Review Article

Skin Hyperpigmentation and its Herbal Treatment: A Review

Archana .P. Jawaje*, Bharti Dongare, Dr.Suhas P.Padmane, Sharad Manapure, Sheelpriya Walde
Department of Quality Assurance, Gurunanak College of Pharmacy, Nagpur, India.
***Corresponding author's E-mail:** Archanajawaje721@gmail.com

Received: 08-04-2023; **Revised:** 20-06-2023; **Accepted:** 26-06-2023; **Published on:** 15-07-2023.

ABSTRACT

A frequent dermatological disorder known as hyperpigmentation is marked by the darkening of specific skin regions. Despite the availability of several conventional treatments, the demand for natural and herbal remedies has been rising as a result of worries about the potential adverse effects of goods made of chemicals. Patients with several skin-related ailments, often known as patients with skin pigmentation, are becoming more and more prevalent. Hyperpigmentation is one of the most prevalent problems in people with skin of colour. As a result, herbal formulations are required for the treatment of hyperpigmentation. This review article discusses the many forms of hyperpigmentation, their causes, and herbal remedies for managing skin hyperpigmentation. As hyperpigmentation, or uneven skin pigmentation, is a frequent skin issue caused by an increase in melanin production, it is important to understand this condition. As a result, blotches or patches of skin may seem darker than the surrounding skin. Due to sun exposure and damage, certain types of hyperpigmentation including post-inflammatory, melasma, and sun spots are more prone to afflict parts of the face, arms, and legs. Although there are several therapies for the problem, which can have some negative side effects, dermatologists still face difficulties in managing hyperpigmentation.

Keywords: Hyperpigmentation, Melasma, Tyrosinase, Age spot, Melanin.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2023.v81i01.016

DOI link: http://dx.doi.org/10.47583/ijpsrr.2023.v81i01.016

INTRODUCTION

Skin hyperpigmentation, a common dermatological disorder, causes the skin's colour to typically darken. Several internal and external causes, such as hormonal shifts, inflammation, injury, acne, eczema, certain medications, UV exposure, etc[1] can cause these changes in skin colouration. The biological mechanisms that result in the generation of the skin pigment melanin by melanocytes in different layers of skin determine the colour and pigmentation of the skin. Skin hyperpigmentation diseases are consequently caused by changes in melanocyte production or melanin distribution[2].

Under the general term "hyperpigmentation," a number of illnesses connected to skin darkening, pigmentation, and discolouration are included. Melasma, post-inflammatory hyperpigmentation, ephelides, lentigines, and many more are examples of prevalent hyperpigmentation conditions. Melasma is a term for an acquired hyper melanosis skin disorder in which sporadic grey-brown lesions or patches of light to dark-brown skin form on exposed areas of the skin[3]. It typically affects the face and neck regions and is more frequently seen in women.), post-inflammatory hyperpigmentation (PIH) is another hyper melanosis skin disease in which dark areas appear after skin damage or inflammation. Solar lentigines, also known as "Age spots" or "Sunspots," are a disorder where areas of darkened retinal lesions result in hyperpigmentation. Ephelides, often known as freckles, is a common condition characterised by darker, reddish to light brown spots that typically appear on the face, neck, and arms. They emerge in the formative years and are more common in people with lighter or fairer skin tones[4].

Although hyperpigmentation is not a dangerous or fatal condition, it can harm patients' quality of life by harming their emotional and psychological well-being. For hyperpigmentation, there are numerous treatment options. These medications are typically used topically as creams, gels, or ointments. However, these topical treatments come with several side effects, including hypopigmentation, peeling, skin drying, and irritation. Long-term treatments that last for months or even years may result in low patient satisfaction and compliance. The need for new treatment alternatives is highlighted by the fact that there is still no effective medication for hyperpigmentation[5].

Why skin hyperpigmentation?

A common cause of hyperpigmentation is an excess production of melanin. Melanin is a pigment that gives skin its colour. It's produced by skin cells called melanocytes. Several different conditions or factors can alter the production of melanin in your body. Certain medications can cause hyperpigmentation. Also, some chemotherapy drugs can cause hyperpigmentation as a side effect.

Pregnancy changes hormone levels and can affect melanin production in some women. A rare endocrine disease called Addison's disease can produce hyperpigmentation that's most obvious in areas of sun exposure, such as the face, neck, and hands, and areas exposed to friction, such as elbows and knees. Hyperpigmentation is a direct result of an increased level of a hormone in your body that results in increased melanin synthesis. Excessive sun exposure can also cause an increase in melanin.

Etiology and Pathophysiology

The biosynthetic route called melanogenesis, which includes a number of enzymes- and chemical-catalyzed events, is how the pigment melanin is created in melanocytes. Melanocytes, which are found inside melanosomes, are where melanin is synthesised. Tyrosinase and related proteins, which are introduced with the aid of particular protein complexes, are melanogenic enzymes that have an impact on melanin synthesis. After being filled with melanin, the melanosomes are then transferred to the keratinocytes [. Skin exposure to UV light stimulates the production of tyrosinase, the primary enzyme in melanogenesis, which is activated. A glycoprotein called tyrosinase is found in the melanosome's membrane. A cytoplasmic domain with 30 amino acids and a brief transmembrane domain follows the catalytic region, which makes up around 90% of the protein, in the inner melanosomal domain. Histidine residues in the inner (catalytic) region of tyrosinase bind the copper ions necessary for tyrosinase action. Ribosomes can synthesise eumelanin and pheomelanin, two different kinds of melanin. Tyrosinase is a protein that catalyses the first two steps of the formation of melanin, which include hydroxylating L-tyrosine to L-dihydroxyphenylalanine (L-DOPA) and then oxidising this o-diphenol to the equivalent quinone, L-dopaquinone. Facilitated diffusion is used to transfer L-tyrosine into the melanosome. The amount of L-tyrosine required for melanogenesis depends primarily on the conversion of L-phenylalanine, an essential amino acid, by intracellular phenylalanine hydroxylase (PAH) activity. In contrast to L-tyrosine, L-phenylalanine is actively transported through the membrane of the melanosome, ensuring a high level of L-tyrosine within this organelle. The melanin pathway splits into the production of reddish-yellow pheomelanin and blackish-brown eumelanin after dopaquinone is formed. Dopachrome is either converted to 5,6-dihydroxy indole spontaneously in the eumelanin pathway or to 5,6-dihydroxyindole-2-carboxylic acid by the enzyme dopachrome tautomerase (DCT), also known as tyrosine related protein-2 (TRP-2). Two tyrosinase-related proteins (TRP), TRP-1 (likely DHICAoxidase), and TRP-2 (DOPAchrome tautomerase), exhibit about 40% homology, suggesting that the genes may have come from a single ancestor. Tyrosinase's stability is believed to be improved by TRP-1. Eumelanin is created via the final polymerization of indoles and quinones. The pheomelanin route splits off from the eumelanin pathway at the L-dopaquinone stage. The amino acid cysteine, which is transported actively through the melanosomal membrane, is crucial to the pheomelanin pathway. Following that, it combines with L-dopaquinone to create cysteinyl-dopa, which is then transformed into quinoline, alanine-hydroxyl dihydrobenzothazine, and pheomelanin. Due to the existence of redox conditions in the melanosomes, the generation of eumelanin and pheomelanin is balanced. Reduced glutathione (GSH) controls the production of both melanin pigments; eumelanin is produced when GSH levels are high, whilst pheomelanin is produced when GSH levels are low. Thus, the expression and functional activity of antioxidant enzymes like catalase, glutathione peroxidase, glutathione reductase, and thioredoxin reductase affect the pathway for melanin synthesis [6].

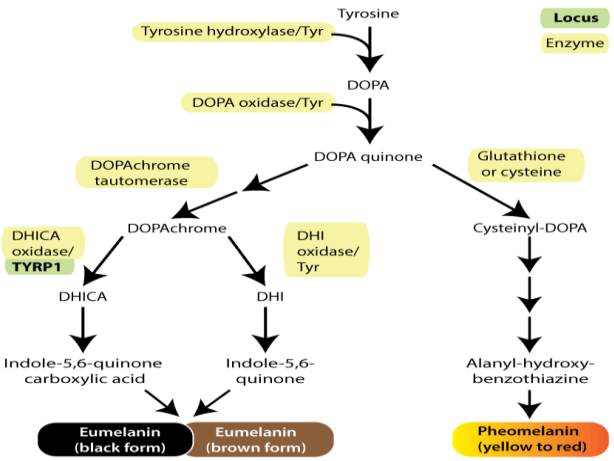

Figure 1: Synthesis of melanin

TYPES OF SKIN HYPERPIGMENTATION[7-9]

Post-inflammatory hyperpigmentation

All skin types are susceptible to this acquired hyper melanosis, which develops following skin inflammation or damage. Infections like dermatophytosis, allergic reactions like mosquito bites, and psoriasis, hypersensitive drug reactions, harm from irritants, or cosmetic operations may all cause it to happen. However, the most typical causes of it are impetigo, atopic dermatitis, and acne vulgaris. Post-inflammatory hyperpigmentation (PIH) is most prevalent in people with dark skin after acne. Melanin overproduction or an erratically distributed pigment following inflammation are the causes of PIH. Melanocyte activity may increase, which may be induced by both reactive oxygen species and inflammatory mediators. Epidermal post-inflammatory hyperpigmentation has a light to dark brown colour, whereas dermal PIH typically has a grey or black colour [7].

Melasma

Melasma is an acquired hyper melanosis that appears on sun-exposed parts of the skin, particularly the face, as asymmetric, brown-coloured, irregular, reticulated macules. But it has been suggested that predisposed genetic background, chronic ultraviolet (UV) exposure, and stimulation of female hormones all contribute to the development of melasma [7]. Additionally, it should be noted that mast cell histamine release in response to UV

exposure has been shown to promote melanogenesis, which is mediated by H2 receptors via protein kinase A activation. It has been proposed that sebocytes have a role in the emergence of melasma. On the function of sebocytes in the pathogenesis of melasma, more research is required [8].

Melasma and Hormonal Effects

Because melasma is frequently associated with pregnancy, the use of hormonal contraceptives, oestrogen therapy for patients with prostate cancer, and the use of conjugated oestrogen by women after menopause, hormones play a role in the pathogenesis of the condition. In particular, oestrogen and progesterone have an impact on the development of melasma. Melasma is more common in females than in males. Unwanted cutaneous side effects of oral contraceptives include melasma. Melasma is frequently thought of as a hormonally induced physiological change in the skin. Oestrogens have a significant impact on both physiological and pathological skin disorders, including pigmentation. The many receptors for oestrogen and progesterone control their biological actions [8-9].

The Potential for Healing

Topical depigmenting remains the mainstay of melasma treatment. The most popular anti-melanogenic drug is hydroquinone, which blocks the competitive tyrosinase enzyme from converting 1-3,4-dihydroxyphenylalanine to melanin. highlighted danger issues such as the risk of malignancy, irreversible depigmentation, and exogenous ochronosis[2]. Topical agents that have been shown to have depigmenting qualities without side effects are being replaced by the following substances: resveratrol, azelaic acid, 4-n-butyl resorcinol, niacinamide, kojic acid, and ascorbic acid [8].

Age SPOT

Age-related signs are the brown dots on the skin, and areas of skin, such as the face and the back of the Hands primarily develop on the area of skin that is frequently exposed to sunlight [10]. The lipofuscin bodies of the basal cells are what give age marks their brown colour. The lysosome's lipid and protein combination known as lipofuscin is where lipids attach to protein fragments via malondialdehyde. Age spots differ in shape, size, colour, and the extent to which they protrude from the skin. Age spots on the skin are created by basal cells that adhere to the epidermis' basement membrane. The stem cells that regenerate and repair the epidermis in new epithelial cells are called basal cells. UV light can harm chemical compounds and basic cells, and some wounded cells can live and deteriorate as a result [11]. Some skin-lightening agents, such as kojic acid, are used to treat age spots [12]. An old cell affects a tissue in two ways: it reduces neighbourhood cell productivity in responding to environmental changes and makes damage more fragile; it also reduces the effectiveness of local tissue repair. As a result, the surrounding cells in an aged cell are more vulnerable to damage and poor maintenance. This mechanism results in the ageing of nearby cells as a result of an ageing cell [11].

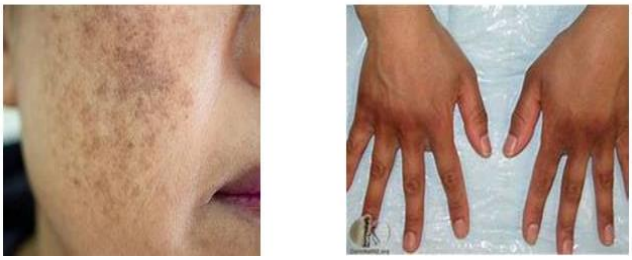

Figure 2: Types of Skin Hyperpigmentation

Hyperpigmentation's causes

There are numerous causes of hyperpigmentation. Addison's disease, Cushing's syndrome, Nelson syndrome, pheochromocytoma, carcinoid, acromegaly, hyperthyroidism, acanthosis nigricans, and diabetes are examples of exogenous and endogenous factors that can affect a person's health. Nutritional factors that contribute to Kwashiorkor include a lack of vitamin B12 [13, 14], folic acid, niacin, tryptophan, and vitamin A. Melasma is an unpleasant skin reaction to hormonal contraception [15].

Effect of tyrosinase inhibition

Tyrosinase is a glycosylated, copper-containing enzyme with many activities that are only present in melanocytes [16]. It catalyses the transformation of lysine into L-DOPA, which is then transformed into dopaquinone and dopachrome[17]. Melanin is produced when dopachrome polymerizes. Tyrosinase enzyme inhibition helps to reduce skin hyperpigmentation by preventing the formation of melanin. Tyrosinase activity is inhibited by extracts of herbal medicines such as liquorice, Aloe vera, Morus alba, and many more.

Herbal remedies for skin hyperpigmentation

In addition to photo safety, several medications and procedures can safely and effectively treat hyperpigmentation of the skin in patients with darker skin. Consequently, herbal remedies and phytoconstituents are a better option for treating skin hyperpigmentation. Treatments like chemexfoliation and laser therapy, as well as substances like hydroquinone, azelaic acid, kojic acid, liquorice extract, and retinoids, may be efficient on their own or in conjunction with other medications [18-19]. Tyrosinase inhibitory, antioxidant, and skin-whitening effects are the three potential modes of action by which herbs are used to treat skin hyperpigmentation.

Aloesin

Aloesin is a substance that is extracted from the aloe plant, and it has been shown to competitively inhibit tyrosinase in human, mushroom, and murine sources [20]. It has also been found that aloesin inhibits tyrosine hydroxylase and DOPA oxidase activities in a dose-dependent manner.

Aloesin and arbutin have been found to cooperatively reduce the synthesis of melanin by inhibiting tyrosinase activity by utilising integrated mechanisms of noncompetitive and competitive inhibitions [21].

Azadirachta indica

Additionally, to having antibacterial and antioxidant properties, *Azadirachta indica* exhibits activity against the tyrosinase enzyme [22]. It includes Nimbin, nimbinene, nimbandiol, and azadirachtin in addition to isomeldenin.

Emblica officinalis

The nutritional value of E. officinalis is well known. Sesquiterpenoids, alkaloids, sugars, amino acids, flavonol glycosides, phenolic glycosides, phenolic acids, and tannins are just a few of the numerous compounds that can be found. Compared to other fruit juice, the juice from E. officinalis has the highest concentration of vitamins C and E. Tyrosinase may be inhibited by the extract by blocking the expression of Trp-1 and the microphthalmia-associated transcription factor (MITF), while Trp-2 may be induced when the extract is applied at low doses. Embrica fruit exhibits an IC50 of 4346.95 166.23 g/mL, which is greater than the IC50 of MPE. Higher antioxidant and anti-melanogenesis effects are provided by ethanol extract [23,24].

Curcuma longa

Some of the active ingredients in *Curcuma longa*, such as curcumin, and bisdemethylcurcumin, have tyrosinase inhibitory or depigmenting properties. Curcumin has the highest rate of tyrosinase inhibition of all of these [25] When compared to a synthetic curcumin analogue, natural curcuminoids exhibit strong inhibitory activity. When combined with the compounds o-diphenols and m-diphenols, the curcumin analogue exhibits stronger tyrosinase activity than other compounds. Curcuminoids reduce tyrosinase activity by preventing L-dopa oxidation[26]. MITF, TRP1, and other tyrosinase protein levels are inhibited by partially purified Curcuma longa (PPC), which also suppresses cells that have been activated by -MSH. PPC's suppression of melanogenesis through a signalling route can activate ERK or PI3K/Akt [27].

Papaya carica

Papain, chymopapain A, and B are present, and they have antioxidant action. Additionally, it contains malic acids, calcium, sugar, fibre, vitamin C, thiamine, riboflavin, and niacin. Proteins and lipids are also a part of it. Carica fruit extract has been reported to have 87% antioxidant activity. There were two main types of phenolic chemicals in papaya fruit. These phenolic compounds are the most significant natural antioxidant groups [28].

Acacia catechu

At a concentration of 120 g/ml, the extract showed strong tyrosinase inhibition activity, with an inhibition percentage of 61.58 compared to a favourable kojic acid regulation [98.73% inhibition] at a concentration equivalent to 120 g/ml. A. cateCHU Whitening cream has retained strong stability for 3 months without preservatives [29].

Panax ginseng

The herb *Panax ginseng* contains many therapeutically useful ginsenosides. P-coumaric acid, which was isolated from fresh Panax ginseng leaves, was utilised to prevent the mushroom tyrosinase-catalyzed oxidation of L-tyrosine. Floralginsenoside [FGA], Ginsenoside [GRd], and Ginsenoside Re [GRe] are the isolates from Panax ginseng berries. By reducing the expression of the microphthalmia-associated factor, floral ginsenoside [FGA] has been found to have a substantial inhibitory effect on melanogenesis [3]. The numerous pharmacological functions of ginseng, including its anticancer and antioxidant properties as well as its anti-ageing, anti-stress, and anti-fatigue effects, are what gives it its significance. PgAuNPs have been found to have strong antioxidant activity because of the DPPH's free radical activity. Additionally, the leaves of Panax ginseng can whiten skin, protect the skin, and retain moisture[30-32].

Herbal treatment for skin hyperpigmentation

The use of herbal remedies as a natural means of treating skin hyperpigmentation has grown in favour. Plant-based ingredients with skin-lightening, antioxidant, and anti-inflammatory effects are frequently used in these therapies. Before applying herbal medicines to the entire face or the problematic area, it is advised to conduct a patch test because individual responses to herbal therapies can differ. Additionally, consistency and regular application are necessary to see discernible hyperpigmentation changes. It is advised to get the advice of a dermatologist or skincare specialist to confirm the safety and efficacy of herbal remedies, particularly if you have underlying skin disorders or are taking other skincare products or pharmaceuticals.

Future perspectives and challenges

This section explores the future perspectives and challenges related to the development and use of herbal skin creams for hyperpigmentation, including emerging trends, technological advancements, and potential research areas. It also discusses the issues related to the standardisation, regulation, and commercialization of herbal products.

CONCLUSION

In this review, we discussed a variety of plants and herbs that are utilised as tyrosinase inhibitors and skin-lightening agents. The most vital component of our body is our skin. The amount of melanin in the skin affects the colour of the skin. The pigment melanin, which is found in the skin, gives plants and mammals their colour. Hyperpigmentation of the skin results from an increase in melanin levels in the skin. Tyrosinase enzyme is primarily responsible for melanin synthesis. The production of melanin in the epidermal layer of skin, which affects skin colour, is facilitated by the conversion of L-tyrosine in L-DOPA and L-DOPA to dopaquinone. *Azadiracta indicia, Aloe sin,*

Emblica officinalis, Curcuma longa, Papaya carica, Acacia catechu, Panax ginseng, and many other plants are utilised as phytoconstituents in herbal cosmetics as anti-hyperpigmentation agents in the cosmetics industry. These herbs contain flavonoids and triterpenoids, some of which have antioxidant and skin-whitening properties.

Acknowledgement: The author is thankful to all the contributors in compiling and preparing a manuscript for this article.

REFERENCES

1. Bernal-P, Pérez-M, M.A & Camacho, F. Management of facial hyperpigmentation. American Journal of Clinical Dermatology, 2000;1(5):261–268.
2. Rossi, A. M., & Perez, M. I. Treatment of hyperpigmentation. Facial Plastic Surgery Clinics of North America, 2011;19(2):313–324.
3. Victor, F., Gelber, J., & Rao, B. Melasma: A review. Journal of Cutaneous Medicine and Surgery: Incorporating Medical and Surgical Dermatology, 2004;8(2):97–102.
4. Ezzedine, K., Mauger, E., Latreille, J., Jdid, R., Malvy, D., Gruber, F., Galan, P., Hercberg, S., Tschachler, E., & Guinot, C. Freckles and solar lentigines have different risk factors in Caucasian women. Journal of the European Academy of Dermatology and Venereology, 2013;27(3):e345–e356.
5. Nautiyal A, Wairkar S. Management of hyperpigmentation: Current treatments and emerging therapies, The official journal of the international federation of pigment cell societies. Society for melanoma research DOI: 10.1111/pcmr.12986 2021;34(6):1000–1014.
6. Goswami P and Sharma H. K. Skin hyperpigmentation disorders and use of herbal extracts: a review Current Trends in Pharmaceutical Research 2020;7(2):18-25, ISSN: 2319-4820.
7. Lee AY. An updated review of melasma pathogenesis. Dermatologica Sin 2014;32(4):233–239. https://doi.org/10.1016/j.dsi.2014.09.006
8. Kwon SH, Na JI, Choi JY, Park KC. Melasma: Updates and perspectives. Exp Dermatol 2019;28(6):704–708.
9. Maddalena I, Jusuf NK, Putra IB. Melasma characteristic in hormonal contraceptive acceptors at Kelurahan Mangga Kecamatan Medan Tuntungan, Medan-Indonesia. Bali Med J 2018;7(3):645–649.
10. Bino S, Duval C, Bernard F. Clinical and biological characterization of skin pigmentation diversity and its consequences on UV impact. Int J Mol Sci 2018;19(9):2668.
11. Wang-Michelitsch J, Michelitsch TM. Development of age spots as a result of the accumulation of aged cells in aged skin. arXiv Prepr arXiv 1505070 2015;12:1–9.
12. Saeedi M, Eslamifar M, Khezri K. Kojic acid applications in cosmetic and pharmaceutical preparations. Biomed Pharmacother 2019;110:582–593. https://doi.org/10.1016/j.biopha.2018.12.006
13. Sarkar SB, Sarkar S, Ghosh S, Bandyopadhyay S. Addison's disease. Contemp Clin Dent 2012;3(4):484–486
14. Cherqaoui R, Husain M, Madduri S, Okolie P, Nunlee-Bland G, Williams J (2013) A Reversible cause of skin hyperpigmentation and postural hypotension. Case Rep Hematol 2013;18(1):1–5. https://doi.org/10.1155/2013/680459
15. Maddalena I, Jusuf NK, Putra IB. Melasma characteristic in hormonal contraceptive acceptors at Kelurahan Mangga Kecamatan Medan Tuntungan, Medan-Indonesia. Bali Med J 2018;7(3):645–649
16. Balakrishnan KP, Narayanaswamy N, Duraisamy A. Tyrosinase inhibition and antioxidant properties of *Muntingia calabura* extracts: In vitro studies. Int J Pharm Bio Sci 2011;2(1):294–303.
17. Shirota S, Miyazaki K, Aiyama R, Ichioka M, Yokokura T. Tyrosinase inhibitors from crude drugs. Biol Pharm Bull 1994;17(2):266–269.
18. Saeedi M, Eslamifar M, Khezri K. Kojic acid applications in cosmetic and pharmaceutical preparations. Biomed Pharmacother 2019;110:582–593. https://doi.org/10.1016/j.biopha.2018.12.006
19. Davis EC, Callender VD. A review of the epidemiology, clinical features and treatment options in skin of colour. J Clin Aesthet Dermatol 2010;3(7):20-25.
20. Jones K, Hughes J, Hong M, Jia Q, Orndorff S. Modulation of melanogenesis by aloesin: A competitive inhibitor of tyrosinase. Pigment Cell Res [Internet]. 2002 [cited 2020 Nov 8];15(5):335–40.
21. Jin YH, Lee SJ, Chung MH, Park JH, Park YI, Cho TH, et al. Aloesin and arbutin synergistically inhibit tyrosinase activity via a different action mechanism. Arch Pharm Res [Internet]. 1999 [cited 2020 Nov 8];22(3):232–6.
22. Chiocchio I, Mandrone M, Sanna C, Maxia A, Tacchini M, Poli F, Screening of a hundred plant extracts as tyrosinase and elastase inhibitors, two enzymatic targets of cosmetic interest. Ind Crop Prod 2018;12:498–505.
23. Variya BC, Bakrania AK, Patel SS. *Emblica officinalis* (Amla): a review for its phytochemistry, ethnomedicinal uses and medicinal potentials concerning molecular mechanisms. Pharmacol Res 2016;11(1):180–200.
24. Sripanidkulchai B, Junlatat J. Bioactivities of alcohol-based extracts of *Phyllanthus emblica* branches: antioxidation, anti-melanogenesis and antiinflammation. J Nat Med 2014;68(3):615–622. https://doi.org/10.1007/s11418-014-0824-1
25. Mukherjee PK, Biswas R, Sharma A, Banerjee S, Biswas S, Katiyar CK. Validation of medicinal herbs for anti-tyrosinase potential. J Herb Med 2018;14:1–16. https://doi.org/10.1016/j.hermed.2018.09.002
26. Du ZY, Jiang YF, Tang ZK, Mo RQ, Xue GH, Lu YJ. Antioxidation and tyrosinase inhibition of polyphenolic curcumin analogues. Biosci Biotechnol Biochem 2011;75(12):2351–2358. https://doi.org/10.1271/bbb.110547
27. Jang JY, Lee JH, Jeong SY, Chung KT, Choi YH, Choi BT. Partially purified Curcuma longa inhibits alpha-melanocyte-stimulating hormone-stimulated melanogenesis through extracellular signal-regulated kinase or AKT activation-mediated signalling in B16F10 cells. Exp Dermatol

2009;18(8):689– 694. https://doi.org/10.1111/j.1600-0625.2009.00857.x

28. Song Y, Jeong SW, Lee WS, Park S, Kim YH, Kim GS et al. Determination of polyphenol components of Korean prostrate spurge (*Euphorbia supina*) by using liquidchromatography–tandem mass spectrometry: Overall contribution to antioxidant activity. J Anal Methods Chem 2014;8:1–8

29. Anurukvorakun O, Boonruang R, Lahpun N. Formulation strategy, stability issues, safety and efficacy evaluations of *Acacia catechu* whitening cream. Int J Appl Pharm 2019;11(2):91–96.

30. Gediya SK, Mistry RB, Patel UK, Blessy M, Jain HN. Herbal plants: used as a cosmetics. J Nat Prod Plant Resour 2011;8(1):24–32.

31. Lee JO, Kim E, Kim JH, Hong YH, Kim HG, Jeong D, Kim J, Kim SH, Park C, Seo DB, Son YJ, Han SY, Cho JY. Antimelanogenesis and skin protective activities of *Panax ginseng* calyx ethanol extract. J Ginseng Res 2018;42(3):389–399. https://doi.org/10.1016/j.jgr.2018.02.007

32. Wang X, Gong X, Zhang H, Zhu W, Jiang Z, Shi Y. *In vitro* anti-ageing activities of *Ginkgo biloba* leaf extract and its chemical constituents. Food Sci Technol 2020;40(2):476–482. https://doi.org/10.1590/fst.02219

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.