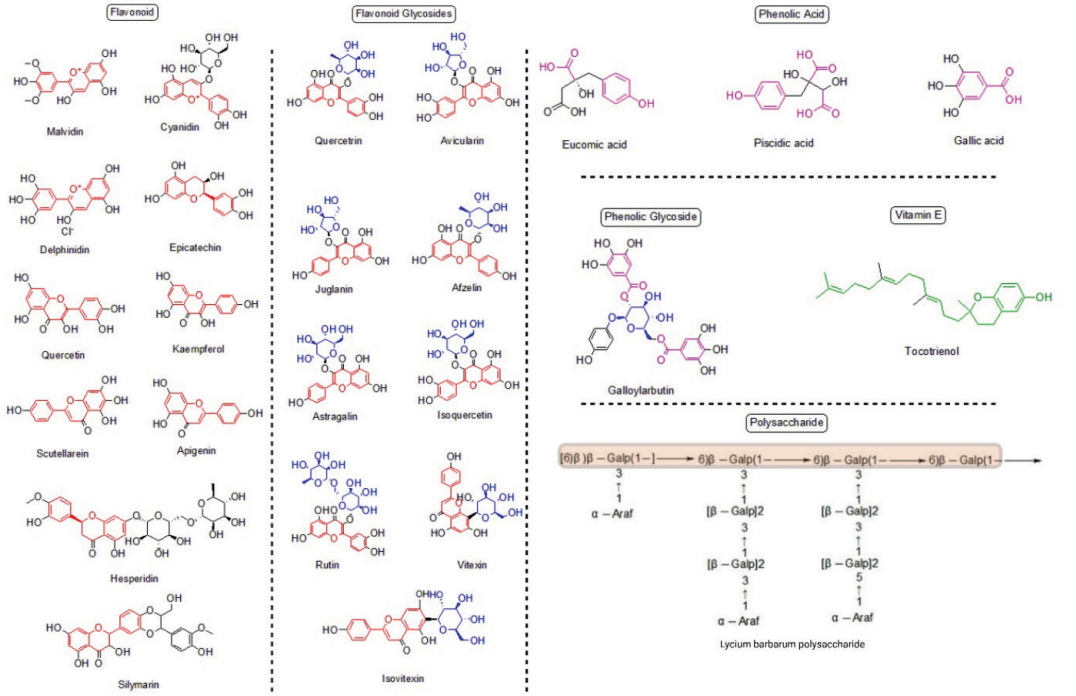

Figure 4: Chemical structures of compounds categorised according to their chemical classes. Core flavonoid structures are highlighted in red, glycoside moieties in blue, phenolic acids in purple, vitamin E derivatives in green, and polysaccharides within a brown box (created using Chemdraw and Biorender software)

polyphenols justifies their remarkable anti-inflammatory properties (Acuña *et al*., 2012). This study also discovered that GbEE extract included 7-Epiclusianone, a benzophenone, as a prominent component, lending credence to the study's findings (Figueiredo *et al*., 2014).

Vaccinium myrtillus

Bilberry, *Vaccinium myrtillus*, possesses antioxidative, antiproliferative, anti-apoptotic, anti-angiogenic, and anti-inflammation activities by activating the ARE (Benzie & Wachtel-Galor, 2011). At a concentration of 320 µg/mL, water-soluble bilberry extract was tested in HaCaT cells for its ability to protect against UVA and UVB-mediated damage. UVA-irradiated cells produced less intracellular ROS when pretreated with *V. myrtillus* extract but not UVB. When UVA-irradiated HaCaT cells were exposed to *V. myrtillus* extract, malondialdehyde, a biomarker for lipid peroxidation was reduced. Similarly, UVB irradiation had a dose-dependent counter effect, except at higher UVA and UVB dosages. In contrast, when UVA and UVB-induced damage were examined, micronucleus generation was reduced. However, pre-treatment with *V. myrtillus* extract dramatically reduced only UVA-induced mitochondrial membrane disruption and apoptosis but not the UVB-irradiated cells (Calò & Marabini, 2014).

Micronuclei are extra-nuclear structures containing damaged chromosomes that are not integrated into the nucleus following cell division. Cell death, genetic instability, or cancer development will result from the production of UV-induced micronuclei formation (Luzhna *et al*., 2013). The ability of *V. myrtillus* to inhibit micronuclei production reinforces its chemotherapeutic potential. Furthermore, anthocyanins in *V. myrtillus* have been shown to interpolate with DNA, resulting in a complex of DNA co-pigmentation that modulates

gene expression whilst protecting DNA from oxidative damage (Benzie & Wachtel-Galor, 2011). As a result, *V. myrtillus* extract is valuable in photoaging and photocarcinogenesis.

Rubus spp.

Blackberries from the *Rubus* genus have a high polyphenol content, including ellagitannins, anthocyanin, and phenolic monomers such as flavonoids and phenolic acids (Mintie *et al*., 2020). Blackberry Extract (BBE) contains six unique anthocyanins, including C3G (Murapa *et al*., 2012). As discussed earlier, C3G reduced UVB-mediated oxidative damage and inflammation in SKH-1 mouse skin (Pratheeshkumar *et al*., 2014). A molecular investigation was conducted to assess the impact of Blackberry Extract (BBE) on SKH-1 mice skin. Topically administered BBE (10% and 20%) altered the MAPK signaling pathway to protect against UVB-induced damages.

Dephosphorylation of Jun-N-terminal kinase (JNK1/2), extracellular-regulated protein kinase (ERK1/2), and p38 was associated with decreased nuclear NF-κB and consequent inflammatory mediators COX-2, iNOS, and prostaglandin E2. BBE also inhibited CPD and consequent 8-oxodG formation (Divya *et al*., 2015). As discussed previously, CPD can cause DNA strand breaks, mutations, and neoplastic transformation (Rastogi *et al*., 2010; Pfeifer & Besaratinia, 2012; Widel *et al*., 2014). Taken together, BBE suppresses UVB-mediated inflammation and carcinogenesis via modulating oxidative stress markers, pro-inflammatory cytokines, and mediators.

Opuntia ficus-indica L.

The cactus pear, often known as the prickly pear cactus (*Opuntia*) is found throughout Mexico, America, Africa, and the Mediterranean. *Opuntia* cladodes are reported to possess antioxidant, wound healing, antimicrobial, and hypoglycemic properties (Di Lorenzo *et al*., 2017). *Opuntia ficus-indica* extract (1 mg/ml) was administered to HaCaT cells to test its UVA protection. Pre-treatment of cells with *O. ficus-indica* Raw Extract (ORE) inhibited stress signalling pathways such as lipid peroxidation, GSH depletion, and free radical generation. There was also a strong photoprotective impact against UVA-induced apoptosis. In the presence of ORE or *O. ficus-indica* small molecular weight fraction, cells showed no caspase-3 and caspase-7 activity, demonstrating that phenolic derivatives, notably piscidic and eucomic acids, protect cells from UVA-mediated stress (Di Lorenzo *et al*., 2017). Interestingly, ORE is high in phenolic derivatives and other bioactive compounds such as mucilage, a carbohydrate-containing polymer (polysaccharide). This molecule was discovered to be beneficial in anti-ageing and wound-healing by modulating stress factors, regulating skin moisture, and promoting cutaneous ameliorative processes (Di Lorenzo *et al*., 2017). Hence, it is apparent that *O. ficus-indica* extract, which is high in polyphenols and polysaccharides is suitable for use as a sun protection agent.

Solanum undatum

Solanum undatum, popularly known as Nightshade apple has anti-cancer and anti-inflammatory characteristics due to its high steroidal glycoalkaloids content, which includes solamargine, solasonine, and solasodine (Al Sinani & Eltayeb, 2017). A prior study discovered that solamargine is critical in inducing cell death via apoptosis (Wu *et al*., 2011). Recently, a study evaluated the effects of *Solanum undatum* extract (SR-T100) on photoaging and photocarcinogenesis in Actinic Keratosis (AK) (Yang *et al*., 2021), using skin samples from 13 AK patients who had previously participated in a phase II study (Wu *et al*., 2011).

The most frequent premalignant skin lesion produced by long-term sun exposure is AK, which manifests as epidermal parakeratosis, keratinocyte atypia, and dermal inflammation with solar elastosis (Jansen *et al*., 2019). As a result, both photocarcinogenic and photoaging processes associated with AK were investigated in this research (Yang *et al*., 2021). In four AK

skins, the SR-T100 gel therapy resulted in partial remission (> 75%) and complete remission (100%) in nine AK skins. Solamargine-containing SR-T100 gel effectively suppressed photocarcinogenesis via decreasing mutant p53 and SOX2 to prevent non-regulated cell proliferation and via NOTCH1 expression, which functions as a tumour suppressor in non-melanoma skin cancers (Nowell & Radtke, 2013; South *et al*., 2014). Furthermore, SR-T100 gel reduced wrinkling in AK skin while enhancing the synthesis of elastic fibres and restoring lamin B1 expression, both of which are photoaging markers (Yang *et al*., 2021). Therefore, the anti-ageing and photochemotherapeutic benefits of *Solanum undatum* gel extract on photodamaged skin with AK were evidenced.

Punica granatum L.

Punica granatum L., Pomegranate Fruit Extract (PFE) is high in anthocyanins (including cyanidin, delphinidin, and pelargonidin), hydrolyzable tannins (including punicalagin, punicalin, and pedunculagin), and ellagitannins (Bar-Ya'akov *et al*., 2019). PFE fed orally (0.2% in water) decreased hyperplasia, cutaneous oedema, leukocyte infiltration, and COX-2 expression in SKH-1 hairless mice. The hyperproliferation of epidermal cells was examined by proliferative markers PCNA and cyclin D1, indicating a lowered proliferative index of PFE as a biomarker of cancer development and progression (Khan *et al*., 2012). PFE also prevented UVB induced NF-κB activation, as evidenced by enhanced IκBα accumulation to keep NF-κB/p65 bound to the cytoplasm and subsequent inhibition of NF-κB and IKKα activation. The study looked at MAPK family upstream regulators of NF-κB. PFE therapy reduces ERK1/2, JNK1/2, and p38, implying that PFE may influence the crosstalk of several pathways that contribute to increase cell viability, proliferation, inflammation, and death, resulting in photo chemoprevention in skin cells (Khan *et al*., 2012).

Citrus sinensis

A study was conducted to assess the *in vivo* skin anti-ageing and photoprotective benefits of consuming a red-orange (*Citrus sinensis* variants Tarocco, Sanguinello, and Moro) extract (Puglia *et al*., 2014). On healthy Caucasian individuals with skin types II, III, and IV, the photoprotective effects of Red Orange Extract (ROE) intake against UV-mediated melanin formation in solar lentigo and skin erythema were evaluated. A regional hyperpigmented lesion or in other words, a senile lentigo or solar lesion, is one of the most obvious changes in photo-damaged skin, particularly in Caucasian and Asian populations (Pollefliet *et al*., 2013); pigmentation above is primarily caused by existing melanin photo-oxidation rather than the synthesis of new pigments and provides only a mild photoprotective benefit (Miyamura *et al*., 2011).

ROE, on the other hand, contains a high concentration of polymethoxyflavonoids, anthocyanins, and other antioxidants such as hydroxycinnamic acids, flavones, and ascorbic acid (Yoshizaki *et al*., 2014). Correspondingly, when human volunteers were given 100 mg of ROE daily for 15 days, there was a significant decrease in the degree of UV-induced cutaneous erythema. Furthermore, red-orange consumption can reduce solar lentigo hyperpigmentation and improve skin appearance and tanning homogeneity by inhibiting UV-induced melanin overproduction. Therefore, ROE can be employed as nutricosmetics due to its anti-ageing and antioxidative properties.

Rubus idaeus L.

Anthocyanins, flavonoids, and phenols are abundant in *Rubus idaeus* L. (red raspberry). The ellagitannins, lambertianin C, and sanguiin H-6 in red Raspberry Extract (RE) exhibit anti-inflammatory and anti-cancer properties (Sangiovanni *et al*., 2013; Lee *et al*., 2016). Research into the influence of 1, 10, and 100 µg/ml of RE on UVB-mediated ageing in NHDFs found that RE inhibits IL-6

and MMP secretion via inhibiting the MAPK/AP-1 signalling pathway. A well-known ROS-sensitive signal pathway is the MAPK family, which includes JNK, ERK, and p38 kinase. The activation of AP-1 by MAPK phosphorylation has been demonstrated to promote MMP gene transcription (Gao *et al*., 2018). As stated, MMPs are involved in connective tissue and elastic fibre degeneration (Cavinato *et al*., 2016; Cavinato & Jansen-Dürr, 2017). Correspondingly, RE was shown to restore p-Smad2/3 and TGF-β1 levels. Furthermore, by suppressing Smad7, a negative regulator in the TGF-β/Smad pathway, RE can potentially promote the expression of type I collagen (Gao *et al*., 2018). Overall, RE is indeed effective in preventing UVB-induced premature ageing.

Fragaria ananassa

A recent *in vitro* study evaluated the ability of the strawberry extract to protect Human Dermal fibroblasts (HuDe) from UVA exposure (Alvarez-Suarez *et al*., 2012). In this work, 24 hours of incubation with 0.5 mg/mL methanolic extracts of the Sveva cultivar (*Fragaria ananassa* Duch.) resulted in dose-dependent photoprotective action, with increased cell viability and decreased DNA damage. These findings are consistent with previous reports indicating the rich content of folate, vitamin C, and phenolic compounds, particularly anthocyanins (Giampieri *et al*., 2012), which have antioxidant, anti-inflammatory, anticarcinogenic, antimutagenic, and photoprotective properties and therefore can regulate enzymatic processes. By neutralising reactive oxygen species and reducing oxidative stress, these compounds prevent the oxidation of key enzyme cofactors and substrates. They also influence enzyme activity by modulating signalling pathways and gene expression related to enzyme synthesis and function, maintaining cellular homeostasis and protecting against damage (Alvarez-Suarez *et al*., 2011; Dogan-Topal *et al*., 2018). In short, the strawberry extract has a great medicinal prospect in preventing UVA-induced damage.

Challenges and Future Perspectives

Developing innovative plant-based sunscreens and supplements for photoprotection and photo chemoprevention presents several challenges. Variability in plant extracts, dose optimization, sustainability, and ethical considerations are critical issues that need addressing. Concerns about organ toxicity, genotoxicity, environmental safety, and bioavailability must also be thoroughly evaluated (Krutmann *et al*., 2020). To mitigate these challenges, research should focus on both acute and chronic effects of experimental formulations, ensuring compliance with International Organization for Standardization (ISO) guidelines and food safety regulations. Meanwhile, individual chemoprotective phytocompounds show promise.

Exploring synergistic effects through combination treatments may enhance efficacy in preventing photoaging and photocarcinogenesis. Comprehensive studies, including pre- and post-UV treatment evaluations under consistent UV conditions are needed to assess the full potential of plant derivatives. Additionally, natural sunscreens and oral supplements should be tailored to diverse skin types and melanin levels. Research on photoprotective plant derivatives for eye health, given the vulnerability of corneal tissue to UV-induced damage like photokeratitis and pterygium is also limited and warrants further investigation (Lee *et al*., 2021).

Conclusions

Plants rich in phytonutrients have been shown to prevent various oxidative and inflammatory-related diseases such as cancer and ageing. Scientific evidence linking a diet rich in herbs and fruits to reduced disease risk has increased rapidly in recent years. This review highlights the potential of phytoderivatives and fruit extracts to prevent UV-induced damage by reducing oxidative stress, inhibiting inflammatory cytokines, preventing DNA damage, and regulating specific biomarkers and enzymes. Further research is needed to

translate results from cell models to human skin treatments and to understand the mechanisms involved. Additionally, exploring UV-induced immunosuppression and the photoprotective effects of biomolecules like lipids, which have been studied less is recommended. It is also crucial to consider environmental concerns when developing UV protection strategies. By integrating environmental considerations into research and development, we can strive towards sustainable UV protection solutions that benefit human health and the planet.

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Conflict of Interest Statement

The authors agree that this research was conducted in the absence of any self-benefits, commercial, or financial conflicts and declare the absence of conflicting interests with the funders.

References

Abel, J., & Haarmann-Stemmann, T. (2010). An introduction to the molecular basics of aryl hydrocarbon receptor biology. *Biological Chemistry*, *391*(11), 1235-1248. https://doi.org/10.1515/bc.2010.128

Acuña, U. M., Dastmalchi, K., Basile, M. J., & Kennelly, E. J. (2012). Quantitative high-performance liquid chromatography photo-diode array (HPLC-PDA) analysis of benzophenones and biflavonoids in eight Garcinia species. *Journal of Food Composition and Analysis*, *25*(2), 215-220. https://doi.org/10.1016/j.jfca.2011.10.006

Al Sinani, S. S. S., & Eltayeb, E. A. (2017). The steroidal glycoalkaloids solamargine and solasonine in Solanum plants. *South African Journal of Botany*, *112*, 253-269. https://doi.org/10.1016/j.sajb.2017.06.002

Alvarez-Suarez, J. M., Dekanski, D., Ristić, S., Radonjić, N. V., Petronijević, N. D., Giampieri, F., Astolfi, P., González-Paramás, A. M., Santos-Buelga, C., Tulipani, S., Quiles, J. L., Mezzetti, B., & Battino, M. (2011). Strawberry Polyphenols Attenuate Ethanol-Induced Gastric Lesions in rats by activation of antioxidant enzymes and attenuation of MDA increase. *PLOS ONE*, *6*(10), e25878. https://doi.org/10.1371/journal.pone.0025878

Ambothi, K., Prasad, N. R., & Balupillai, A. (2015). Ferulic acid inhibits UVB-radiation induced photocarcinogenesis through modulating inflammatory and apoptotic signaling in Swiss albino mice. *Food and Chemical Toxicology*, *82*, 72-78. https://doi.org/10.1016/j.fct.2015.04.031

Aslam, B., Awadh Alrowaili, Z., Khaliq, B., Manzoor, J., Raqeeb, S., & Ahmad, F. (2021). Ozone depletion identification in stratosphere through faster region-based convolutional neural network. *Computers, Materials & Continua*, *68*(2), 2159-2178. https://doi.org/10.32604/cmc.2021.015922

Baeyens, A., Abrantes, A. M., Ahire, V., Ainsbury, E. A., Baatout, S., Baselet, B., Botelho, M. F., Boterberg, T., Chevalier, F., Da Pieve, F., Delbart, W., Edin, N. F. J., Fernandez-Palomo, C., Geenen, L., Georgakilas, A. G., Heynickx, N., Meade, A. D., Michaelidesova, A. J., Mistry, D., Montoro, A., Mothersill, C., Pires, A. S., Reindl, J., Schettino, G., Socol., Y., Selvaraj, V. K., Sminia, P., Vermeulan, K., Vogin, G., Wked, A., & Wozny, A.-S. (2023). Basic concepts of radiation biology. In S. Baatout (Ed.), *Radiobiology textbook* (pp. 25-81). Springer International Publishing. https://doi.org/10.1007/978-3-031-18810-7_2

Bahner, J. D., & Bordeaux, J. S. (2013). Non-melanoma skin cancers: Photodynamic therapy, cryotherapy, 5-fluorouracil, imiquimod, diclofenac, or what? Facts and

controversies. *Clinics in Dermatology*, *31*(6), 792-798. https://doi.org/10.1016/j.clindermatol.2013.08.020

Baldwin, M. P., & Lenton, T. M. (2020). Solving the climate crisis: Lessons from ozone depletion and COVID-19. *Global Sustainability*, *3*, e29. https://doi.org/10.1017/sus.2020.25

Balupillai, A., Prasad, R. N., Govindasamy, K., Ramasamy, K., Muthusamy, G., Shanmugham, M., Devadasan, V., & Dhanapalan, A. (2016). Caffeic Acid Inhibits Chronic UVB-Induced Cellular Proliferation through JAK-STAT3 signaling in mouse skin. *Photochemistry and Photobiology*, *92*(3), 467-474. https://doi.org/10.1111/php.12588

Balupillai, A., Prasad, R. N., Ramasamy, K., Muthusamy, G., Shanmugham, M., Govindasamy, K., & Gunaseelan, S. (2015). Caffeic Acid Inhibits UVB-induced Inflammation and Photocarcinogenesis through activation of Peroxisome Proliferator-activated Receptor- *γ* in mouse skin. *Photochemistry and Photobiology*, *91*(6), 1458-1468. https://doi.org/10.1111/php.12522

Bar-Ya'akov, I., Tian, L., Amir, R., & Holland, D. (2019). Primary metabolites, anthocyanins, and hydrolyzable tannins in the pomegranate fruit. *Frontiers in Plant Science*, *10*, 620. https://doi.org/10.3389/fpls.2019.00620

Bastos, E. L., Quina, F. H., & Baptista, M. S. (2023). Endogenous Photosensitizers in human skin. *Chemical Reviews*, *123*(16), 9720-9785. https://doi.org/10.1021/acs.chemrev.2c00787

Bens, G. (2014). Sunscreens. In J. Reichrath, *Sunlight, vitamin D and skin cancer* (pp. 429-463). New York: Springer. https://doi.org/10.1007/978-1-4939-0437-2_25

Benzie, I. F. F., & Wachtel-Galor, S. (2011). Bilberry (vaccinium myrtillus L.). In *Herbal Medicine: Biomolecular and clinical aspects* (2nd ed., pp. 55-71). CRC Press.

Bernerd, F., Passeron, T., Castiel, I., & Marionnet, C. (2022). The damaging effects of long UVA (UVA1) rays: A major challenge to preserve skin health and integrity. *International Journal of Molecular Sciences*, *23*(15), 8243. https://doi.org/10.3390/ijms23158243

Bhattacharjee, D., Preethi, S., Patil, A. B., & Jain, V. (2021). A comparison of natural and synthetic sunscreen agents: A review. *International Journal of Pharmaceutical Research*, *13*(01). https://doi.org/10.31838/ijpr/2021.13.01.524

Brand, R. M., Wipf, P., Durham, A., Epperly, M. W., Greenberger, J. S., & Falo, L. D. (2018). Targeting Mitochondrial Oxidative stress to mitigate UV-induced skin damage. *Frontiers in Pharmacology*, *9*, 920. https://doi.org/10.3389/fphar.2018.00920

Calò, R., & Marabini, L. (2014). Protective effect of Vaccinium myrtillus extract against UVA- and UVB-induced damage in a human keratinocyte cell line (HaCaT cells). *Journal of Photochemistry and Photobiology B: Biology*, *132*, 27-35. https://doi.org/10.1016/j.jphotobiol.2014.01.013

Cavinato, M., & Jansen-Dürr, P. (2017). Molecular mechanisms of UVB-induced senescence of dermal fibroblasts and its relevance for photoaging of the human skin. *Experimental Gerontology*, *94*, 78-82. https://doi.org/10.1016/j.exger.2017.01.009

Cavinato, M., Koziel, R., Romani, N., Weinmüllner, R., Jenewein, B., Hermann, M., Dubrac, S., Ratzinger, G., Grillari, J., Schmuth, M., & Jansen-Dürr, P. (2016). Uvb-induced senescence of human dermal fibroblasts involves impairment of proteasome and enhanced autophagic activity. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *72*(5), 632-639. https://doi.org/10.1093/gerona/glw150

Cavinato, M., Waltenberger, B., Baraldo, G., Grade, C. V. C., Stuppner, H., & Jansen-Dürr, P. (2017). Plant extracts and natural compounds used against UVB-induced photoaging. *Biogerontology*, *18*(4), 499-516. https://doi.org/10.1007/s10522-017-9715-7

Cheynier, V., Comte, G., Davies, K. M., Lattanzio, V., & Martens, S. (2013). Plant phenolics: Recent advances on their biosynthesis, genetics, and ecophysiology. *Plant Physiology and Biochemistry*, *72*, 1-20. https://doi.org/10.1016/j.plaphy.2013.05.009

Cortat, B., Garcia, C. C. M., Quinet, A., Schuch, A. P., De Lima-Bessa, K. M., & Menck, C. F. M. (2013). The relative roles of DNA damage induced by UVA irradiation in human cells. *Photochemical & Photobiological Sciences*, *12*(8), 1483-1495. https://doi.org/10.1039/c3pp50023c

Dai, J., Ma, H., Fan, J., Li, Y., Wang, J., Ni, H., Xia, G., & Chen, S. (2011). Crude polysaccharide from an anti-UVB cell clone of Bupleurum scorzonerifolium protect HaCaT cells against UVB-induced oxidative stress. *Cytotechnology*, *63*(6), 599-607. https://doi.org/10.1007/s10616-011-9381-6

Dare, R. G., Oliveira Ferreira, L. dos A., Ribeiro, F. M., Visentainer, J. V., Nakamura, C. V., & Torrado Truiti, M. da C. (2021). Photochemoprotective effects of Ethyl Acetate Fraction from Senegalia polyphylla Leaves in Ultraviolet-Irradiated L929 Fibroblasts. *Free Radicals and Antioxidants*, *11*(1), 7-12. https://doi.org/10.5530/fra.2021.1.2

De Oliveira, A. C., Miyagawa, L. M., Monteiro, K. M., Dias, A. L. S., Longato, G. B., Spindola, H., Vendramini-Costa, D. B., Quetin-Leclercq, J., Carvalho, J. E., & Rogez, H. (2021). Phenolic composition, antiproliferative and antiulcerogenic activities of a polyphenol-rich purified extract from açai (*Euterpe oleracea*) fruits. *International Journal of Food Science & Technology*, *56*(12), 6626-6634. https://doi.org/10.1111/ijfs.15332

Decean, H., Fischer-Fodor, E., Tatomir, C., Perde-Schrepler, M., Somfelean, L., Burz, C., Hodor, T., Orasan, R., & Virag, P. (2016). Vitis vinifera seeds extract for the modulation of cytosolic factors Bax-α and NF-kB involved in UVB-induced oxidative stress and apoptosis of human skin cells. *Medicine and Pharmacy Reports*, *89*(1), 72-81. https://doi.org/10.15386/cjmed-508

Di Lorenzo, F., Silipo, A., Molinaro, A., Parrilli, M., Schiraldi, C., D'Agostino, A., Izzo, E., Rizza, L., Bonina, A., Bonina, F., & Lanzetta, R. (2017). The polysaccharide and low molecular weight components of Opuntia ficus indica cladodes: Structure and skin repairing properties. *Carbohydrate Polymers*, *157*, 128-136. https://doi.org/10.1016/j.carbpol.2016.09.073

Dias, M. M. dos S., Martino, H. S. D., Noratto, G., Roque-Andrade, A., Stringheta, P. C., Talcott, S., Ramos, A. M., & Mertens-Talcott, S. U. (2015). Anti-inflammatory activity of polyphenolics from açai (Euterpe oleracea Martius) in intestinal myofibroblasts CCD-18Co cells. *Food & Function*, *6*(10), 3249-3256. https://doi.org/10.1039/C5FO00278H

Divya, S. P., Wang, X., Pratheeshkumar, P., Son, Y.-O., Roy, R. V., Kim, D., Dai, J., Hitron, J. A., Wang, L., Asha, P., Shi, X., & Zhang, Z. (2015). Blackberry extract inhibits UVB-induced oxidative damage and inflammation through MAP kinases and NF-κB signaling pathways in SKH-1 mice skin. *Toxicology and Applied Pharmacology*, *284*(1), 92-99. https://doi.org/10.1016/j.taap.2015.02.003

Dogan-Topal, B., Uslu, B., & Ozkan, S. A. (2018). Detection of prevented DNA damage by therapeutic foods. In *Genetically Engineered Foods* (pp. 281-309). Elsevier. https://doi.org/10.1016/B978-0-12-811519-0.00011-X

D'Orazio, J., Jarrett, S., Amaro-Ortiz, A., & Scott, T. (2013). UV radiation and the skin. *International Journal of Molecular Sciences*, *14*(6), 12222-12248. https://doi.org/10.3390/ijms140612222

Doré, J.-F., & Chignol, M.-C. (2012). Tanning salons and skin cancer. *Photochemical and Photobiological Sciences*, *11*(1), 30-37. https://doi.org/10.1039/C1PP05186E

dos Anjos Oliveira Ferreira, L., de Paula Barros de Melo, C., Saito, P., Iwanaga, C. C., Nakamura, C. V., Casagrande, R., & da Conceição Torrado Truiti, M. (2020). Nectandra cuspidata fraction and the isolated polyphenols protect fibroblasts and hairless mice skin from UVB-induced inflammation and oxidative stress. *Journal of Photochemistry and Photobiology B: Biology*, *205*, 111824. https://doi.org/10.1016/j.jphotobiol.2020.111824

Dos Santos, M., Mamede, R., Rufino, M., De Brito, E., & Alves, R. (2015). Amazonian native palm fruits as sources of antioxidant bioactive compounds. *Antioxidants*, *4*(3), 591-602. https://doi.org/10.3390/antiox4030591

Dupont, E., Gomez, J., & Bilodeau, D. (2013). Beyond UV radiation: A skin under challenge. *International Journal of Cosmetic Science*, *35*(3), 224-232. https://doi.org/10.1111/ics.12036

Esser, C., Bargen, I., Weighardt, H., Haarmann-Stemmann, T., & Krutmann, J. (2013). Functions of the aryl hydrocarbon receptor in the skin. *Seminars in Immunopathology*, *35*(6), 677-691. https://doi.org/10.1007/s00281-013-0394-4

Farivar, N. (2019). *UV-Induced DNA damage response in blood cells as a potential method for cancer detection* [University of British Columbia]. https://doi.org/10.14288/1.0378307

Figueiredo, S. A., Vilela, F. M. P., Silva, C. A. da, Cunha, T. M., dos Santos, M. H., & Fonseca, M. J. V. (2014). *In vitro* and *in vivo* photoprotective/photochemopreventive potential of Garcinia brasiliensis epicarp extract. *Journal of Photochemistry and Photobiology B: Biology*, *131*, 65-73. https://doi.org/10.1016/j.jphotobiol.2014.01.004

Gallay, C., Dumont, S., & Kherad, O. (2019). Effectiveness of sunscreen against melanoma. *Revue Medicale Suisse*, *15*(635), 198-201.

Gao, W., Wang, Y., Hwang, E., Lin, P., Bae, J., Seo, S. A., Yan, Z., & Yi, T.-H. (2018). Rubus idaeus L. (red raspberry) blocks UVB-induced MMP production and promotes type I procollagen synthesis via inhibition of MAPK/AP-1, NF-κβ and stimulation of TGF-β/Smad, Nrf2 in normal human dermal fibroblasts. *Journal of Photochemistry and Photobiology B: Biology*, *185*, 241-253. https://doi.org/10.1016/j.jphotobiol.2018.06.007

Giampieri, F., Alvarez-Suarez, J. M., Tulipani, S., Gonzàles-Paramàs, A. M., Santos-Buelga, C., Bompadre, S., Quiles, J. L., Mezzetti, B., & Battino, M. (2012). Photoprotective potential of strawberry (*Fragaria* × *ananassa*) extract against UV-A irradiation damage on human fibroblasts. *Journal of Agricultural and Food Chemistry*, *60*(9), 2322-2327. https://doi.org/10.1021/jf205065x

Giampieri, F., Tulipani, S., Alvarez-Suarez, J. M., Quiles, J. L., Mezzetti, B., & Battino, M. (2012). The strawberry: Composition, nutritional quality, and impact on human health. *Nutrition*, *28*(1), 9-19. https://doi.org/10.1016/j.nut.2011.08.009

Godic, A., Poljšak, B., Adamic, M., & Dahmane, R. (2014). The role of antioxidants in skin cancer prevention and treatment. *Oxidative Medicine and Cellular Longevity*, *2014*, 1-6. https://doi.org/10.1155/2014/860479

Gruber, P., & Zito, P. M. (2023, May 14). *Skin cancer*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK441949/

Gunaseelan, S., Balupillai, A., Govindasamy, K., Muthusamy, G., Ramasamy, K., Shanmugam, M., & Prasad, N. R. (2016). The preventive effect of linalool on acute and chronic UVB-mediated skin carcinogenesis in Swiss albino mice. *Photochemical & Photobiological Sciences*, *15*(7), 851-860. https://doi.org/10.1039/C6PP00075D

Halliday, G. M., Byrne, S. N., & Damian, D. L. (2011). Ultraviolet A radiation: Its role in immunosuppression and carcinogenesis. *Seminars in Cutaneous Medicine and Surgery*, *30*(4), 214-221. https://doi.org/10.1016/j.sder.2011.08.002

Harris, B. W., Crane, J. S., & Schlessinger, J. (2023, June 28). *Solar urticaria*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK441986/

Holderness, J., Schepetkin, I. A., Freedman, B., Kirpotina, L. N., Quinn, M. T., Hedges, J. F., & Jutila, M. A. (2011). Polysaccharides isolated from Açaí fruit induce innate immune responses. *PLOS ONE*, *6*(2), e17301. https://doi.org/10.1371/journal.pone.0017301

Hseu, Y.-C., Tsai, Y.-C., Huang, P.-J., Ou, T.-T., Korivi, M., Hsu, L.-S., Chang, S.-H., Wu, C.-R., & Yang, H.-L. (2015). The dermato-protective effects of lucidone from Lindera erythrocarpa through the induction of Nrf2-mediated antioxidant genes in UVA-irradiated human skin keratinocytes. *Journal of Functional Foods*, *12*, 303-318. https://doi.org/10.1016/j.jff.2014.10.019

Hui, C., Qi, X., Qianyong, Z., Xiaoli, P., Jundong, Z., & Mantian, M. (2013). Flavonoids, flavonoid subclasses and breast cancer risk: A meta-analysis of epidemiologic studies. *PLOS ONE*, *8*(1), e54318. https://doi.org/10.1371/journal.pone.0054318

Itoh, T., Fujita, S., Koketsu, M., & Hashizume, T. (2021). Citrulluside H and citrulluside T from young watermelon fruit attenuate ultraviolet B radiation-induced matrix metalloproteinase expression through the scavenging of generated reactive oxygen species in human dermal fibroblasts. *Photodermatology, Photoimmunology & Photomedicine*, *37*(5), 386-394. https://doi.org/10.1111/phpp.12669

Iwanaga, C. C., Ferreira, L. A. O., Rodrigues, C. C. A., Pinto, I. C., Romagnolo, M. B., Nakamura, C. V., Casagrande, R., & Truiti, M. C. T. (2021). Photochemoprotective Potential of the Ethyl Acetate Fraction from *Eugenia hiemalis* leaves and its 2,6-Di-*O*-galloylarbutin isolate against UVB-Induced Photodamage. *Photochemistry and Photobiology*, php.13420. https://doi.org/10.1111/php.13420

Jansen, M. H. E., Kessels, J. P. H. M., Nelemans, P. J., Kouloubis, N., Arits, A. H. M. M., van Pelt, H. P. A., Quaedvlieg, P. J. F., Essers, B. A. B., Steijlen, P. M., Kelleners-Smeets, N. W. J., & Mosterd, K. (2019). Randomized trial of four treatment approaches for Actinic Keratosis. *New England Journal of Medicine*, *380*(10), 935-946. https://doi.org/10.1056/NEJMoa1811850

Kahremany, S., Hofmann, L., Gruzman, A., Dinkova-Kostova, A. T., & Cohen, G. (2022). NRF2 in dermatological disorders: Pharmacological activation for protection against cutaneous photodamage and photodermatosis. *Free Radical Biology and Medicine*, *188*, 262-276. https://doi.org/10.1016/j.freeradbiomed.2022.06.238

Kang, J., Thakali, K. M., Xie, C., Kondo, M., Tong, Y., Ou, B., Jensen, G., Medina, M. B., Schauss, A. G., & Wu, X. (2012). Bioactivities of açaí (Euterpe precatoria Mart.) fruit pulp, superior antioxidant and anti-inflammatory properties to Euterpe oleracea Mart. *Food Chemistry*, *133*(3), 671-677. https://doi.org/10.1016/j.foodchem.2012.01.048

Kang, J., Xie, C., Li, Z., Nagarajan, S., Schauss, A. G., Wu, T., & Wu, X. (2011). Flavonoids from acai (Euterpe oleracea Mart.) pulp and their antioxidant and anti-

inflammatory activities. *Food Chemistry*, *128*(1), 152-157. https://doi.org/10.1016/j.foodchem.2011.03.011

Kapoor, D., Bhardwaj, S., Landi, M., Sharma, A., Ramakrishnan, M., & Sharma, A. (2020). The impact of drought in plant metabolism: How to exploit tolerance mechanisms to increase crop production. *Applied Sciences*, *10*(16), 5692. https://doi.org/10.3390/app10165692

Khan, N., Syed, D. N., Pal, H. C., Mukhtar, H., & Afaq, F. (2012). Pomegranate fruit extract inhibits uvb-induced inflammation and proliferation by modulating nf-κb and mapk signaling pathways in mouse skin†. *Photochemistry and Photobiology*, *88*(5), 1126-1134. https://doi.org/10.1111/j.1751-1097.2011.01063.x

Komatsu, T., Sasaki, S., Manabe, Y., Hirata, T., & Sugawara, T. (2017). Preventive effect of dietary astaxanthin on UVA-induced skin photoaging in hairless mice. *PLOS ONE*, *12*(2), e0171178. https://doi.org/10.1371/journal.pone.0171178

Krutmann, J., Passeron, T., Gilaberte, Y., Granger, C., Leone, G., Narda, M., Schalka, S., Trullas, C., Masson, P., & Lim, H. W. (2020). Photoprotection of the future: Challenges and opportunities. *Journal of the European Academy of Dermatology and Venereology*, *34*(3), 447-454. https://doi.org/10.1111/jdv.16030

Kwon, S. W., Ko, H. J., Bae, J. T., Kim, J. H., Lee, G. S., & Pyo, H. B. (2016). Cell protective effects of enzymatic hydrolysates of citrus peel pectin. *Journal of the Society of Cosmetic Scientists of Korea*, *42*(1), 75-85. https://doi.org/10.15230/SCSK.2016.42.1.75

Kytidou, K., Artola, M., Overkleeft, H. S., & Aerts, J. M. F. G. (2020). Plant Glycosides and Glycosidases: A treasure-trove for therapeutics. *Frontiers in Plant Science*, *11*. https://doi.org/10.3389/fpls.2020.00357

Lee, D., Ko, H., Kim, Y.-J., Kim, S.-N., Choi, K.-C., Yamabe, N., Kim, K. H., Kang, K. S., Kim, H. Y., & Shibamoto, T. (2016). Inhibition of a2780 human ovarian carcinoma cell proliferation by a *rubus* component, sanguiin h-6. *Journal of Agricultural and Food Chemistry*, *64*(4), 801-805. https://doi.org/10.1021/acs.jafc.5b05461

Lee, J., Kim, U., Lee, Y., Han, E., Ham, S., Lee, W., Choi, W., & Kang, S. (2021). Sunlight exposure and eye disorders in an economically active population: Data from the KNHANES 2008-2012. *Annals of Occupational and Environmental Medicine*, *33*. https://doi.org/10.35371/aoem.2021.33.e24

Lee, J. W., Ratnakumar, K., Hung, K.-F., Rokunohe, D., & Kawasumi, M. (2020). Deciphering UV-induced dna damage responses to prevent and treat skin cancer. *Photochemistry and Photobiology*, *96*(3), 478-499. https://doi.org/10.1111/php.13245

Li, H., Li, Z., Peng, L., Jiang, N., Liu, Q., Zhang, E., Liang, B., Li, R., & Zhu, H. (2017). *Lycium barbarum* polysaccharide protects human keratinocytes against UVB-induced photo-damage. *Free Radical Research*, *51*(2), 200-210. https://doi.org/10.1080/10715762.2017.1294755

Li, Q., Wang, D., Bai, D., Cai, C., Li, J., Yan, C., Zhang, S., Wu, Z., Hao, J., & Yu, G. (2020). Photoprotective effect of Astragalus membranaceus polysaccharide on UVA-induced damage in HaCaT cells. *PLOS ONE*, *15*(7), e0235515. https://doi.org/10.1371/journal.pone.0235515

Li, W., Mu, X., Wu, X., He, W., Liu, Y., Liu, Y., Deng, J., & Nie, X. (2022). Dendrobium nobile Lindl. Polysaccharides protect fibroblasts against UVA-induced photoaging via JNK/c-Jun/MMPs pathway. *Journal of Ethnopharmacology*, *298*, 115590. https://doi.org/10.1016/j.jep.2022.115590

Li, Y., Fan, J., Ma, H., Shen, F., Zhang, G., Wang, J., Xia, G., Fan, D., & Chen, S. (2011). Elevated level of polysaccharides in a high level UV-B tolerant cell line of Bupleurum scorzonerifolium Willd. *African Journal of Biotechnology*, *10*(29), 5578-5586. https://doi.org/10.5897/AJB10.2160

Long, Y., Wang, W., Zhang, Y., Du, F., Zhang, S., Li, Z., Deng, J., & Li, J. (2023). Photoprotective effects of Dendrobium nobile Lindl. Polysaccharides against UVB-Induced Oxidative Stress and Apoptosis in HaCaT cells. *International Journal of Molecular Sciences*, *24*(7), 6120. https://doi.org/10.3390/ijms24076120

Lucas, R. M., Byrne, S. N., Correale, J., Ilschner, S., & Hart, P. H. (2015). Ultraviolet radiation, vitamin D and multiple sclerosis. *Neurodegenerative Disease Management*, *5*(5), 413-424. https://doi.org/10.2217/nmt.15.33

Luzhna, L., Kathiria, P., & Kovalchuk, O. (2013). Micronuclei in genotoxicity assessment: From genetics to epigenetics and beyond. *Frontiers in Genetics*, *4*, 131. https://doi.org/10.3389/fgene.2013.00131

Mansuri, R., Diwan, A., Kumar, H., Dangwal, K., & Yadav, D. (2021). Potential of natural compounds as sunscreen agents. *Pharmacognosy Reviews*, *15*(29), 47-56. https://doi.org/10.5530/phrev.2021.15.5

Mao, G.-X., Xing, W.-M., Wen, X.-L., Jia, B.-B., Yang, Z.-X., Wang, Y.-Z., Jin, X.-Q., Wang, G.-F., & Yan, J. (2015). Salidroside protects against premature senescence induced by ultraviolet B irradiation in human dermal fibroblasts. *International Journal of Cosmetic Science*, *37*(3), 321-328. https://doi.org/10.1111/ics.12202

Martins, F. T., dos Santos, M. H., Coelho, C. P., Barbosa, L. C. A., Dias, G. C., Fracca, M. P., Neves, P. P., Stringheta, P. C., & Doriguetto, A. C. (2011). A powder X-ray diffraction method for detection of polyprenylated benzophenones in plant extracts associated with HPLC for quantitative analysis. *Journal of Pharmaceutical and Biomedical Analysis*, *54*(3), 451-457. https://doi.org/10.1016/j.jpba.2010.09.010

Merin, K. A., Shaji, M., & Kameswaran, R. (2022). A review on sun exposure and skin diseases. *Indian Journal of Dermatology*, *67*(5), 625. https://doi.org/10.4103/ijd.ijd_1092_20

Mintie, C. A., Singh, C. K., & Ahmad, N. (2020). Whole fruit phytochemicals combating skin damage and carcinogenesis. *Translational Oncology*, *13*(2), 146-156. https://doi.org/10.1016/j.tranon.2019.10.014

Miyamura, Y., Coelho, S. G., Schlenz, K., Batzer, J., Smuda, C., Choi, W., Brenner, M., Passeron, T., Zhang, G., Kolbe, L., Wolber, R., & Hearing, V. J. (2011). The deceptive nature of UVA tanning versus the modest protective effects of UVB tanning on human skin: UVA versus UVB tanning of human skin. *Pigment Cell & Melanoma Research*, *24*(1), 136-147. https://doi.org/10.1111/j.1755-148X.2010.00764.x

Mohan, S., Azmi, W. A., Santhanam, R., Rahman, N. E. A., & Ismail, W. I. W. (2024). Photoprotective Properties of Four Structure Propolis from Heterotrigona itama Stingless Beehive: Fractionation, Bioactivity Analysis, and Chemical Profiling. *Heliyon, 10*(20), e39164. https://doi.org/10.1016/j.heliyon.2024.e39164

Mohiuddin, A. (2019). An extensive review of sunscreen and Suntan preparations [Preprint]. *Medicine & Pharmacology*. https://doi.org/10.20944/preprints201904.0327.v1

Murapa, P., Dai, J., Chung, M., Mumper, R. J., & D'Orazio, J. (2012). Anthocyanin-rich fractions of blackberry extracts reduce uv-induced free radicals and oxidative damage in keratinocytes: Blackberry extracts reduce uv oxidative damage in keratinocytes. *Phytotherapy Research*, *26*(1), 106-112. https: //doi.org/10.1002/ptr.3510

Nahm, W. J., Gwillim, E. C., Badiavas, E. V., Nichols, A. J., Kirsner, R. S., Boggeln, L. H., & Shen, J. T. (2021). Treating melanoma in situ during a pandemic with telemedicine and a combination of imiquimod, 5-fluorouracil, and tretinoin. *Dermatology and Therapy*, *11*(1), 307-314. https://doi.org/10.1007/s13555-020-00473-w

National Cancer Institute (US). (2024, March 11). *Skin Cancer Treatment (PDQ®)*. PDQ Cancer Information Summaries - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK65928/

Neves, L. M. G., Tim, C. R., Floriano, E. M., da Silva de Avó, L. R., Fernandes, J. B., Parizotto, N. A., & Cominetti, M. R. (2021). Lycium barbarum polysaccharide fraction associated with photobiomodulation protects from epithelium thickness and collagen fragmentation in a model of cutaneous photodamage. *Lasers in Medical Science*, *36*(4), 863-870. https://doi.org/10.1007/s10103-020-03132-w

Nowell, C., & Radtke, F. (2013). Cutaneous notch signaling in health and disease. *Cold Spring Harbor Perspectives in Medicine*, *3*(12), a017772-a017772. https://doi.org/10.1101/cshperspect.a017772

O'Leary, R. E., Diehl, J., & Levins, P. C. (2014). Update on tanning: More risks, fewer benefits. *Journal of the American Academy of Dermatology*, *70*(3), 562-568. https://doi.org/10.1016/j.jaad.2013.11.004

Oliveira, M. M. de, Daré, R. G., Barizão, É. O., Visentainer, J. V., Romagnolo, M. B., Nakamura, C. V., & Truiti, M. da C. T. (2018). Photodamage attenuating potential of Nectandra hihua against UVB-induced oxidative stress in L929 fibroblasts. *Journal of Photochemistry and Photobiology B: Biology*, *181*, 127-133. https://doi.org/10.1016/j.jphotobiol.2018.03.008

Paixão, T. P., Silva, M. T., De Andrade, M. A., Raposo, N. R. B., & Vieira, J. L. F. (2023). Plants from Brazil with potential photoprotective activity: A review. *Pharmacognosy Reviews*, 204-213. https://doi.org/10.5530/097627870191

Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: An overview. *Journal of Nutritional Science*, *5*. https://doi.org/10.1017/jns.2016.41

Patwardhan, J., & Bhatt, P. (2015). Ultraviolet-B protective effect of flavonoids from Eugenia Caryophylata on human dermal fibroblast cells. *Pharmacognosy Magazine*, *11*(44), 397. https://doi.org/10.4103/0973-1296.168979

Patwardhan, J., & Bhatt, P. (2016). Flavonoids derived from Abelmoschus esculentus Attenuates UV-B induced cell damage in Human Dermal Fibroblasts through Nrf2-ARE pathway. *Pharmacognosy Magazine*, *12*(Suppl. 2), S129-S138. https://doi.org/10.4103/0973-1296.182175

Patwardhan, J., & Bhatt, P. (2019). Protective effect of flavonoids from Foeniculum vulgare against ultraviolet-B-induced oxidative stress in human dermal fibroblasts. *Biomedical Research Journal*, *6*(2), 62. https://doi.org/10.4103/BMRJ.BMRJ_22_19

Peixoto, H., Roxo, M., Krstin, S., Röhrig, T., Richling, E., & Wink, M. (2016). An Anthocyanin-Rich extract of Acai (*Euterpe precatoria* Mart.) increases stress resistance and retards aging-related markers in *Caenorhabditis elegans*. *Journal of Agricultural and Food Chemistry*, *64*(6), 1283-1290. https://doi.org/10.1021/acs.jafc.5b05812

Perveen, S. (2018). Introductory Chapter: Terpenes and terpenoids. In S. Perveen & A. Al-Taweel (Eds.), *Terpenes and terpenoids*. IntechOpen. https://doi.org/10.5772/intechopen.79683

Petruk, G., Del Giudice, R., Rigano, M. M., & Monti, D. M. (2018). Antioxidants from plants protect against skin photoaging. *Oxidative Medicine and Cellular Longevity*, *2018*, 1-11. https://doi.org/10. 1155/2018/1454936

Petruk, G., Di Lorenzo, F., Imbimbo, P., Silipo, A., Bonina, A., Rizza, L., Piccoli, R., Monti, D. M., & Lanzetta, R. (2017). Protective effect of Opuntia ficus-indica L. cladodes against UVA-induced oxidative stress in normal human keratinocytes. *Bioorganic & Medicinal Chemistry Letters*, *27*(24), 5485-5489. https://doi.org/10.1016/j.bmcl.2017.10.043

Petruk, G., Illiano, A., Del Giudice, R., Raiola, A., Amoresano, A., Rigano, M. M., Piccoli, R., & Monti, D. M. (2017). Malvidin and cyanidin derivatives from açai fruit (Euterpe oleracea Mart.) counteract UV-A-induced oxidative stress in immortalized fibroblasts. *Journal of Photochemistry and Photobiology B: Biology*, *172*, 42-51. https://doi.org/10.1016/j.jphotobiol.2017.05.013

Pfeifer, G. P. (2020). Mechanisms of UV-induced mutations and skin cancer. *Genome Instability & Disease*, *1*(3), 99-113. https://doi.org/10.1007/s42764-020-00009-8

Pfeifer, G. P., & Besaratinia, A. (2012). UV wavelength-dependent DNA damage and human non-melanoma and melanoma skin cancer. *Photochemical & Photobiological Sciences*, *11*(1), 90-97. https://doi.org/10.1039/C1PP05144J

Pluemsamran, T., Onkoksoong, T., & Panich, U. (2012). Caffeic Acid and Ferulic Acid inhibit UVA-Induced Matrix Metalloproteinase-1 through regulation of antioxidant defense system in Keratinocyte HaCaT cells. *Photochemistry and Photobiology*, *88*(4), 961-968. https://doi.org/10.1111/j.1751-1097.2012.01118.x

Pollefliet, C., Corstjens, H., González, S., Hellemans, L., Declercq, L., & Yarosh, D. (2013). Morphological characterization of solar lentigines by *in vivo* reflectance confocal microscopy: A longitudinal approach. *International Journal of Cosmetic Science*, *35*(2), 149-155. https://doi.org/10.1111/ics.12016

Pratheeshkumar, P., Son, Y.-O., Wang, X., Divya, S. P., Joseph, B., Hitron, J. A., Wang, L., Kim, D., Yin, Y., Roy, R. V., Lu, J., Zhang, Z., Wang, Y., & Shi, X. (2014). Cyanidin-3-glucoside inhibits UVB-induced oxidative damage and inflammation by regulating MAP kinase and NF-κB signaling pathways in SKH-1 hairless mice skin. *Toxicology and Applied Pharmacology*, *280*(1), 127-137. https://doi.org/10.1016/j.taap.2014.06.028

Puglia, C., Offerta, A., Saija, A., Trombetta, D., & Venera, C. (2014). Protective effect of red orange extract supplementation against UV-induced skin damages: Photoaging and solar lentigines. *Journal of Cosmetic Dermatology*, *13*(2), 151-157. https://doi.org/10.1111/jocd.12083

Rabinovich, L., & Kazlouskaya, V. (2018). Herbal sun protection agents: Human studies. *Clinics in Dermatology*, *36*(3), 369-375. https://doi.org/10.1016/j.clindermatol.2018.03.014

Rastogi, R. P., Richa, Kumar, A., Tyagi, M. B., & Sinha, R. P. (2010). Molecular mechanisms of ultraviolet radiation-induced dna damage and repair. *Journal of Nucleic Acids*, *2010*, 1-32. https://doi.org/10.4061/2010/592980

Reilly, D. M., & Lozano, J. (2021). Skin collagen through the lifestages: Importance for skin health and beauty. *Plastic and Aesthetic Research*, *2021*. https://doi.org/10.20517/2347-9264.2020.153

Ribeiro, F. M., Volpato, H., Lazarin-Bidóia, D., Desoti, V. C., de Souza, R. O., Fonseca, M. J. V., Ueda-Nakamura, T., Nakamura, C. V., & Silva, S. de O. (2018). The extended production of UV-induced reactive oxygen species in L929 fibroblasts is attenuated by posttreatment with Arrabidaea chica through scavenging mechanisms. *Journal of Photochemistry and Photobiology B: Biology*, *178*, 175-181. https://doi.org/10.1016/j.jphotobiol.2017.11.002

Rojas Camargo, J., Londono Giraldo, C. A., & Ciro Monsalve, Y. A. (2016). *The health benefits of natural skin UVA photoprotective compounds found in botanical sources*.

https://bibliotecadigital.udea.edu.co/handle/10495/35731

Rufino, M. do S. M., Pérez-Jiménez, J., Arranz, S., Alves, R. E., de Brito, E. S., Oliveira, M. S. P., & Saura-Calixto, F. (2011). Açaí (Euterpe oleraceae) 'BRS Pará': A tropical fruit source of antioxidant dietary fiber and high antioxidant capacity oil. *Food Research International*, *44*(7), 2100-2106. https://doi.org/10.1016/j.foodres.2010.09.011

Ryšavá, A., Vostálová, J., & Rajnochová Svobodová, A. (2021). Effect of ultraviolet radiation on the Nrf2 signaling pathway in skin cells. *International Journal of Radiation Biology*, *97*(10), 1383-1403. https://doi.org/10.1080/09553002.2021.1962566

Sangiovanni, E., Vrhovsek, U., Rossoni, G., Colombo, E., Brunelli, C., Brembati, L., Trivulzio, S., Gasperotti, M., Mattivi, F., Bosisio, E., & Dell'Agli, M. (2013). Ellagitannins from rubus berries for the control of gastric inflammation: *In vitro* and *in vivo* studies. *PLOS ONE*, *8*(8), e71762. https://doi.org/10.1371/journal.pone.0071762

Santa-Cecília, F. V., Vilela, F. C., da Rocha, C. Q., Dias, D. F., Cavalcante, G. P., Freitas, L. A. S., dos Santos, M. H., & Giusti-Paiva, A. (2011). Anti-inflammatory and antinociceptive effects of Garcinia brasiliensis. *Journal of Ethnopharmacology*, *133*(2), 467-473. https://doi.org/10.1016/j.jep.2010.09.036

Santhanam, R., Karunakaran, T., Sowndhararajan, K., Zulkifli, M. F., Kothandaraman, M. G., Aravindhan, V., & Ismail, W. I. W. (2022b). Photoprotective potential, cytotoxicity, and UPLC-QTOF/MS Analysis on bioactive solvent fractions of Moringa concanensis Nimmo Bark. *Evidence-based Complementary and Alternative Medicine*, *2022*, 1-10. https://doi.org/10.1155/2022/3781189

Santhanam, R. K., Fakurazi, S., Ahmad, S., Abas, F., Ismail, I. S., Rukayadi, Y., Akhtar, M. T., & Shaari, K. (2018). Inhibition of UVB-induced pro-inflammatory cytokines and MMP expression by Zanthoxylum rhetsa bark extract and its active constituent hesperidin. *Phytotherapy Research*, *32*(8), 1608-1616. https://doi.org/10.1002/ptr.6092

Schuch, A. P., Machado Garcia, C. C., Makita, K., & Menck, C. F. M. (2013). DNA damage as a biological sensor for environmental sunlight. *Photochemical & Photobiological Sciences*, *12*(8), 1259-1272. https://doi.org/10.1039/c3pp00004d

Schuch, A. P., Moreno, N. C., Schuch, N. J., Menck, C. F. M., & Garcia, C. C. M. (2017). Sunlight damage to cellular DNA: Focus on oxidatively generated lesions. *Free Radical Biology and Medicine*, *107*, 110-124. https://doi.org/10.1016/j.freeradbiomed.2017.01.029

Shusterove, L., & Romero, J. (2020). *The importance of coral reefs and how to ensure their longevity, a one health approach*, *12*. https://scholarworks.boisestate.edu/vip_2020/12

Siraichi, J. T. G., Felipe, D. F., Brambilla, L. Z. S., Gatto, M. J., Terra, V. A., Cecchini, A. L., Cortez, L. E. R., Rodrigues-Filho, E., & Cortez, D. A. G. (2013). Antioxidant capacity of the leaf extract obtained from *Arrabidaea chica* cultivated in Southern Brazil. *PLOS ONE*, *8*(8), e72733. https://doi.org/10.1371/journal.pone.0072733

Sliney, D. (2013). Balancing the risk of eye irritation from UV-C with infection from bioaerosols. *Photochemistry and Photobiology*, *89*(4), 770-776. https://doi.org/10.1111/php.12093

Sobiepanek, A., Milner-Krawczyk, M., Bobecka-Wesołowska, K., & Kobiela, T. (2016). The effect of delphinidin on the mechanical properties of keratinocytes exposed to UVB radiation. *Journal of Photochemistry and Photobiology B: Biology*, *164*, 264-270. https://doi.org/10.1016/j.jphotobiol.2016.09.038

South, A. P., Purdie, K. J., Watt, S. A., Haldenby, S., den Breems, N. Y., Dimon, M., Arron, S. T., Kluk, M. J., Aster, J. C., McHugh, A., Xue, D. J., Dayal, J. H. S., Robinson, K. S., Hasan Rizvi, S. M., Proby, C. M., Harwood, C. A., & Leigh, I. M. (2014). Notch1 mutations occur early during cutaneous squamous cell carcinogenesis. *Journal of Investigative Dermatology*, *134*(10), 2630-2638. https://doi.org/10.1038/jid.2014.154

Staniforth, V., Huang, W.-C., Aravindaram, K., & Yang, N.-S. (2012). Ferulic acid, a phenolic phytochemical, inhibits UVB-induced matrix metalloproteinases in mouse skin via posttranslational mechanisms. *The Journal of Nutritional Biochemistry*, *23*(5), 443-451. https://doi.org/10.1016/j.jnutbio.2011.01.009

Sun, Z., Hwang, E., Lee, H. J., Lee, T. Y., Song, H. G., Park, S.-Y., Shin, H.-S., Lee, D.-G., & Yi, T. H. (2015). Effects of Galla chinensis extracts on UVB-irradiated MMP-1 production in hairless mice. *Journal of Natural Medicines*, *69*(1), 22-34. https://doi.org/10.1007/s11418-014-0856-6

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209-249. https://doi.org/10.3322/caac.21660

Svobodová, A. R., Galandáková, A., Šianská, J., Doležal, D., Lichnovská, R., Ulrichová, J., & Vostálová, J. (2012). DNA damage after acute exposure of mice skin to physiological doses of UVB and UVA light. *Archives of Dermatological Research*, *304*(5), 407-412. https://doi.org/10.1007/s00403-012-1212-x

Svobodová, A., & Vostálová, J. (2010). Solar radiation induced skin damage: Review of protective and preventive options. *International Journal of Radiation Biology*, *86*(12), 999-1030. https://doi.org/10.3109/09553002.2010.501842

Takshak, S., & Agrawal, S. B. (2019). Defense potential of secondary metabolites in medicinal plants under UV-B stress. *Journal of Photochemistry and Photobiology B: Biology*, *193*, 51-88. https://doi.org/10.1016/j.jphotobiol.2019.02.002

Tamayoa, M. V., Schuch, A. P., Suárez, H. R. C., Salabarria, I. S., Pérez, T. H. G., Fuentes, C. E. P., Menck, C. F. M., & Sánchez-Lamar, A. (2018). Photoprotection of fractions obtained from Phyllanthus Orbicularis Extract against UVB -induced DNA damage. *Journal of Dermatologic Surgery, Research and Therapy*, 1-7. https://doi.org/10.29199/DERM.101011

Tarasova, O., Vermeulen, A., Sawa, Y., Houweling, S., & Dlugokencky, E. (2023, May 15). *The state of greenhouse gases in the atmosphere using global observations through 2021*. https://doi.org/10.5194/egusphere-egu23-15201

Terra, V. A., Souza-Neto, F. P., Frade, M. A. C., Ramalho, L. N. Z., Andrade, T. A. M., Pasta, A. A. C., Conchon, A. C., Guedes, F. A., Luiz, R. C., Cecchini, R., & Cecchini, A. L. (2015). Genistein prevents ultraviolet B radiation-induced nitrosative skin injury and promotes cell proliferation. *Journal of Photochemistry and Photobiology B: Biology*, *144*, 20-27. https://doi.org/10.1016/j.jphotobiol.2015.01.013

U.S. Food and Drug Administration. (2020, August 19). *Ultraviolet (UV) radiation* [Organization]. FDA. https://www.fda.gov/radiation-emitting-products/tanning/ultraviolet-uv-radiation

U.S. Food and Drug Administration. (2021, February 1). *UV lights and lamps: Ultraviolet-C radiation, disinfection, and coronavirus*. FDA. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/uv-lights-and-lamps-ultraviolet-c-radiation-disinfection-and-coronavirus

Verma, A., Zanoletti, A., Kareem, K. Y., Adelodun, B., Kumar, P., Ajibade, F. O.,

Silva, L. F. O., Phillips, A. J., Kartheeswaran, T., Bontempi, E., & Dwivedi, A. (2023). Skin protection from solar ultraviolet radiation using natural compounds: A review. *Environmental Chemistry Letters*. https://doi.org/10.1007/s10311-023-01649-4

Vogeley, C., Esser, C., Tüting, T., Krutmann, J., & Haarmann-Stemmann, T. (2019). Role of the Aryl Hydrocarbon Receptor in environmentally induced skin aging and skin carcinogenesis. *International Journal of Molecular Sciences*, *20*(23), 6005. https://doi.org/10.3390/ijms20236005

Wang, B., Jiang, H., Ma, N., & Wang, Y. (2016). Phosphorylated-p38 mitogen-activated protein kinase expression is associated with clinical factors in invasive breast cancer. *SpringerPlus*, *5*(1), 934. https://doi.org/10.1186/s40064-016-2636-0

Warren, L., & Casey, G. (2019). Photoprotection. In P. Hoeger, V. Kinsler, A. Yan, J. Harper, A. Oranje, C. Bodemer, M. Larralde, D. Luk, V. Mendiratta, & D. Purvis (Eds.), *Harper's textbook of pediatric dermatology* (1st ed., pp. 969-982). Wiley. https://doi.org/10.1002/9781119142812.ch79

Widel, M., Krzywon, A., Gajda, K., Skonieczna, M., & Rzeszowska-Wolny, J. (2014). Induction of bystander effects by UVA, UVB, and UVC radiation in human fibroblasts and the implication of reactive oxygen species. *Free Radical Biology and Medicine*, *68*, 278-287. https://doi.org/10.1016/j.freeradbiomed.2013.12.021

World Meteorological Organization. (2021, January 6). *Record-breaking 2020 ozone hole closes*. https://public.wmo.int/en/media/news/record-breaking-2020-ozone-hole-closes

Wu, C.-H., Liang, C.-H., Shiu, L.-Y., Chang, L.-C., Lin, T.-S., Lan, C.-C. E., Tsai, J.-C., Wong, T.-W., Wei, K.-J., Lin, T.-K., Chang, N.-S., & Sheu, H.-M. (2011). Solanum incanum extract (SR-T100) induces human cutaneous squamous cell carcinoma apoptosis through modulating tumor necrosis factor receptor signaling pathway. *Journal of Dermatological Science*, S0923181111001216. https://doi.org/10.1016/j.jdermsci.2011.04.003

Xiao, J., Liong, E. C., Ching, Y. P., Chang, R. C. C., Fung, M. L., Xu, A. M., So, K. F., & Tipoe, G. L. (2013). Lycium barbarum polysaccharides protect rat liver from non-alcoholic steatohepatitis-induced injury. *Nutrition & Diabetes*, *3*(7), e81-e81. https://doi.org/10.1038/nutd.2013.22

Yamano, N., Kunisada, M., Kaidzu, S., Sugihara, K., Nishiaki-Sawada, A., Ohashi, H., Yoshioka, A., Igarashi, T., Ohira, A., Tanito, M., & Nishigori, C. (2020). Long-term effects of 222-nm ultraviolet radiation C sterilizing lamps on mice susceptible to ultraviolet radiation. *Photochemistry and Photobiology*, *96*(4), 853-862. https://doi.org/10.1111/php.13269

Yang, C.-C., Wu, C.-H., Wong, T.-W., Lai, F.-J., Wei, K.-C., Lin, T.-K., Lin, C.-S., Zhao, J., Xiang, L., Kao, C.-H., Wang, Y.-J., Lan, C.-C. E., & Sheu, H.-M. (2021). Effects of Solanum undatum extract (SR-T100) on photocarcinogenesis and photoaging of actinic keratosis. *The Journal of Dermatology*, *48*(3), 344-352. https://doi.org/10.1111/1346-8138.15703

Yang, Y., Li, W., Li, Y., Wang, Q., Gao, L., & Zhao, J. (2014). Dietary Lycium barbarum Polysaccharide Induces Nrf2/ARE Pathway and Ameliorates Insulin Resistance Induced by High-Fat via Activation of PI3K/AKT Signaling. *Oxidative Medicine and Cellular Longevity*, *2014*, 145641. https://doi.org/10.1155/2014/145641

Yap, W. N. (2018). Tocotrienol-rich fraction attenuates UV-induced inflammaging: A bench to bedside study. *Journal of Cosmetic Dermatology*, *17*(3), 555-565. https://doi.org/10.1111/jocd.12421

Yoshizaki, N., Fujii, T., Masaki, H., Okubo, T., Shimada, K., & Hashizume, R. (2014). Orange peel extract, containing high levels

of polymethoxyflavonoid, suppressed UVB-induced COX-2 expression and PGE_2 production in HaCaT cells through PPAR-γ activation. *Experimental Dermatology*, *23*, 18-22. https://doi.org/10.1111/exd.12394

Yuan, X.-Y., Pang, X.-W., Zhang, G.-Q., & Guo, J.-Y. (2017). Salidroside's protection against UVB-mediated oxidative damage and apoptosis is associated with the upregulation of Nrf2 expression. *Photomedicine and Laser Surgery*, *35*(1), 49-56. https://doi.org/10.1089/pho.2016.4151

Zinovkina, L. A. (2018). Mechanisms of Mitochondrial DNA repair in mammals. *Biochemistry (Moscow)*, *83*(3), 233-249. https://doi.org/10.1134/S0006297918030045