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Exploring the plant kingdom for the development of novel sunscreen formulations

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Exposure to solar radiation, particularly to its ultraviolet (UV) components has a variety of harmful effects on human skin, ranging from mild inflammatory effects to as severe as causing several types of cancers. Thus, synthetic sunscreens have been introduced to the market to be used as protectants against harmful UV radiation. However, with the realization of the adverse effects associated with the synthetic sunscreen products, there is an increasing demand for sunscreens of herbal origins. Dr. Mayuri Napagoda and her team explain here the significance of plant extracts and plant secondary metabolites for the development of sunscreens with high efficiency and low side-effect profiles while sharing their latest research findings in the field.

Too much sunlight damage your skin

Life on earth is impossible without the sun. However, as the famous quote says “too much of everything is as bad as too little,” the excessive exposure to sunlight is as unhealthy as receiving no sunlight at all. To get a better understanding of the impact of excessive solar radiation, a brief overview of the solar electromagnetic spectrum is given below.

Sunlight is electromagnetic energy that propagates as both electrical and magnetic waves in the form of packets of energy known as “photons.” Depending on the frequency or wavelength of the electromagnetic radiation, the electromagnetic spectrum is divided into different regions from the lowest to the highest frequency as radio waves, microwaves, infrared, visible light, ultraviolet, X-rays, and gamma rays (Fig 1). The most critical components of the solar electromagnetic radiation are infrared radiation (IR) which is the primary source of heat, visible light to which the human eye is most sensitive and ultraviolet (UV) radiation which can ionize atoms.

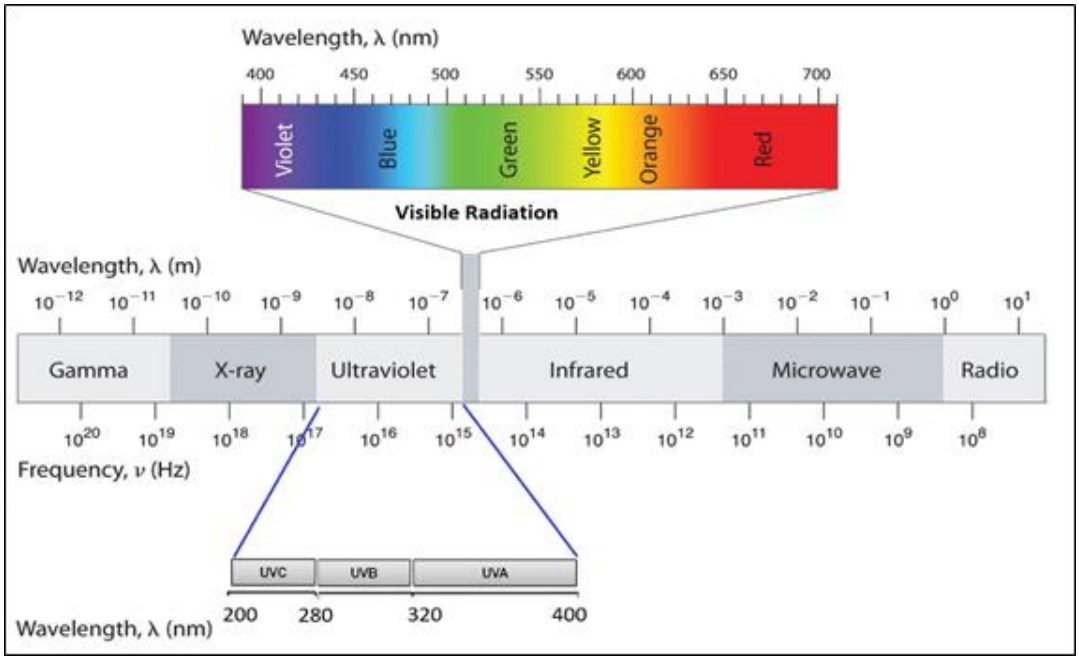

Fig. 1: Electromagnetic spectrum
(Origin of the picture: https://www.google.com/search)

The solar UV radiation is classified into three major categories depending on the wavelength; UV-A (320-400 nm), UV-B (280-320 nm) and UV-C (200-280 nm). Over 90% of solar UV light is comprised of UV-A which is capable of penetrating deep into the epidermis which is the outer most layer of the skin as well as into the dermis which lies beneath the epidermis and consists of dense irregular connective tissues. UV-A radiation is known as “aging rays” and could result in premature photoaging (accelerated skin aging) and necrosis (death) of endothelial cells thus damaging dermal blood vessels. Besides, it can lead to structural damage of the DNA and impairment of the immune system resulting in high susceptibility to infections and even malignant melanoma, a type of skin cancer that accounts for about 75% of skin cancer deaths worldwide. UV-B radiation makes up 4 to 5% of solar UV light and is known as “burning rays” that acts mainly in the epidermal basal cell layer of the skin. It is more genotoxic than UV-A and is primarily responsible for sunburn, erythema (superficial reddening of the skin), inflammation, hyperpigmentation, wrinkling, local immunosuppression, photoaging, and photo-carcinogenesis. Although UV-C possesses the highest potential for biological damage in all forms of life, it gets efficiently filtered by the stratospheric ozone layer, thus not yet considered a major factor in solar exposure of human beings (Clydesdale et al., 2001: Trautinger 2001: Afaq and Mukhtar, 2002).

During the past few decades, the anthropogenic activities led to substantial damage to the protective ozone layer and resulted in a significant increase in solar radiation reaching the earth. Thus, the incidence of various diseases related to the excessive exposure to UV radiation has exponentially increased over the recent years (Napagoda et al., 2016). The strength of sunburn-producing UV radiation at a particular place and time is given as the UV Index or UVI (Fig 2) which is usually used as an indicator of the

potential for skin damage. The UVI was developed by World Health Organization (WHO) and World Meteorological Organization (WMO) with the collaboration of several other international agencies to raise public awareness and also to alert people about the need of adopting protective measures when exposed to UV radiation.

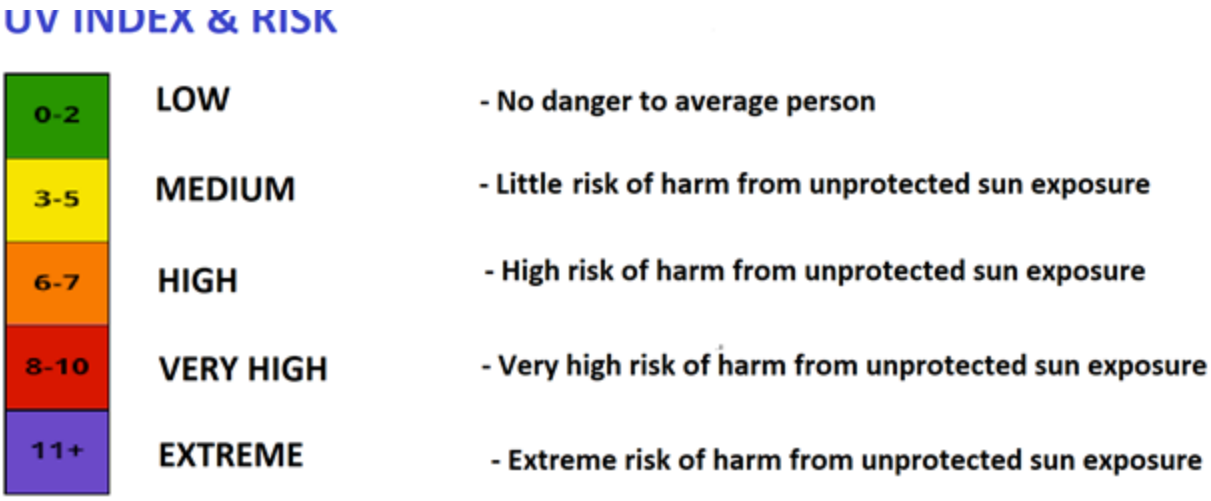

Fig.2: The UV index
(Origin of the picture: https://www.optika.com.mt/eye-health/uv-rays/uv-index-chart/)

To protect against UV damage, human skin is equipped with an elaborate defense system; however, the intense or overexposure to UV radiation would overwhelm these defense mechanisms. Staying in the shade and abstain from outdoor activities in high sunlight intensity is the best method to avoid the exposure to solar UV radiation, yet it is impractical and not always possible. Thus, various other preventive measurements such as the use of protective clothing, hats, and glasses, application of topical sunscreens on the skin, consumption of oral photoprotective agents, have been adopted by people to reduce the harmful effects caused by UV radiation.

Sunscreens as skin saviors

Sunscreen is a product which is applied to the skin and contains UV-absorbing, reflecting and/or scattering active molecules. The active particles on the sunscreens are also called photoprotective agents and they can either prevent the damage of the UV radiation or modulate different cellular responses to UV radiation to stop tumor promotion and progression. Topical sunscreens are broadly categorized into physical blockers and chemical absorbers. Physical blockers reflect or scatter UV photons while chemical absorbers absorb high-intensity UV photons (Gupta, 2013). Physical blockers include inorganic substances like titanium dioxide and zinc oxide while organic substances like oxybenzone, octylmethoxy cinnamate, etc. are examples of chemical absorbers. Although UV filters like titanium dioxide and zinc oxide are effective as

sunscreens, they tend to be opaque and white on the skin and consequently are unacceptable for cosmetic use.

SPF (sun protection factor) value is an indicator in sunscreens that is defined as the level of photoprotection offers by a sunscreen product when it is applied at a thickness of 2 mg/cm^3 skin. The protection percentage from UV radiation differs in each sunscreen product depending on its SPF value. Sunscreens are usually categorized as minimal sun protection products (SPF < 12), moderate sun protection products (SPF 12-30) or high sun protection products (SPF ≥ 30). When SPF is 15, it provides > 93% protection against UV-B, and SPF +30 provides 97% protection from UV-B. Generally, sunscreens with an SPF value of 15 or higher are highly recommended (Napagoda et al., 2016). SPF reflects mainly the acute protection against UV-B, but it does not indicate a product's protection against UV-A. It is not applicable to indicate SPF value related to UV-A, because UV-A is thousand times less likely to cause erythema when compared with UV-B. Though there is no uniformly accepted indicator for UV-A protection, critical wavelength, minimal persistent pigment darkening (MPPD) and UV-A/UV-B ratio are sometimes used to assess UV-A protection.

Although the ideal sunscreen should provide good protection throughout the whole UV spectrum (i.e., a broad range of protection), most of the commercial sunscreen products are highly effective against UV-B, but not against UV-A. Besides, a broad spectrum sunscreen should be photostable and remain in place after perspiration or swimming. Moreover, it should be chemically inert, non-toxic and should not cause irritation or contact allergy (Ho, 2001). These should be formulated in a cosmetically acceptable form. Thus, commonly sunscreen agents are incorporated as creams, gels, oils, and lotions.

Compounds, such as bemotrizinol, avobenzone, bisoctizole, benzophenone-3, and octocrylene, are broad-spectrum agents and have proven to be effective against a broad range of solar spectrum both in experimental models and outdoor settings. However, the adverse side effects such as the development of irritant dermatitis, hypersensitivity, allergies, and even melanoma are associated with the use of products containing synthetic sunscreen agents. Therefore, the usage of natural/herbal sunscreens has gained considerable attention over the recent years, and several natural compounds with UV absorption property have been used to substitute for or to reduce the number of synthetic sunscreen agents (Napagoda et al., 2016).

Green sunscreens

Natural remedies have been used for centuries for treating skin conditions and a wide variety of dermatological disorders including inflammation, phototoxicity, psoriasis, atopic dermatitis, etc. Herbal materials to alleviate these conditions have presumably been selected by process of "trial and error," and the chemical composition and the pharmacological properties of some of these herbal remedies have been investigated in the quest of finding out more effective and safer topical photoprotective agents. Recent

studies have indicated that a wide variety of phytochemicals are capable of altering/correcting undesired cellular functions and thereby leading to a photoprotection. For example, green tea, black tea, *Aloe vera*, walnut extract, avocado, *Ginkgo biloba* have been evaluated for their protective effect against damage induced by UV radiation in cells, tissues, animals, and humans. Also, a wide variety of natural plant extracts such as *Mentha piperita*,*Azadirachta indica*, *Ocimum sanctum, Lycopersicon esculentum*, *Carica papaya, Rosa damascene*, *Hamamelis virginiana, Matricaria recutita, Aesculus hippocastanum, Rhamnus purshiana, Cinnamomum zeylanicum*, *Dracocephalum moldavica* and *Viola tricolor* have been reported with vigorous photoprotective activities. These extracts consist of numerous phytochemicals that could provide better effects on the skin due to the antioxidant, anti-inflammatory, melanin inhibiting, anti-mutagenic, anti-aging properties, etc (Zhao et al., 1999: Adhami et al., 2008: Gupta, 2013). Especially the presence of antioxidants like carotenoids, flavonoids, phenolics that are capable of interfering into free radical chain reactions would impart photoprotection against UV radiation. Moreover, antioxidants such as resveratrol, hydroxycinnamic acid, curcumin, caffeic acid, quercetin, etc. have been already exerted inhibitory effects on a plethora of cellular events at various stages of carcinogenesis (Zhao et al., 1999: Adhami, et al., 2008).

As natural molecules derived from plant extracts are offering an exciting avenue for further research, Dr. Napagoda and her colleagues initiated a comprehensive pharmacological and phytochemical study on the plants that have been utilized in Sri Lanka for skin care and dermatological disorders.

A way towards the development of herbal sunscreen formulations from Sri Lankan plants

The application of herbal formulations to enhance the complexion and to treat dermatological disorders has been practicing in Sri Lanka for over a thousand years. These traditional uses suggest that Sri Lankan flora is rich in phytochemicals that could be utilized in the pharmaceutical and cosmetic industry. However, this potential remains largely unexplored. To fulfill this knowledge gap, a preliminary study had been conducted to evaluate the photoprotective activity of eleven medicinal plants that have been employed in the indigenous medicine in Sri Lanka for dermatological disorders. This study has revealed an in-vitro SPF value ≥ 25 for six plant extracts: *Atalantia ceylanica* (Family: Rutaceae), *Hibiscus furcatus* (Family: Malvaceae), *Leucas zeylanica* (Family: Lamiaceae), *Mollugo cerviana* (Family: Molluginaceae), *Olax zeylanica* (Family: Olacaceae) and *Ophiorrhiza mungos* (Family: Rubiaceae). Several extracts were found to be photostable without any significant reduction in the SPF after exposition to direct solar radiation for 21 days. Moreover, strong radical scavenging potential was observed in some of the extracts signifying that sunscreens developed with those could boost the body's defense system against the formation of UV induced free radicals, thus resulting in superior photoprotection.

Inspired by these highly promising observations, initial experiments were conducted to develop sunscreen formulations from the hydroalcoholic extracts of these potent extracts (Fig 3). The UV absorption measurements were obtained for each formulation to determine its UV filtering potential and subsequently the SPF. To compare the efficacy of the herbal formulations, a commercial synthetic sunscreen, and the aqueous cream base was used as positive and negative controls respectively. Most of the formulations displayed high SPF, photostability and broad-spectrum of UV absorption and interestingly, the commercial synthetic sunscreen product was also not found to be superior to these herbal formulations (Napagoda et al., 2018 a: Napagoda et al., 2018 b). Therefore, this study demonstrated the suitability of Sri Lankan medicinal plants to be developed into commercial herbal sunscreens and the experiments are underway to enhance the bioavailability via nanotechnology, as well as to evaluate possible cytotoxicity on human skin.

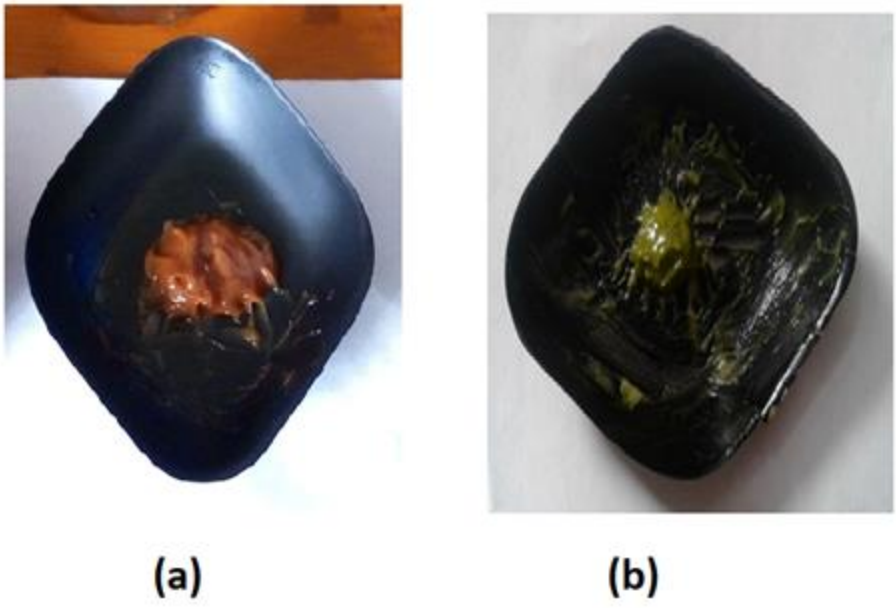

Fig. 3: Herbal sunscreen formulations developed from
(a) Leucas zeylanica
(b) Ophiorrhiza mungos

Novel approaches to enhance the sunscreen potential in herbal extracts

It has been reported that the efficacy of some of the photoprotective herbal extracts could be significantly increased due to improved solubility, permeability, and stability when those were formulated as nano-preparations.

One of the major concerns in the usage of herbal cosmetics is lower penetration and high compound instability of various cosmetic products for sustained and enhanced compound delivery. To overcome these disadvantages, nano-sized delivery systems have been introduced for sustained and improved delivery of phyto-derived bioactive

compounds in cosmeceutical products. Nanosizing of phyto-compounds also boosts the aesthetic value in various cosmeceutical products with enhanced skin protecting activities. A wide array of nano-sized delivery systems such as stable lipid nanoparticles, nanostructured lipid carriers, fullerenes, liposomes, etc. are emerging for the enhanced delivery of phyto-compounds in skin care. Curcumin, resveratrol, quercetin, vitamins C and E, genistein, and green tea catechins were successfully nanosized using various delivery technologies and incorporated into gels, lotions, and creams.

Furthermore, advanced lipid nanocarriers based on renewable vegetable resources (rice bran oil and raspberry seed oil) were developed by Niculae et al. and were incorporated into creams containing synthetic UV-B and UV-A filters, butylmethoxydibenzoylmethane and octocrylene. Both sunscreens exhibited improved photoprotection due to the synergistic effect between rice bran and raspberry seed oil and organic filters. The outcomes of this study could be considered as a milestone in both nanotechnology and skin cosmetology, paving the way towards the development of safer cosmetic formulations with antioxidant and photoprotective properties. Furthermore, this study revealed that an effective co-release of active ingredients could be achieved because of the high nano-structured vegetable oil content combined with a low amount of synthetic UV filters in the same carrier system (Niculae et al. 2014). Similarly, green coffee oil in combination with the synthetic sunscreen ethylhexyl methoxycinnamate showed a significant increase in SPF, highlighting the synergistic effect between plant oils and organic filters (Chiari et al., 2014). In a more recent study, novel sunscreen creams containing polymeric nanoparticles of morin, a plant flavonoid possessing both antioxidant and UV protection properties, were prepared and optimized. These formulations did not exhibit any cytotoxicity and showed high SPF values and antioxidant effects. When formulations were developed with morin nanoparticles along with physical sunscreen agents, excellent results were obtained (Shetty et al., 2015). These observations further support that nanoparticulate forms of polyphenols or other agents in sunscreen products along with physical sunscreen agents would provide additional desirable effects mainly due to the synergism in the photoprotective property.

With these latest developments, it is possible to hypothesize that more effective sunscreens of herbal origin would dominate the cosmeceutical market in a few years.

Conclusion:

Numerous studies have demonstrated that the herbal extracts and phytochemicals are highly efficient as sunscreen agents and nanotechnology-based techniques could offer innovative sunscreen products with enhanced bioavailability of the active ingredients with increased aesthetic value and prolonged effects. However, more research work is still required, especially to evaluate the cytotoxicity of these novel formulations before introducing them to the market.

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