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Cosmetics for the treatment of cutaneous hyperpigmentation

Corresponding author
Stela Regina Ferrarini
Universidade Federal de Mato Grosso
stela.ferrarini@ufmt.br

Natielle Moreira Costa
Universidade Federal de Mato Grosso

Livia Teixeira Oliveira
Universidade Federal de Mato Grosso

Abstract. Skin hyperpigmentation is a dermatological condition characterized by darkening of the skin due to increased melanin production. Various factors such as excessive sun exposure, skin inflammation, hormonal imbalance, and genetic predisposition can contribute to the development of these conditions, significantly affecting quality of life. This work aims to explore the efficacy of cosmeceuticals in the treatment of hyperpigmentation, focusing on products available in tropical regions like Brazil. To achieve this, a narrative literature review with a qualitative approach based on scientific articles, dissertations, and journals obtained through the Google Scholar, PubMed, and Science Direct platforms using the following search keywords: cosmeceuticals, cosmetics, skin lightening, skin regeneration, published between 2003 and 2023, in Portuguese and English languages, was conducted. The different types of hyperpigmentation, such as melasma, post-inflammatory hyperpigmentation, and solar lentigines, were discussed, addressing their clinical characteristics and pathophysiologies, presenting the main mechanisms involved in the formation of skin hyperpigmentation. Subsequently, the main active ingredients used in the treatment of hyperpigmentation were highlighted, such as niacinamide, retinol, vitamin C, kojic acid, arbutin, and hydroquinone. The mechanisms of action of each active ingredient and their scientific evidence of efficacy are discussed. Through a literature analysis, recommendations were provided for the appropriate and safe use of cosmetics in the treatment of skin hyperpigmentation, considering factors such as skin type, dermatological conditions, and sun protection measures. The work aims to contribute to advancing knowledge about the treatment of skin hyperpigmentation, providing updated information on the role of cosmeticals in this context.
Keywords: skin hyperpigmentation; skin lightening; lightening cosmetics

Introduction

Cutaneous hyperpigmentation is one of the signs of photoaging and is a dermatological concern that affects individuals of all ages and ethnicities (Draelos, Z. D., 2014; Martin, K. I.; Glaser, D. A., 2011). Hyperpigmentation occurs due to an increase in the production or deposition of melanin. Melanin is the primary molecular determinant of skin color that provides protection by limiting the absorption of solar radiation by approximately 50% to 70%. The biosynthesis of melanin takes place in melanocytes, cells with tyrosinase enzymes responsible for the transformation of melanin (Leal, C. A. E; Lara, S. G., 2019).

Excessive pigmentation can be caused by various factors, including, among them, age, hormonal imbalance, endocrine disorders, inflammation, and/or excessive sun exposure (Leal, C. A. E; Lara, S. G., 2019; Juhaszz, M. L.; Levin, M. K., 2018). Resulting in different patterns such as hyperpigmentation in the form of small lentigines on the cheeks due to cumulative sun exposure, pigmentation in the form of melasma present on the sides of the forehead, lateral jawline, and upper lip, and another form is post-inflammatory hyperpigmentation, which is a consequence of trauma or inflammation causing irregularities in the skin and dark spots in the affected areas (Plensdorf, S.; Livieratos, M.; Dada, N., 2017).

Each type of hyperpigmentation presents characteristics and ways of onset, and they respond differently to treatments (Oliveira, J. C.; De Andrade Sena, C. F., 2018). The pigments can be in the layers of the dermis and epidermis of the skin, and treatments need to penetrate these layers to take effect, and this is one of the difficulties in the treatment of skin blemishes. Usually, several active ingredients and different methods are used to achieve good results.(Draelos, Z. D., 2009).

Cosmeceuticals emerged in 1984 through Dr. Albert Kligman, noted dermatologist who invented this term to describe a category of products positioned between cosmetics and pharmaceuticals, which are intended to improve the appearance and the health of the skin (Sotiropoulou, G.; Zingkou, E.; Pampalakis, G., 2021). Cosmeceuticals demonstrate the ability to improve skin function by incorporating potent ingredients that work to prevent melanin synthesis and influence the biological function of the skin while providing nutrients to promote healthy skin (Brandt, F. S.; Cazzaniga, A.; Hann, M., 2011).

The correct use of sunscreens can prevent the appearance of dyschromias, which in turn prevents skin cancer. Sunscreens are used to protect the skin against solar rays, preventing spots and dyschromias. Sunscreen filters need to be applied several times a day. Sunscreens can be classified into physical or chemical filters, which have been replaced by inorganic and organic filters (Cabral et al, 2011).

Inorganic filters protect the skin from ultraviolet radiation by reflecting, dispersing, and/or absorbing radiation. Inorganic blockers are used in children and patients with a history of allergies (Vasconcelo, 2014). On the other hand, organic filters have a different mechanism of action; their conjugated aromatic compounds convert luminous energy into thermal energy, and the electrons are energized into an excited transient state. Thus, chemical filters act as energy catalysts, transforming ultraviolet radiation into heat (Lupi et al, 2009). Furthermore, organic filters are divided according to their action spectrum into UVB and/or UVA agents. A new UVB sunscreen protection grading system has been suggested: low protection, medium protection, high protection, and very high protection (Lupi et al, 2009).

The aim of this work was to develop a narrative literature review with a qualitative approach, focusing on cosmetics used in the treatment of cutaneous hyperpigmentation, a very common topical issue in tropical countries such as Brazil. This review was composed of electronic books, articles, dissertations, and journals obtained through research platforms such as Google Scholar, Pubmed, and Science Direct, using the following search keywords: cosmeceuticals, cosmetics, skin whitening, skin regeneration. The search covered the period from 2003 to 2023 and included publications in both languages Portuguese and English. Articles that presented free and fully accessible content addressing the objective of this review were selected. A total of 106 articles were found, of which 67 duplicate articles and those not relevant to the topic were excluded.

Contextualization and analysis

The beauty and uniformity of the skin are important aspects in society, potentially causing a negative impact on an individual's well-being, social life, and self-esteem. Facial hyperpigmentation is a common alteration in the general population, characterized by the appearance of dark and irregular spots on the skin where excessive melanocyte stimulation triggers the overproduction of melanin, dysregulating pigmentation control (Moura et al., 2017; Peretti et al., 2015). This disorder can occur due to two factors: extrinsic factors influenced by UV radiation exposure, such as lentigines, and intrinsic factors resulting from internal stimuli within the body, such as hormonal changes and post-inflammatory hyperchromias. Thus, cutaneous hyperpigmentation can be classified as melasma, post-inflammatory hyperpigmentation and solar lentigines (Oliveira, J. C.; De Andrade Sena, C. F., 2018).

Melasmas are skin spots, mainly present in exposed areas such as the face, particularly on the forehead and cheeks. They are caused by an acquired hyperpigmentation disorder resulting in increased melanin production in the skin. Melasmas have a brownish and grayish coloration and are typically acquired through sun exposure, hormonal changes, ultraviolet radiation, genetic influences, and predominantly occur during the reproductive period. Therefore, their higher incidence is observed in women than in men (Batista, E. F.; Mejia, D. P. M., 2011). Melasma is challenging to treat and the results are often unsatisfactory. Since it is a hyperpigmentation in easily visible areas, it not only affects the skin but also impairs the individual's self-esteem (Rodrigues, J. C., 2021).

Post-inflammatory hyperpigmentation is characterized by macules and patches with irregular shapes and dark pigmentation. It is triggered by traumas that cause lesions or inflammation such as acne, psoriasis, atopic dermatitis, among other reasons that lead to increased melanogenesis through cytokines released during the inflammation process (Da Silva, J. P. C.; Fernandes, F. P., 2019). This hyperpigmentation can occur at any age and the intensity of the spots' pigmentation varies according to the individual's skin phototype. When they are dark brown, they can remain on the skin for months or years, potentially worsening if exposed to UV radiation (Rodrigues, J. C., 2021).

Solar lentigines are macular lesions and rounded spots caused by acute or chronic exposure to sunlight, occurring due to changes in signaling in melanin production on the face (Plensdorf, S.; Martinez, J., 2009). During this proliferation, melanin produced in excess is stored in melanosomes in the basal layer of the epidermis, staining regions of the body that are more exposed to the sun, such as the

face, chest, arms, and hands. People with light skin generally have a higher likelihood of developing solar lentigines compared to those with darker skin tones (Plensdorf, S.; Livieratos, M.; Dada, N., 2017).

In light of this, skin-lightening cosmeceuticals have been an important ally in the treatment of cutaneous hyperpigmentation for skin tone uniformity through constituents that provide beauty-enhancing benefits. Some of these skin conditions can be difficult to treat, and cosmeceuticals are options that offer a potentially safer and more effective alternative in treatment, whether used alone or in conjunction with other established treatments (Sarkar, R.; Arora, P.; Garg, K., 2013). Below, Table 1 lists the main types of cutaneous hyperpigmentation and their characteristics.

Table 1. Presentation of the main types of cutaneous hyperpigmentation

Types of Hyperpigmentation	Characteristics	Main Causes	References
Melasma	Brownish and grayish spots.	Hypersensitivity to UV radiation and hormonal factors.	Rodrigues, J., C., 2021; Batista, E. F.; Mejia, D. P. M., 2012.
Post-inflammatory hyperpigmentation	Irregular macules and spots with dark pigmentation.	Traumas caused by lesions or inflammation on the skin.	Da Silva, J. P. C.; Fernandes, F. P., 2019; Rodrigues, J. C., 2021
Solar lentigines	Hyperpigmented and well-circumscribed macular lesions, varying in color from yellowish to dark brown.	Chronic and acute exposure to UV radiation and changes in melanin production signaling.	Plensdorf, S.; Livieratos, M.; Dada, N.,2017; Plensdorf, S.; Martinez, J., 2009

Main cosmeceuticals for the treatment of cutaneous hyperpigmentation

The treatment of cutaneous hyperpigmentation is based on the application of depigmenting or skin-lightening agents that act by inhibiting the biosynthesis of tyrosine. Melanin is the main responsible for skin pigmentation and has a beneficial effect in photoprotection against harmful UV lesions, been produced from epidermal melanocytes with basal keratinocytes (Moura M. C. et al., 2017; Pillaiyar, T.; Manickam, M., Namasivayam, V., 2017). Melanin is synthesized through the process of melanogenesis involving a combination of enzymatic and chemical catalytic reactions. It starts with the oxidation of L-tyrosine by tyrosinase into L-Dopa, thus converting into two types of melanins: eumelanin (black-brown) and pheomelanin (yellow-red), stored in melanosomes and found within keratinocytes (Bagatin, J. T., 2018).

Depigmenting cosmeceutical products aim to reduce hyperpigmentation and their formulations contain different types of active ingredients that act on all steps of the melanogenesis process (Da Silva, J. P. C.; Fernandes, F. P., 2019).

Main Depigmenting Actives
Niacinamide

Niacinamide, also known as nicotinamide (3-pyridine-carboxamide), is a water-soluble, physiologically active amide of niacin (vitamin B3) (Boonme, P. et al., 2009). Niacin is involved in the synthesis of the enzymes Nicotinamide Adenine Dinucleotide (NAD) and Nicotinamide Adenine Dinucleotide Phosphate (NADP) necessary for cellular metabolism and participates in various oxidation-reduction reactions, exerting multiple effects on the skin (Sarkar, R.; Arora, P.; Garg, K., 2013).

Topical use of niacinamide has been shown to be effective in reducing hyperpigmentation by modulatingindirectly the protease-activated receptor (PAR-2) and reducing the transfer of melanosomes to circulating keratinocytes. The results obtained may be due to the balance between positive regulation of melanogenesis in the hyperpigmented area and negative regulation by niacinamide (Silva, B. C. C., 2015; Sarkar, R.; Arora, P.; Garg, K., 2013). In other words, niacinamide is an active ingredient that contributes to improving skin appearance bylighteningand improvinghydration. The effects of niacinamide were observed in women with melasma who used niacinamide lotion for 6 weeks and showed improvements in skin tone by reducing spots (Vasconcelos, R. A. B., 2022).

Niacinamide is one of the main ingredients in cosmeceuticals commonly used for treatment of hyperpigmentation, with anti-inflammatory, antibacterial, and sebum-regulating actions. Therefore, it is also indicated for acne treatment, reducing significantly lesions caused by acne and preventing post-inflammatory hyperpigmentation. It was found that niacinamide concentrations of 2%, 2.5%, and 5% provided acceptable effects for consumers and it can be applied during the day

(Rodrigues, J. C., 2021; Pandey, A.; Jatana, G. K.; Sonthalia, S., 2023).

Retinoids

Retinoids are natural or synthesized components derived from vitamin A, an important nutrient for skin cell renewal. These actives are commonly used in the treatment of various pigmentation disorders such as melasma and post-inflammatory hyperpigmentation (Sarkar, R.; Arora, P.; Garg, K., 2013).

Retinoids are liposoluble molecules and therefore able to cross the cell membrane easily. When inside the cells, they bind to specific nuclear receptors (retinoic acid receptors) and modulate the expression of genes involved in cell proliferation and differentiation, regulating the production of specific proteins and enzymes (Babamiri. K; Nassab, R., 2010). Retinoids's effects on pigmentation can be explained through various mechanisms, including inhibition of oxidative stress, reduction of melanosome transfer and regeneration of the cellular matrix (Searle. T. A. F.; Ali, F. R., 2020).

The conversion of retinol occurs through oxidation to retinaldehyde, which is further oxidized to retinoic acid, its biologically active form. Topical retinoic acid is widely used in the treatment of melasma, acne and post-inflammatory hyperpigmentation due to its ability to reduce hyperpigmentation through epidermal cell renewal (Araujo, I. L.; Mejia, D. P. M., 2014). This process occurs because retinoids interfere with pigment transfer to keratinocytes, limiting contact between melanocytes and keratinocytes, favoring the loss of pigmentation through a process called epidermopoiesis (Sarkar, R.; Arora, P.; Garg, K., 2013).

Retinoids are potent depigmenting agents, with topical use recommended in concentrations of 0.3 to 1%. Clinical studies have even shown efficacy at a dose of 0.05% (Babamiri. K; Nassab, R., 2010; Bissett, D. L., 2009). Retinoids produce erythema, peeling, and are phototoxic. During the day, the use of sunscreens is recommended. The concentration depends on the therapeutic response, but the concentrations currently used range between 1 and 10% (Borges, 2010). Retinoids can be applied during the day or at night, but it is suggested that they be applied primarily at night because sunlight can sensitize the skin in some people.

Vitamin C (Ascorbic Acid)

Vitamin C, also known as ascorbic acid, is a water-soluble compound that oxidizes readily in an aqueous environment (Batista, E. F.; Mejia, D. P. M., 2012). Ascorbic acid exhibits anti-free radical action and acts as a cofactor in the hydroxylation of protein and lysine, amino acids involved in collagen production. It also serves as an electron donor in the aqueous compartment of cells, neutralizing free radicals produced by UV radiation and protecting intracellular structures from oxidative stress (Batista, E. F.; Mejia, D. P. M., 2012).

Studies reveal that vitamin C acts on the skin as an inhibitor of melanin formation by restricting the formation of o-quinone and oxidized melanin, resulting in skin spot lightening and increased collagen synthesis. In addition to its antioxidant action, it combats free radicals, preventing sun damage and avoiding premature skin aging (Nogueira, R. F. et al., 2018).

The topical use of vitamin C provides various effects for the skin, showing high relevance in cosmetic, nutricosmetic, and cosmeceutical products, such effects as: inhibition of melanin formation, aiding in the treatment of hyperpigmentation, anti-inflammatory effect and antioxidant action (Batista, E. F.; Mejia, D. P. M., 2012; Nogueira, R. F. et al., 2018). In cosmeceuticals, three active forms of Vitamin C can be used: L-ascorbic acid being the most biologically active form, however, it shows limited penetration into the skin because it is water-soluble; ascorbyl-6-palmitate and magnesium ascorbyl phosphate (MAP) are lipophilic and have a skin-lightening effect, being more stable in aqueous formulations in neutral pH (Pandey, A.; Jatana, G. K.; Sonthalia, S., 2023).

Vitamin C is widely used as an active ingredient due to its multifunctional properties in skincare (Mangela, T.; Martins, A., 2021). Its use in cosmeceuticals occurs at concentrations ranging from 3 to 10% of the active ingredient. Concentrations higher than this do not increase the biological effect and may cause some irritation. At these ideal concentrations, the active ingredient provides a regenerative effect, participates in the synthesis process of collagen and elastin and also lightens the skin in hyperchromic treatments, can be applied to the skin during the day (Oliveira, J. C.;Sena, C. F. A., 2018). However, Vitamin C has the disadvantage of its low stability and being a thermolabile substance, able to oxidize easily due to high temperatures, alkaline pH, or in contact with air and light, causing problems in handling and storage of this substance.

Kojic Acid

Kojic acid (5-hydroxy-4-pyrone-2-methyl) is a natural substance produced through the fermentation of carbohydrates such as glucose, sucroseand maltose by strains of fungi or bacteria, such as *Aspergillus*, *Penicillium*, or *Acetobacter*spp (Sarkar, R.; Arora, P.; Garg, K., 2013). There is evidence demonstrating that kojic acid acts as a depigmenting agent by chelating copper ions, thereby preventing the increase in tyrosinase activity and interfering with melanin formation (Gao, X. H. et al., 2008).

Kojic acid exhibits skin-lightening, antioxidant and photoprotective action. This active ingredient has low potential for irritation and is not photosensitive, making it a very good alternative treatment for hyperpigmentation when patients cannot tolerate hydroquinone use (Oliveira, J. C.; Sena, C. F. A., 2018).

The depigmenting activity of kojic acid occurs in cosmeceutical formulations when present in concentrations of up to 1.5%, however concentrations between 1 to 4% have been reported. Despite being easily incorporated into formulations due to its water solubility, kojic acid is an ingredient extremely unstable in cosmetics formulations, developing brown color and losing its efficacy when exposed to light and air (Oliveira, J. C.;Sena, C. F. A., 2018; Chávez, C. X.B.; Dorea, J. S.; Pinheiro, R. C. S. P., 2019). Kojic acid can be applied both at night and in the morning, as long as it is combined with sunscreen. It is important to emphasize that kojic acid should be stored in places with moderate temperature, not exceeding 40°C, as oxidation may occur. Additionally, kojic acid should be kept in closed places that do not come directly into contact with light (Oliveira, et al., 2021).

Hydroquinone

Hydroquinone is a natural compound found in plants such as bearberry, vegetables and foods. It presents a phenolic structure acquired from the endogenous metabolism of benzene and is well known for its suppressive effect on melanin synthesis, degradation of melanosomes, destruction of melanocytes and synthesis of RNA and DNA (Bodo, L. F. L.; Rodrigues, T. S.; Rabito-Melo, M. F., 2019; Boonme, P. et al. 2009; Limberger, T. N. J., 2015).

Hydroquinone is one of the most efficient skin-lightening agents, available in various pharmaceutical forms for topical use, and has been considered the best treatment for melasma, post-inflammatory hyperpigmentation, senile lentigines and freckles (Limberger, T. N. J., 2015; Ayres , E. L. et al., 2016; Rodrigues, J. C., 2021). This active ingredient acts as an inhibitor of melanin formation by interacting with copper at the enzyme site of tyrosinase, thus interfering with RNA and DNA synthesis and degrading melanosomes. Concurrently, it affects the cellular metabolism of the lipoprotein membranes of cytoplasmic organelles, leading to their disruption (Limberger, T. N. J., 2015; Boonme, P. et al. 2009).

Hydroquinone is used in topical cosmeceuticals at concentrations of 1.5 to 5% alone or in combination with other pharmaceutical agents. Since 2001, in European Union countries, hydroquinone is no longer authorized in cosmetic formulations, and its use is prohibited by the European Committee (24ª Diretiva 2000/6 / CE) (EMAD, MOEZZI, DASTGHEIB, 2013; KOLBE et al., 2013; SHIN, PARK, 2014).

Hydroquinone is unstable, mainly when in combination with other active ingredients, and can undergo oxidation, making it essential to use opaque containers to avoid exposure to light and air (Gao, X. H. et al., 2008; Rodrigues, C. J., 2021). Due to its potential adverse effects its use must be carefully, under the supervision of a healthcare professional and for a short period of time (Boonme, P. et al. 2009; Bodo, L. F. L.; Rodrigues, T. S.; Melo, M. F. R., 2018). Therefore, it is being progressively replaced by other compounds that are less irritating (Nicoletti, 2002).

Arbutin

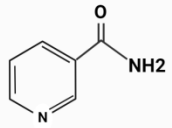
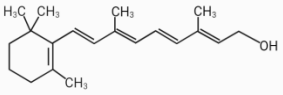
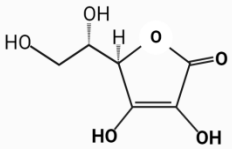
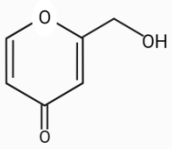
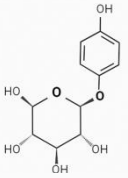
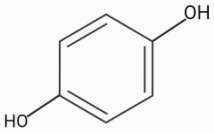
Arbutin (β-D-glucopyranoside) is a natural derivative of hydroquinone in which a molecule of D-glucose is attached to hydroquinone. This active ingredient is found in the leaves of bearberry, cranberry, mulberry bushes and in the vast majority of pears (Sarkar, R.; Arora, P.; Garg, K., 2013).

It is also possible to obtain pure forms of arbutin derivatives, such as α-arbutin, β-arbutin and deoxyarbutin by enzymatic and chemical synthesis. These are considered more potent for skin whitening because they are more effective inhibitors of human tyrosinase when compared tothe natural form, arbutin. Additionally, the synthetic form has been evaluated to be safer than the natural form (Boonme, P. et al., 2009; Gao, X. H. et al., 2008).

The pH in formulations containing arbutin must be controlled,because it can be hydrolyzed into hydroquinone in acidic or basic environments. Due to the high polarity of the molecule, topic absorption is challenging due toits low permeation in the stratum corneum (Rodrigues, J. C., 2021). Arbutin has been employed more than Hydroquinone because sensitization reactions have not been observed, and is more chemically stable. Arbutin is an important skin lightener and widely used in concentrations of 1 to 5%. This active ingredient is less effective than hydroquinone and kojic acid and is normally used in association with other skin-lightening agents(Boonme, P. et al., 2009; Boo, Y.C. 2021).

Mechanisms of action and biological cutaneous effects of these main cosmeceutical actives will be discussed for different types of hyperpigmentation (Table 2).

Table 2. Presentation of the main properties of cosmeceuticals in the treatment of cutaneous hyperpigmentation.

Active Ingredients	Mechanism of Action	Usage Concentration	Chemical Structure	References
Niacinamide	Melanosome transfer inhibitor	2 to 5 %		Vasconcelos, R. A. B., 2022; Rodrigues, J. C., 2021; Pandey, A.; Jatana, G. K.; Sonthalia, S., 2023.
Retinol	Glycosylation inhibition	0,3 to 1 %		Azulay, M. M.; Bagatin, E. 2009; Babamiri. K; Nassab, R., 2010; Bissett, D. L., 2009.
Vitamin C	Tyrosinase inhibitor	3 to 10 %		Oliveira, J. C.; Sena, C. F. A., 2018; Pandey, A.; Jatana, G. K.; Sonthalia, S., 2023; Azulay, M. M.; Bagatin, E., 2011.
Kojic Acid	Tyrosinase inhibitor	1 to 4 %		Oliveira, J. C.; Sena, C. F. A., 2018; Chávez, C. X. B.; Dorea, J. S.; Pinheiro, R. C. S. P.,2019.
Arbutin	Tyrosinase inhibitor	1 to 5 %		Boonme, P. el al.,2009; Boo, Y.C. 2021
Hydroquinone	Tyrosinase inhibitor	2 to 4 %		Boo, Y.C. 2021; Rodrigues, C. J., 2021; Gao, X. H. *et al.,* 2008

Contraindications and Adverse Reactions

In addition to providing benefits to the skin, whitening cosmetics can cause some unwanted effects and have some contraindications. The interaction between the skin and the product can interfere with cutaneous biological function and alter its physiology (Chorilli, M.; Scarpa, M. V.; Corrêa, M. A., 2007). The most common adverse effects are skin irritability, contact dermatitis, photosensitivity, hypopigmentation, infectivity, carcinogenicity and even systemic adverse effects (Gao, X. H. et al., 2008).

Among the active ingredients presented in this review, some are capable of causing adverse reactions while others were not found in the articles reviewed.

Niacinamide presents few adverse effects, which facilitates its topical use, being an efficient alternative in the treatment of skin blemishes (Vasconcelos, R. A. B., 2022). The adverse effects observed with the use of this active ingredient are skin irritation, redness, itching, or burning sensation. These adverse reactions are generally mild and temporary and can often be avoided by starting with a lower concentration of niacinamide and gradually increasing its use (Navarette-Sollis, 2011). It is suggested to discontinue the use of this active ingredient if allergic reactions are observed, such as rashes, swelling, or difficulty breathing (Vasconcelos, 2022).

Topical retinoids can cause skin irritation, with the appearance of redness, dryness, swelling, peeling, and subjective sensations such as itching, burning, and stinging (Gao, X. H. et al., 2008). Among the retinoids, retinol, retinal, retinoic acid, and retinyl palmitate, authors observed that retinol caused greater damage than retinal, followed by retinoic acid which caused less damage, and retinyl palmitate had no significant effect (Gimeno, 2004).

The use of Vitamin C in the treatment of melasma has shown absence of events of adverse effects (Espinal-Perez et al, 2004). According to Sandoval, Caixeta and Ribeiro (2015), the pure vitamin C is highly tolerable and compatible with the skin. However Vitamin C is a weak acid and can cause skin irritation, especially if used in high concentrations. This can lead to redness, itching, peeling and a burning sensation.

There are reports that kojic acid may cause contact allergy and skin irritability, but there are few reports on the local or systemic adverse effects of this active ingredient (Gao, X. H. et al., 2008). The

use of kojic acid improves the texture and tone of the area affected by melasma; currently, it is one of the safest depigmenting agents for treatment (Borges, 2022).

One of the most common problems caused by the use of hydroquinone is skin irritation, leading to contact dermatitis, especially when used in high concentrations, above 5% (Gao, X. H. et al., 2008). Moreover, erythema, peeling, permanent depigmentation, and exogenous ochronosis are also observed. Another adverse effect is exogenous ochronosis, a less common effect characterized by progressive darkening of the skin area exposed to the use of hydroquinone. The adverse effects of hydroquinone can often impair health, which is why in some countries the use of this active ingredient in cosmetic formulations is no longer authorized, or over-the-counter formulations are approved at concentrations of up to 2%, and if it exceeds the established limit, sales should be made only with a medical prescription (Bodo, L. F. L., 2018). In general, skin-lightening cosmetics have been widely used to treat various hyperpigmentation conditions such as melasma, sunspots, freckles, among others. However, it is crucial to recognize that these products can also present significant contraindications and adverse reactions. It is important to highlight that some depigmenting agents may not be suitable for all skin types. For example, products containing acids like glycolic acid or salicylic acid can be very irritating for individuals with sensitive or allergy-prone skin. Therefore, individuals with a history of skin sensitivity should avoid these ingredients or consult a dermatologist before using them.

Furthermore, some skin-lightening cosmetics may be contraindicated during pregnancy and lactation, such as hydroquinone and retinoic acid. Regarding adverse reactions, it is common for some users to experience irritation, redness, peeling, or a burning sensation when using depigmenting products, especially at the beginning of treatment. These reactions are usually mild and temporary, but in some cases, they may persist or worsen over time. If severe or persistent reactions occur, it is essential to discontinue the use of the product and seek professional guidance.

Conclusion

Cutaneous hyperpigmentation is a common aesthetic problem among people and can arise from genetic alterations and/or sun exposure. Regardless of the type of hyperpigmentation, its location, and the intensity of its coloration, it is known that these disorders are caused by an increase in melanin production by the enzyme tyrosinase.

Cosmeceuticals with depigmenting actives have the potential to reverse these skin alterations, serving as a promising tool to treat hyperpigmentation in a minimally aggressive manner, with mild adverse reactions and offering good results. There are various cosmeceutical actives that have efficacy in reducing specific hyperpigmentations, but in addition to the cosmeceuticals researched for the treatment of cutaneous hyperpigmentation, it is important to emphasize the use of moisturizers and sunscreen to prevent or delay the appearance of new spots.

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