



## PRODUCTS FROM MEDICINAL PLANTS WITH CHARACTERISTICS OF PHOTOPROTECTION AND ANTIOXIDANT -A REVIEW

### Biological Science

**Bruno Oliveira de Veras\*** Department of Biochemistry, Federal University of Pernambuco, Av. Prof. Moraes Rego, 1235, Recife, Brazil. \*Corresponding Author

**Fernanda Granja da Silva Oliveira** Department of Biochemistry, Federal University of Pernambuco, Av. Prof. Moraes Rego, 1235, Recife, Brazil.

**Penha Patricia Cabral Ribeiro** Department of Nutrition, Federal University of Rio Grande do Norte, Av. Sen. Salgado Filho, 3000 - Lagoa Nova, Brazil

**Raphael de Oliveira Nascimento Lacerda** Department of Biochemistry, Federal University of Pernambuco, Av. Prof. Moraes Rego, 1235, Recife, Brazil.

**Jackelly Felipe de Oliveira** Department of Biotechnology, Federal University of Paraiba, Castelo Branco – João Pessoa, Brazil.

### ABSTRACT

Formulations have undergone changes due to the requirement of consumers for products that have natural compounds in their composition. As one of the functions of cosmetics is the skin protection, the use of photoprotectors is currently considered the most effective measure for the prevention of damage caused by solar radiation, including against skin cancer. Thus, plants have the characteristic of producing various antioxidants secondary metabolites, such as flavonoids and phenolic compounds, substances considered great candidates for the development of eco-sustainable and low cost photoprotectors. This work aims to review the use of secondary metabolites of plant origin with antioxidant capacity, as well as its mechanism of action that confers photoprotective property, with a focus on cosmetic development.

### KEYWORDS

Plants; Antioxidant; Photoprotection; Ultraviolet Radiation.

### 1. INTRODUCTION

The development and production of cosmetics has been highly focused on natural cosmetics, and consumers have shown preference in using products that use natural raw materials, especially vegetable derivatives [1]. Natural products with antioxidant activity have gained prominence due to the decrease of undesirable effects in relation to synthetic antioxidants [2]. Following this trend in the world cosmetic sector, the insertion of raw materials with antioxidant activity is currently employed in the segments that aim at the inclusion of natural products and plant extracts in the formulations, as well as the development of photoprotectors and antioxidants [3,4,5].

Photoprotectors are compositions that protect the skin from solar radiation specifically to ultraviolet UV radiation. UV radiation is a range of the electromagnetic spectrum that lies between 100-400 nm and is divided into UVA (320-400 nm), UVB (290-320 nm) and UVC (100-290 nm) radiation [6]. In addition to sunburn and skin cancer, exposure to UV radiation is also related to early cutaneous aging, which can be explained by the reduction of reactive oxygen species (ROS), which are extremely harmful to tissues [7]. Natural chemical compounds with antioxidant and photoprotective activities are synthesized by plants as secondary metabolites, for example phenolic compounds and flavonoids, and these have shown important pharmaceutical and cosmetic potential, due to their biological actions already reported.

Thus, the proposal of this work is to bring an approach on the formulation of photoprotectors linking to the ability of plants to synthesize secondary metabolites with antioxidant capacity of great applicability in this segment.

### 2. BIBLIOGRAPHICAL REVIEW

#### 2.1. Secondary metabolites from plants

Plant metabolism can be divided into primary and secondary metabolism. Primary or basal metabolism can be defined as the set of common processes that are similar in plant species, leading to the synthesis of substances important for the maintenance of the plant's primary vital processes, such as carbohydrates, proteins, lipids and nucleic acids. In addition, these biosynthetic processes generate, in

addition to intermediates for other metabolic pathways, energy and compounds with reducing power, and occur from oxidation-reduction reactions of organic compounds [8]. In contrast, secondary (or special) metabolism results in the biosynthesis of highly complex compounds that do not have well-defined functions in plant metabolism, since they do not participate in the generation of energy, growth or cell division. These compounds are characterized by low molecular mass and restricted distribution among plants, being important for chemotaxonomy and systematics among families, genera and often even species [8,9].

In addition to protecting the plant against fungi, bacteria and other pathogens and mechanical damage, the secondary metabolites are believed to have a protective effect against oxygen-rich environments with antioxidant action. It can also act as attractive or repellent of pollinating insects, plant-feeding animals, protection against ultraviolet radiation, intraspecific signaling, allelopathy, water stress, among other functions [8]. The biosynthesis of secondary metabolites, in turn, is based on the formation of building blocks, which originate from the simple metabolites of amphibole metabolism. Glycolysis, Krebs cycle and pentoses cycle (Calvin cycle) give the compounds from these pathways which represent sources of carboxylic acids and sugars [9].

The classification of natural products is generally organized according to its biosynthetic pathway, since few of the pathways originate these metabolites, and because of this, there are few groups in which the secondary metabolites are classified (Table 1).

**TABLE 1.** Secondary metabolites with therapeutic interest and their biosynthetic origin [4, 8, 9, 13].

Biosynthetic Route	Metabolites
Acetyl-CoA	Polyacetylenes
	Polyketides
Amino acids	Flavonoids and stilbenes
	Amines
	True alkaloids
	Glycosinolates

	Cyan glycosides
1-deoxy-D-xylulose	Triterpenes
	Hemiterpene building block
	Diterpenes
	Monoterpenes
Mevalonate	Triterpenes and steroids
	Sesquiterpenes
Cinnamic acid	Cumarinas
	Phenylpropanoids
	Phenyl carboxylic acids

## 2.2. Phenolic compounds

Featuring both simple and complex structures, being comprised of at least one aromatic ring substituted by at least one hydroxyl group, phenolic compounds are secondary metabolites originating from plants and fungi. They are produced to protect against UV rays, insects, viruses and bacteria, and some species produce phenolic compounds to inhibit the growth of other plants (allelopathy) [10,11]. They also play an important role in breeding, protection against pathogens and predators, as well as contribute to the color and sensory characteristics of fruits and vegetables [12].

Phenolic compounds are considered as metabolites with a mixed biosynthetic pathway, since they are synthesized from two main metabolic pathways: the shikimic acid pathway and the mevalonic acid pathway [13]. They may occur in free form (aglycones), linked to sugars (glycosides), and also linked to proteins, and other secondary metabolites [8]. Phenols are commonly found in herbs, fruits, vegetables, grains, among others [15]. This class of compounds has been related to the health benefits derived from the consumption of high levels of fruits and vegetables, which can be used as dyes and flavoring agents, and are part of the human diet and have been associated with its antioxidant activity [16]. As examples of phenolic substances, coumarins, phenolic acids, quinones, tannins, lignins, besides stilbenes, phenylpropanoids and flavonoids can be mentioned [8]. Due to their structural diversity, this class of metabolites has been referred to as "polyphenols". The most natural form of occurrence is in the form conjugated to mono and polysaccharides, linked to one or more phenolic groups, and can occur as functional derivatives, such as esters and methyl esters [12]. Although such structural diversity results in the wide range of phenolic compounds, phenolic acids, flavonoids and tannins are considered the main phenols of the diet [17].

## 2.3. Flavonoids

Flavonoids are the largest group of phenolic compounds of plant origin, accounting for more than half of the eight thousand phenolic compounds that occur naturally. They are compounds with low molecular weight, with 15 carbons arranged in the configuration C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub> [12]. The basic chemical structure of flavonoids is based on two aromatic rings A and B, joined by a 3-carbon bridge, usually a heterocyclic ring. Ring A is derived from the acetate / mevalonate pathway, while ring B is derived from phenylalanine via the chiquimate pathway. Ring A is fused to the sixth carbon of ring C and at the 2-position there is a phenyl group as substituent. Ring C may be a heterocyclic pyran ring, which gives rise to the basic structures of leucoanthocyanins and anthocyanidins, called the flavana nucleus. Because the C-ring presents as a pyrone, the formation of the flavones, flavonols, flavanones, isoflavones, chalcones and aurones occurs, receiving the denomination of 4-oxo-flavonoid nucleus [12, 18].

In addition, flavonoids exhibit a characteristic antioxidant activity, which is related to their ability to eliminate free radicals, to donate hydrogen atoms or electrons, or chelates of cations of metal compounds [12]. The complex chemical structure of flavonoids, as well as the diversity of their molecules, makes the structure-activity relationship more complicated than phenolic acids. Some of the structural features and nature of the substitutions in rings B and C may determine the antioxidant activity of flavonoids. The degree of hydroxylation and the positions of the hydroxyl groups on ring B, in particular a ring B ortho-dihydroxy structure in the positions (known as the "catechol" group), results in an increased activity as greater radical stability is conferred by relocation [12], or may also act as a preferred bonding site for metals. The presence of the so-called pyrogallol group (hydroxyl groups at the 3', 4' and 5' positions in the B ring) may increase the antioxidant activity of flavonoids compared to those with a single hydroxyl group. These compounds can act as pro-oxidative substances [19].

Another feature that can be mentioned about the antioxidant structure-activity relationship of flavonoids is the presence of a double bond between carbon 2 and 3, conjugated with the 4-oxo group, in ring C, which would increase antioxidant capacity [20]. These double bonds at carbons 2 and 3, associated with the hydroxyl group at carbon 3 in ring C, would increase antioxidant activity, as an example of the kaempferol molecule [19]. In addition to the remarkable antioxidant activity, the flavonoids present other activities, such as antitumor, antiviral, anti-inflammatory and photoprotective [12]. These biological activities make flavonoids an important source of bioactive compounds, which may contribute to the development of new drugs.

## 1.3. Natural photoprotectors and antioxidants from medicinal plants

Based on the chemical structure of organic sunscreens, we can verify the presence of aromatic rings, as well as the use in the cosmetic sector of organic filters derived from cinnamic acid and salicylate, products of natural origin. Additionally, with the constant search for new photostable molecules for use in sunscreens, the development of photoprotectors with filters based on natural products has been outstanding. This research involves, mainly, the absorption capacity of ultraviolet light by the chromophore groups of the molecule, associated to the possible antioxidant activity [21].

Several natural compounds, mainly from vegetal species, can fulfill these requirements, and the scientific literature has presented several vegetal derivatives with antioxidant activity, which chemical composition presents substances with aromatic rings, as for example propiophenones, caffeic acid derivatives, lignans and flavonoids [3,21,22]. Thus, the antioxidant and photoprotective activity of vegetable derivatives rich in these classes of secondary metabolites represents, therefore, great potential for the development of formulations.

## 2.5. The role of antioxidants

The aerobic metabolism involves several chemical reactions, among them mechanisms of oxide-reduction and transfer of electrons. In this way, free radicals can be considered as one of the mediators of cellular metabolism and are molecules that have a pair of highly reactive, unpaired electrons. The free radicals are essential for the processes of energy production, cell growth, chemical signaling and synthesis of important biomolecules [23]. Free radicals are deactivated by endogenous agents, such as enzymes (S-glutathione peroxidase, catalase and superoxide desmutase), or by substances obtained through ingestion, such as vitamins, minerals and substances derived from the secondary metabolism of plants, which are characterized by its antioxidant capacity [24].

Oxidative stress is a condition due to the imbalance between the production of free radicals and the stabilization of these by endogenous or exogenous antioxidants. The main agents that induce oxidative stress related pathogens are reactive species that have an unpaired electron in an oxygen atom, thus characterizing the Reactive Oxygen Species (ROS) or nitrogen (RNS). Generally, antioxidants are those that can slow, prevent or repair the oxidative damage caused by ROS to a target molecule. Antioxidants can protect skin from free radicals by various means, and can be incorporated into cosmetic products, such as sunscreens, to reduce the oxidative damage caused by sun-induced ROS. Several studies have demonstrated the beneficial effects of the association between sunscreens and antioxidants, and these associated formulations have obtained better results in protection against UV radiation damage [26,27].

## 2.6. Skin and solar radiation

Solar radiation comprises part of the electromagnetic spectrum, and is emitted in different wavelength ranges, ranging from 290 nm to 3000 nm, and includes ultraviolet radiation, ranging from UVC (200-290 nm), UVB (290- 320 nm) and UVA (320-400 nm); (760-3000 nm) [28,29]. The infrared radiation can be detected in the form of heat, the visible radiation detected by the optical system through the colors and the ultraviolet radiation through the photochemical reactions [30]. UVC radiation, in turn, is completely absorbed by the ozone layer and therefore does not reach the Earth's surface, while 90% of UVB radiation is absorbed by ozone in the stratosphere and UVA radiation passes into the atmosphere almost without being absorbed [29].

The human skin is a complex organ, composed of three distinct tissues structurally and functionally: the epidermis, dermis and hypodermis.

The epidermis is the outermost layer, composed of keratinocytes, which make up the stratified squamous epithelium [29, 31]. This apparatus plays an extremely important role in protecting the organism against external agents. However, despite all structure, it is not able to completely block the penetration of solar radiation. Thus, the penetration depth of wavelength-oriented radiation, in which shorter wavelengths such as UVB radiation can reach the epidermis, while long wavelengths such as infrared radiation can reach the subcutaneous tissue [32]. In this way, the different regions of the solar spectrum can promote different damages to the skin, being the UVB radiation the most deleterious among them, because despite its penetration only in the epidermis, it has greater associated energy, and promotes greater damage to the skin, causing direct damages to cells and DNA, which can promote mutations [29].

Physiologically, the skin has mechanisms of natural protection against solar radiation, which presents satisfactory effectiveness only in certain limits of exposure. Among these mechanisms, melanin synthesis, thickening of the stratum corneum and epidermis, formation of urocanic acid, mechanisms of DNA repair and activation of endogenous antioxidants [29] can be mentioned. Since these mechanisms are limited, the need for photoprotection is very important, which involves the use of clothing, hats and sunglasses specific to sun protection, as well as the correct use of photoprotective cosmetic products [33].

When these radiation protection mechanisms fail the effects of ultraviolet radiation are problematic, such as the onset of erythema (sunburn), photoaging, changes in the immune system and skin cancer, and UVB radiation is completely carcinogenic after prolonged exposure. Skin cancer and photoaging have been gaining great prominence given the presented marked growth over the years throughout the planet, presenting epidemic proportions. According to data from the Brazilian National Cancer Institute, the lethality of melanoma, the most frequent type of cancer, is high [34]. In this way, skin protection against solar radiation gain great relevance for the preservation of human health and photoprotectors are currently considered as the most effective measure for the prevention of damages caused by solar radiation, including against skin cancer [32, 33].

## 2.7. Development of cosmetic formulations

The development of cosmetics from natural raw materials requires a serious and thorough study, with the proper characterization of the botanical, agronomic, phytochemical, pharmacological, toxicological, pharmacotechnical aspects and development of analytical methodologies [35]. For the development of a photoprotective product, several characteristics must be considered before choosing the pharmaceutical form, in addition to safety and efficacy. The type of product, target consumer, body part, additional activities inserted to the product (antioxidant substances), aspect (color, odor), solubility of the sunscreen in the vehicle, are some examples of important characteristics to be analyzed [36]. In this way, it becomes possible to choose the ideal pharmaceutical form for the incorporation of the sunscreen.

The evaluation of the effectiveness of photoprotectors is performed by analyzing their ability to protect the skin against erythema and edema, reducing the risk of burns and carcinoma of basal and thorny layer cells [37]. One of the most used ways of evaluating the effectiveness of the protectors is the determination of the Solar Protection Factor (SPF) [38].

The determination of SPF can be performed by *in vitro* and *in vivo* methodologies, and *in vitro* tests have advantages such as speed, reproducibility, lower cost and non-exposure to risks by volunteers or animals. These methods use serial dilutions and spectrophotometric analysis [38, 39]. The spectrophotometric method of diluted alcohol solutions is one of the most widely used *in vitro* methods, as it has been shown to be fast, efficient and has good correlation with *in vivo* tests, having as a disadvantage the restricted use of substances insoluble in the solvent suggested by the method, such as for example the physical filters [6, 39].

Cosmetic formulations with photoprotective action usually have a combination of two or more sunscreens, aiming at raising the SPF (Sun Protection Factor) and making protection in the UVA and UVB bands more effective. The sunscreens used in the formulations can be classified into organic (also called chemical) or inorganic (also called physical); and in UVA, UVB or UVA/UVB filters, based on the region of the ultraviolet spectrum in which they absorb radiation [25, 33].

Inorganic filters are those that form a physical barrier against the penetration of solar radiation through the skin, reflecting UV-Vis radiation, and therefore are also considered "physical" filters. The main inorganic filters available today are zinc oxide (ZnO), which provides UVA / UVB protection, and titanium dioxide (TiO<sub>2</sub>), which provides UVB protection. These filters are recommended for the formulation of photoprotectors for children's use, sensitive and pregnant skin, as well as raising FPS, since they are considered safer and more photostable filters than organic filters [29, 33]. Organic sunscreens are aromatic compounds conjugated to a carbonyl group and to a radical in the "ortho" and "para" positions, with electron donor groups replacing these positions in the aromatic ring. The absorption of the radiation occurs at a certain wavelength, passing the molecule to a more excited, higher energy state, and when they return to ground state, they emit the energy absorbed into the atmosphere at a longer wavelength, less harmful to the skin. Due to this process, they are also considered "chemical" filters. They recover the ability to absorb UV radiation repeatedly, thus characterizing their photostability [29, 33]. As examples of organic sunscreens, there may be mentioned *p*-aminobenzoic acid and derivatives, cinnamic acid derivatives, salicylates, benzophenones, camphor derivatives, dibenzoylmethane derivatives and anthranilates [29, 33].

In addition to the choice of sunscreens, it is important to plan the influence of the other ingredients in the photoprotective formulation, and the choice of the vehicle is an important factor for a better acceptance of the product and obtaining the desired FPS level. Several pharmaceutical forms can be used for the incorporation of a sunscreen and can be classified according to the solubility in vehicles based on water, oil, water and oil, ethanol and oil or on consistency [36]. Emulsions have been the most used forms in the preparation of photoprotectors in recent years, as they allow the incorporation of lipo and hydrophilic filters, which can act synergistically, thus improving the effectiveness of the product. Some authors consider the best vehicles for products for this purpose, but, although widely used, this type of vehicle has disadvantages, such as instability of the preparations, which occurs due to the presence of molecules with different solubilities, requiring the use of substances which prevent phase separation, which may be a pharmacotechnical and cost problem for the formulation.

The effectiveness of the photoprotective formulation, in turn, is directly linked to consumer acceptance of the product, since it is not only the levels of FPS that guarantee sun protection, but also the amount, form and frequency of application of the photoprotective product to the skin to be protected [33, 40]. In this way, product quality is an important parameter both for product acceptance and for consumer safety, since products that do not meet the quality parameters can cause degradation of the components of the formula, giving rise to substances with high toxicity and health risks. Therefore, studies of quality control and stability of cosmetics play a key role in the development of formulations [40].

By evaluating the stability of the cosmetic product, it is possible to evaluate the performance of the product exposed to environmental conditions, from the manufacturing to the shelf life. Thus, the stability study provides important information on the safety and efficacy of the product, as well as a prediction of consumer acceptance, as these studies are considered predictive under conditions that are also intended to accelerate possible changes that may occur under normal conditions of the market and transportation [42]. Therefore, the stability study of cosmetic products contributes to the development of the formulation, besides providing important information about the storage [42].

Some aspects should be considered in stability studies. Physical factors encompass the original physical properties like appearance, color, odor and uniformity. Chemical factors should involve the chemical integrity of the active components as well as the contents of these ingredients. Regarding the microbiological factors, cosmetic products must maintain the microbiological characteristics, according to specified requirements [42]. Taking these factors into account, tests should be performed to obtain information about the stability of the products in a short period of time. Therefore, samples should be stored under both extreme conditions and recommended storage conditions to accelerate changes that may occur within the expiration date. Stability tests follow a sequence of tests called preliminary, accelerated and shelf tests [42].

### 3. CONCLUSION

Due to the worldwide trend towards the development of cosmetics from natural products, some secondary metabolites originating from medicinal plants, such as phenolic compounds and flavonoids, have gained prominence. With a marked antioxidant capacity, an important feature to avoid the oxidative stress due to the exposure of the skin to ultraviolet light, vegetal extracts show an important pharmaceutical and cosmetic potential for the development of new cosmetics with photoprotective and antioxidant capacity.

### REFERENCES

- [1] Iha S.M. et al. (2008). "Estudo fitoquímico de goiaba (*Psidium guajava* L.) com potencial antioxidante para o desenvolvimento de formulação fitocosmética". *Brazilian Journal of Pharmacognosy*, 3,387-93.
- [2] Krishnaiah D., Rosalam S., Rajesh N. (2011) "A review of the antioxidant potential of medicinal plant species", *Food and Bioproducts Processing*, 2017-2033.
- [3] Oliveira-Júnior, R.G. et al. (2012) "Phytochemical screening, antioxidant and antibacterial activity of extracts from the flowers of *Neoglaziovia variegata* (Bromeliaceae)", *Journal of Chemical and Pharmaceutical Research*, 4, 4489-4494.
- [4] Almeida J.R.G.S. et al. (2012) "Antinoceíptiva activity of ethanol extract from *Duguetia chrysoarpa* Maas (Annonaceae)". *The Scientific World Journal*, 1-6.
- [5] Polonini H.C. et al. (2011) "Fotoprotetores naturais como instrumento de ação primária na prevenção do câncer de pele", *Revista de Atenção Primária à Saúde*, 14, 216-223.
- [6] Nascimento C.S. et al. (2009) "Incremento do FPS em formulação de protetor solar utilizando extratos de própolis verde e vermelha", *Revista Brasileira de Farmácia*, 30, 334-339.
- [7] Velasco M.V.R. et al. (2008) "Associação da Rutina com p-Metoxicinamato de Octila e Benzofenona-3: Avaliação In Vitro da Eficácia Fotoprotetora por Espectrofotometria de Refletância", *Latin American Journal of Pharmacy*, 27(1), 23-27.
- [8] Rezende, F.M., Rosado D. Moreira F.A., Carvalho W.R.S. (2016) "Vias de síntese de metabólitos secundários em plantas". In: PENA, M.H. [et al.]. (Org.). *VI Botânica no Inverno 2016*. 1ª Ed. São Paulo: Instituto de Biociências da Universidade de São Paulo, 93-104.
- [9] Kreis W. et al. (2016) "Biossíntese de metabólitos primários e secundários". In: SIMÕES, C. M. O.; SCHENKEL, E. P.; GOSMANN, G.; et al, *Farmacognosia: da Planta ao medicamento*, Porto Alegre/Florianópolis Ed. Universidade/UFRGS/Ed. Da UFSC, p. 69-81.
- [10] Simões C.M.O., Schenkel E.P., (2002) "A pesquisa e a produção brasileira de medicamentos a partir de plantas medicinais: a necessária interação da indústria com a academia", *Revista Brasileira de Farmacognosia*, 12(1),35-40.
- [11] Heleno S.A., Ferreira I.C.F.R., Calheta R.C., Esteves A.P., Queiroz M.J.R.P. (2015) "Cytotoxicity of *Coprinopsis atramentaria* extract, organic acids and their synthesized methylated and glucuronate derivatives", *Food Research International*, 55, 170–175.
- [12] Balasundram N.A.B., Sundram K.B., Samman S.A. (2006) "Phenolic compounds in plants and agri-industrial by-products: Antioxidant activity, occurrence, and potential uses", *Food Chemistry*, 99(1), 191–203.
- [13] Vizzotto M., Krolow A.C.R., Weber G.E.B. (2010) "Metabólitos encontrados em plantas e sua importância. Embrapa Clima Temperado-Documentos", Embrapa Clima Temperado, 16.
- [14] Psotova J., Svobodova A., Kolarova H., Walterova D. (2006) "Photoprotective properties of *Prunella vulgaris* and rosmarinic acid on human keratinocytes", *Journal of Photochemistry and Photobiology B: Biology*, 84, 167-174.
- [15] Svobodová A., Popova J., Walterová D. (2003) "Natural phenolics in the prevention of UV-induced skin damage", *Biomed Papers*, 147(2) 137–145.
- [16] Heim K.E., Tagliaferro A.R., Bobilya D.J. (2002) "Flavonoid antioxidants: chemistry, metabolism and structure-activity relationship", *Journal of Nutritional Biochemistry*, 13(10), 572-584.
- [17] King A., Young G. (1999) "Characteristics and occurrence of phenolic phytochemical", *Journal of the American Dietetic Association*, 99, 213-218.
- [18] Coutinho M.A.S., Muzitano M.F., Costa S.S. (2009) "Flavonoides: potenciais agentes terapêuticos para o processo inflamatório", *Revista Virtual de Química*, 1(3), 241-256.
- [19] Seeram N.P., Nair M.G. (2002) "Inhibition of lipid peroxidation and structure-activity-related studies of the dietary constituents' anthocyanins, anthocyanidins, and catechins", *Journal of Agricultural and Food Chemistry*, 50(19), 5308–5312.
- [20] Souza-Moreira T.M., Salgado H.R.N., Pietro R.C.L.R. (2010) "O Brasil no contexto de controle de qualidade de plantas medicinais", *Brazilian Journal of Pharmacognosy*, 20(3), 435-440.
- [21] Guaratini T., Callejon D.R., Pires D.C., Lopes J.N.C. (2009) "Fotoprotetores derivados de produtos naturais: perspectivas de mercado e interações entre o setor produtivo e centros de pesquisa" *Química Nova*, 32(3), 717-721.
- [22] Alencar-Filho J.M.T. et al. (2016) "Flavonoids as photoprotective agents: a systematic review", *Journal of Medicinal Plants Research*, 20(47), 848-864.
- [23] Barreiros L.B.S., David J.M., David J.P. (2006) "Estresse oxidativo: relação entre geração de espécies reativas e defesas do organismo", *Química Nova*, 29(1), 113-123.
- [24] Alves R.E., Brito E.A., Rufino M.S.M., Sampaio C.G. (2008) "Antioxidant activity measurement in tropical fruits: A case study with acerola", *Acta Horticulturae*, 1, 299-305.
- [25] Barel A., Paye M., Maibach H. (2009) "Handbook of cosmetic science and technology" 668.
- [26] Wang M. et al. (2016) "Sharing and community curation of mass spectrometry data with Global Natural Product Social Molecular Networking", *Nature Biotechnology*, 34(8), 828-837.
- [27] Haag S.F. et al. (2014) "Enhancement of skin radical scavenging activity and stratum corneum lipids after application of a hyperforin-rich cream" *European Journal of Pharmaceutics and Biopharmaceutics*, 86(2), 227-233.
- [28] Akhalaya M.Y., Maksimov G.V., Rubin A.B., Lademann J., Darvin M.E. (2014) "Molecular action mechanisms of solar infrared radiation and heat on human skin" *Ageing Res. Rev*, 16, 1–11.
- [29] Souza A.A., Laverde-Júnior A. (2002) "Aplicação da espectroscopia de ressonância magnética nuclear para estudos de difusão molecular em líquidos: a técnica DOSY", *Química Nova*, 15(6) 1022-1026.
- [30] Flor J., Davolos M.R., Correa M.A. (2007) "Protetores solares", *Química Nova*, 30(1),153-158.
- [31] Marionnet C., Pierrard C, Golebiewski C., Bernerd F. (2014) "Diversity of Biological Effects Induced by Longwave UVA Rays (UVA1) in Reconstructed Skin", *PLoS ONE*, 9(8):e105263.
- [32] Sargent V.E, Travers J.B. (2016) "Examining the Differences in Current Regulatory Processes for Sunscreens and Proposed Safety Assessment Paradigm" *Regul Toxicol Pharm*, 79, 125-141.
- [33] Corrêa M.A. (2012) "Cosmetologia Ciência e Técnica", *Medfarma*, 194.
- [34] Instituto Nacional de Câncer. "Pele e Melanoma". [Online]. Available: [http://www2.inca.gov.br/wps/wcm/connect/tiposdecancer/site/home/pele\\_melanoma](http://www2.inca.gov.br/wps/wcm/connect/tiposdecancer/site/home/pele_melanoma). [Accessed: April. 30, 2018].
- [35] Klein S.M. et al. (2009) "In vitro studies investigating the effect of subcutaneous phosphatidylcholine injections in the 3T3-L1 adipocyte model: lipolysis or lipid dissolution?", *Plastic and Reconstructive Surgery*, 124(2):419-27.
- [36] Surman L.L. et al. (2009) "Potencialidades de Veículos Microemulsionados para Fotoprotetores Físicos", *Latin American Journal of Pharmacy*, 28(1), 133-140.
- [37] Violante I.M.P. et al. (2008) "Estudo preliminar da atividade fotoprotetora in vitro de extratos vegetais do cerrado de Mato Grosso" *Revista Brasileira de Farmacognosia*, 89(3): 175-179.
- [38] Andrade B.A. (2015) "Atividade fotoprotetora in vitro de espécies medicinais da caatinga pernambucana e incorporação em gel dermatológico", Universidade Federal de Pernambuco, Recife, 2015.
- [39] Mansur J.S., Breder M.V.R., Mansur M.C.A., Azulay R.D. (1986) "Determinação do fator de proteção solar por espectrofotometria", *Anais Brasileiros de Dermatologia*, 61, 121-124.
- [40] Milesi S.S., Guterres S.S. (2002) "Fatores Determinantes da Eficácia de Fotoprotetores" *Caderno de Farmácia*, 13(2) 81-87.
- [41] Mishra A.K., Mishra A., Chattopadhyay P. (2012) "Assessment of physical stability and photoprotective activity of topical formulations added with calendula oil", *Oriental Pharmacy and Experimental Medicine*, 12(1), 35-40.
- [42] Brazil, National Health Surveillance Agency (ANVISA) (2004) "Guia de Estabilidade de Produtos Cosméticos", 52.