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Mini Review

SKIN HYPERPIGMENTATION DISORDERS AND USE OF HERBAL EXTRACTS: A REVIEW

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Abstract

Background: *Problems pertaining to the skin pigmentation is one of the major concerns that affect the quality of life of human beings especially women. The disturbances in the melanin production mainly results in skin pigmentation disorders. For centuries natural ingredients have been used in the treatment of skin hyperpigmentation disorders. Since synthetic cosmetic ingredients can have potential side effects, emphasis has been given on the herbal products, which are considered to be mild and biodegradable, exhibiting low toxicity.* ***Objective:*** *The objective of this review is to provide a brief understanding about the skin hyperpigmentation disorders and the use of various herbal extracts as a notable approach for its treatment.* ***Methods:*** *A narrative literature review was conducted with the extraction of information, which was analyzed from various databases viz. Google scholar, Science Direct, PubMed, Wiley Online Library etc.,* ***Results and Discussions:*** *The preferences of the people for the use of herbal skin-lightening agents over the synthetic ones have gained wide spread popularity. Potentially active compounds that have been extracted from the plants have been identified which provide scope for its use a novel depigmenting agent. The improvement in the efficacy of the herbal extracts is mainly due to synergism, and hence this property yields great results when used in cosmetic formulations.* ***Conclusion:*** *Plant extracts have been found to improve the conditions of skin hyperpigmentation along with its utility in other skin related problems. Use of herbal extracts as a skin care agent is gaining popularity as it offers more benefits than the synthetic skin-care formulations.*

Keywords: Photoprotective; Keratinocytes; Tyrosinase; Melanoblasts; Herbal

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Introduction

The world is becoming a Global village where humans are completely engrossed in their day to day activity giving less priority to their health and especially in terms of skincare. Incidences of skin disorders are reported every year and the most common includes those disorders pertaining to skin pigmentation. Urbanization and changes in lifestyle and diet also increases the susceptibility to skin disorders. Humans have undergone evolution by adapting themselves in response to environmental changes; similarly the human skin color has evolved as a result of differences in melanin secretion which is an adaptive phenomenon and has been maintained by natural selection [1]. The human skin colour is influenced by both the quantity and distribution of melanocytes. Variation in basal epidermal melanin amount and type is a major factor that contributes to inborn coloration of human skin [2]. Melanin protects the skin from the damages caused due to exposure to UV radiation. The disturbance in the normal homeostasis of melanin synthesis in an individual leads to skin pigmentation disorders. So proper understanding of the skin pigmentation and the prognosis of such disorders are important for its treatment and to set up various strategies for its prevention and cure. This review begins with a brief insight about skin pigmentation, melanogenesis and pigmentation disorders and addresses the causes of skin hyperpigmentation followed by the description of the common hyperpigmentation disorders and summarizes the use of herbal extracts i.e., the naturally derived ingredients to improve the skin lightness.

Skin Pigmentation

The pigmentation in human skin is mostly derived from melanin which is an extremely dense, virtually insoluble, and high molecular weight polymer attached to a structural protein .The brownish-black eumelanin and the reddish-yellow pheomelanin are the two types of melanin present on the human skin. Darker skin phenotypes are characterized by high concentration of eumelanin including tanned skin. There is considerable variation in the concentration of pheomelanin within any given human group [1]. The synthesis and distribution of the pigmented biopolymer melanin is specialized by a very minor population of cells called melanocytes and these are derived from precursor cells called melanoblasts during embryological development. The melanoblasts originate from the neural crest cells.

Melanocytes are localized at the dermal/epidermal border of human skin in a characteristic regularly dispersed pattern [3]. One of the beneficial properties of pigmentation in human skin is protection against the exposure to UV radiation and other environmental stresses. Hence, the darker skin is notably more resistant to the damaging effects caused by ultraviolet (UV) radiation, which includes photocarcinogenesis and photoaging, than the lighter skin. Melanin is remarkably photoprotective and as a result the epidermal cells in darker skin are subjected to less DNA damage than do those in lighter skin [4].

Malanogenesis

The pigment melanin is produced in melanocyte by means of biosynthetic pathway called melanogenesis which involves a series of enzymes and chemical catalyzed reactions [5]. Synthesis of melanin takes place in melanocytes which are located inside melanosomes. The melanin syntheisis is influenced by the melanogenic enzymes (tyrosinase and related proteins) which are introduced with the help of specific protein complexes. The melanosomes which gets loaded with melanin are then transported to keratinocytes [6]. Exposure of skin to UV radiation provides an impetus to melanogenesis by activating the key enzyme of melanogenes i.e., tyrosinase. (Tyrosinase is a glycoprotein which is located in the membrane of the melanosome). The catalytic region (approximately 90% of the protein) is present in the inner melanosomal domain, followed by a short transmembrane domain and acytoplasmic domain comprising of 30 amino acids [7]. The inner (catalytic) portion of tyrosinase contain histidine residues which bind copper ions required for tyrosinase activity [8]. Two types of melanin namely eumelanin and pheomelanin are synthesized within ribosomes [9]. The first two steps of melanin production is catalyzed by tyrosinase which involves the hydroxylation of L-tyrosine to L-dihydroxyphenylalanine (L-DOPA) and the subsequent oxidation of this *o*-diphenol to the corresponding quinone, L-dopaquinone [10]. L-tyrosine is transported into the melanosome by facilitated diffusion [11]. The concentration of L-tyrosine for melanogenesis depends primarily on the conversion of the essential amino acid L-phenylalanine by intracellular phenylalanine hydroxylase (PAH) activity and as compared to L-tyrosine, L-phenylalanine is actively transported through the membrane of

melanosome, so that a high content of L-tyrosine inside this organelle is ensured [12]. After the formation of dopaquinone, the melanin pathway bifurcates into synthesis of the black-brownish eumelanin and red-yellow pheomelanin [13]. In the pathway of eumelanin, there is either spontaneous conversion of dopachrome to 5,6-dihydroxyindole or its enzymatic conversion to 5,6-dihydroxyindole-2-carboxylic acid by dopachrome tautomerase (DCT) also known as tyrosine related protein-2 (TRP-2). About 40% homology is shown by two tyrosinase-related proteins (TRP), TRP-1 (probably DHICAoxidase) and TRP-2 (DOPAchrome tautomerase), which shows the possibility of inheriting the genes from a common ancestor [14]. TRP-1 is said to enhance the stability of enzyme tyrosinase [15]. The indoles and quinones are finally polymerized to form eumelanin. At the L-dopaquinone step, the pheomelanin pathway branches from the eumelanin pathway. The pheomelanin pathway is highly dependent on the amino acid cysteine which passes through the melanosomal membrane by means of active transport. It then reacts with L-dopaquinone to form cysteinyl-dopa which is then converted to quinoleimine, alanine-hydroxyl dihydrobenzothazine and polymerizes to pheomelanin [16].

The production of eumelanin and pheomelanin are balanced due to the presence of redox conditions in the melanosomes. Reduced glutathione (GSH) determines the formation of both the melanin pigments as presence of high GSH is indicated for eumelanin and low GSH for pheomelanin. Therefore, the pathway for melanin synthesis gets modified based on the expression and functional activity of antioxidant enzymes such as catalase, glutathione peroxidase, glutathione reductase and thioredoxin reductase [17].

Skin pigmentation disorder: A brief insight

The disorders pertaining to skin pigmentation mainly involve the disturbances of pigmentation which involve melanin. An increase in amount, a decrease in amount or an abnormal location or distribution of melanin pigment in the skin or hair mainly contribute to such disturbances. These disturbances in fact are dependable on the either of the following factors.

1. Changes in the number of melanocytes, their locations or shapes;

2. Changes in melanin producing activity of these cells;
3. Changes in the rate or manner of loss of melanin pigment from the skin [18].

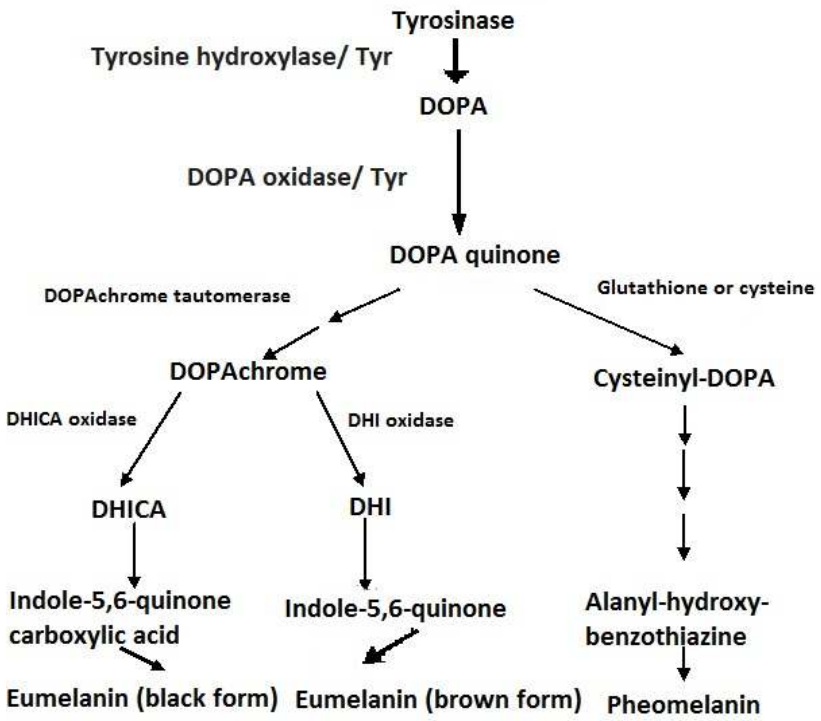

Fig 1: Pathway of melanin synthesis

Several genes with great number of alleles control the type and amount of melanin which results in wide variation of skin colours. Regardless of the degree of pigmentation the human epidermis comprises approximately 74% of eumelanin and 26% pheomelanin. Pigmentation of skin in human is variable and has evolved predominantly in response to the penetration of UV levels [19]. In addition to UV radiation melanin synthesis is also influenced by hormones and biochemical subtances. The hormones that possess melanocyte stimulating activity includes hypophyseal hormones such as melanocyte stimulating hormones (MSH, melatonin), β-lipotropin, and to a lesser extent adrenocorticotropic hormone (ACTH). Hyperpigmentation of skin are usually caused due to an increased number, or activity, of melanocytes and tyrosinase as well as delayed breakdown and removal of

melanin. Common etiologies include postinflammatory hyperpigmentation, melasma, solar lentigines, ephilides and café-au-lait macules. The increase in melanin in epidermis usually enhance with a Wood lamp, but does not enhance its increase in the dermis. Dermal and epidermal changes can be observed in some disorders such as melasma and can be classified as mixed. Reduction of melanocytes or an inability of melanocytes to produce melanin or abnormal transfer of melanosomes to neighbouring keratinocytes are the main factors that contribute to hyperpigmentation. Hypopigmentation can be either diffuse or localized, congenital or acquired, and is often associated with a specific distribution pattern. The most common causes of pigment loss include vitiligo, pityriais alba, tinea versicolor, and the postinflammatory effect [20].

Hyperpigmentation Disorders

Skin hyperpigmentation is a significant cosmetic problem which is often common in middle-aged women. It causes severe impact on patient's quality of life [21]. They can be either congenital with respect to different patterns of inheritance or acquired as a result of skin problems, systemic disease or secondary to environmental factors [22]. The most common acquired pigmentary disorders include melasma and postinflammatory hyperpigmentation [23]. Facial hyperpigmentation is a broad term which is usually associated with the increase in the amount of melanin within the epidermis, the dermis or both. A large number of factors are responsible for facial hypertension and the increase in the melanin pigment might be a local phenomenon or a manifestation of a generalized disorder [24].

Melasma

Melasma is derived from the Greek word *melas,* which means black. It is also known as chloasma and mask of pregnancy. Melasma is the most common cause of facial hyperpigmentation. This disease mainly affects the women whereas men comprises of only 10% of all cases [25]. In addition to the genetic influences and continuous exposure to UV radiation other factors such as hormonal therapies, pregnancy, phototoxic drugs, cosmetics and even antiseizure medications contribute to the pathogenesis of melasma [26]. Exposure to sunlight is a major factor in the development of melasma and usually occurs in face which is the sun exposed body site and the condition generally worsens in summer. People suffering from melasma have a

hypersensitivity to UV radiation which means even a brief exposure to sunlight can stimulate hyperpigmentation. Melanocortin within melanocytes and keratinocytes are induced by UV radiation which justifies the involvement of this hormone in the pathogenesis of the disease. Recently it was suggested that increased in the pigmentation in melasma is also contributed by high intensity visible light. Pregnancy and use of hormonal birth control also contribute as a factor for occurrence of this disease. Presence of excess melanin in both the epidermis and upper dermis is often observed in melasma lesions [27].

Classification

The following three patterns of melasma are recognized in accordance to the distribution of lesions:

1. The centrofacial pattern which involves the forhead, cheeks, upper lip, nose, and chin is the most common pattern.
2. The cheek and bones comes under the malar pattern while the ramus of the mandible constitute the mandibular pattern.

   Similarly the wood's light examination helps to classify melasma into four histologic types:

   1. The most common type of melasma is called as the epidermal type and its pigmentation is intensified under Wood's light examination. It is characterized by increase in melanin in all epidermal layers.
   2. Presence of many melanophages throughout the entire dermis constitute the Dermal type and there is no increase in pigmentation in the wood light examination.
   3. Increase in melanin in the epidermis as well as presence of many dermal melanophages constitute the mixed type. The pigmentation becomes more apparent only in some areas under Wood's light examination.
   4. Indeterminate type are the individuals with skin type VI where Wood's light examination is of no benefit [28].

Postinflammatory hyperpigmentation

A common sequelae of inflammatory dermatoses is the postinflammatory hyperpigmentation that usually affect with considerable frequency and severity in the darker skinned patients [29]. It is one of the most common causes of altered skin colour and is a frustrating problem that affects many dermatology patients, particularly the dark skinned individuals [30]. The darker Fitzpatrick skin types IV, V, VI are more prone to postinflammatory hyperpigmentation with no gender preferences as it occurs with equal incidences in males and females of all ages. Patients with inflammatory diseases that disrupt the epidermal basal layer suffers the worst effect of PIH [31]. A variety of inflammatory conditions can result in PIH which can originate from endogenous or exogenous sources. Lichen planus, psoriasis, atopic dermatitis and acne vulgaris are the endogenous sources whereas non-ionizing radiation, phototoxic reactions, laser procedures and chemical peels constitutes the exogenous causes of PIH [32]. Hyperpigmentation that occurs after skin pigmentation involves the occurrence of two major processes. The first process involves the destruction of basal cell layer in the inflamed skin which is referred to as the incontinentia pigmenti which is a result of accumulation of melanophages in the upper dermis. The degenerated basal keratinocytes and melanocytes which contain a large number of melanin and are then phagocytosed by macrophages [33]. Epidermal inflammatory response constitute the other process that results in the release and oxidation of arachidonic acid to prostaglandins and leukotrienes. These mediators stimulates the epidermal melanocytes by altering the activity of melanocytes and immune cells and subsequently the synthesis of melanin increases leading to the transfer of pigment to the surrounding keratinocytes. This excess stimulation and subsequent transfer of melanin granules results in epidermal hypermelanosis [34]. Variation in size and shape and along with colour ranging from light brown to black can be observed in the lesions caused as a result of PIH [35].

Solar (actinic) lentigo

Letigines, age spots and liver spots are also used to refer to these hyperpigmented spots. The parts of the body exposed to sun (in particular, the hands, arms, and face) are likely to get affected and the chances becomes more due to chronic exposure of skin to UV resulting in chronic

inflammation [36]. Local proliferation of melanocytes which is caused due to UV radiation results in the accumulation of melanin in skin cells (keratinocytes). A solar lentigo or solar lentigines are commonly seen in elderly patients [37]. The molecular mechanism which involves the initiation of solar lentigo is not fully understood but through research it has been found that keratinocytes stimulated by UVB to produce interlukin-1 alpha induces keratinocyte growth factor (KGF) secretion which thereby increases the pigment production in pigmented epidermal equivalents as well as in human skin explants [38].

Ephelides

These are generally benign pigmented spots that are mainly observed in Caucasians and Asians. They are mostly found on the face, neck, chest and arms. They are characterized by appearance of small pigmented spots (generally 1-2mm, but can be larger) and are usually red to light brown in colour. Within the age of 2-3 yr they first appear and eventually increase during adolescesnce and partly fade away with age. Individuals with fair skin and/or red-hair are commonly susceptible to this disease [39]. They are caused due to an increase in the photoinduced melanogenesis which involves the transfer of a large number of fully melanized melanosomes from melanocytes to keratinocytes. The hyperpigmented macules are generally round, oval or irregular in shape without any propensity for malignant transformation [40]. A subtype of solar lentigo is often represented by some ephelides [41].

Café-Au-Lait Macules

One of the common hyperpigmented and flat skin lesions known as Café-au-lait-macules (CALMs) are found in the general population which represents a localized area of melanin formation. Increased melanin in melanocytes and basal keratinocytes mainly contribute to the occurance of the disease. They are congenital i.e., present at birth or appear in early part of life. It is difficult to visualize the CALMs which are congenital therefore Wood's lamp may help in improving the visibility. With the advancing age they increase in number and size with variation from light brown to dark brown in colour. The term cafe-au-lait is derived from French word which means "coffee with milk". Individuals with several genetic syndromes like neurofibromatosis (NF1, NF2), McCune-Albright syndrome, ring chromosomes syndromes,

constitutional repair mismatch deficiency, tuberous sclerosis, Fanconi anaemia, Bloom syndrome and Silver-Russell syndrome are more prone to CALMs. 95% of NF1 patients suffer from CALMs. In general population, the solitary CALMs are usually common which is inherited as autosomal dominant [42,43].

Utilities of herbal extracts in skin hyperpigmentation

Synergism is one of the phenomenon observed in herbal extracts that helps in improving the efficacy and is often used in cosmetic formulations. Hydroquinone, vitamin C or ascorbic acid, arbutin, kolijic acid and its derivatives are the commonly used agents. In addition to this mulberry, artocarpus and orchid extracts are also utilized in cosmetic formulations [44,45]. Hydroquinone is considered as superior quality among tropical treatments for hypigmentation. Skin irritation, exogenous ochronosis and contact dermatitis are the adverse effects that has been associated with its use in dark skinned people. Even long term use of corticosteroids causes local or systemic side effects. Therefore natural plant extracts has been investigated that led to identification of many potentially active compounds which can be used as a novel depigmenting agents [46].

Arbutin

A naturally occurring β-D-glucopyranoside derivative of hydroquinone known as arbutin are found in the dried leaves of definite species of plant. Bearberry is one such plant. Rather than preventing the synthesis and expression of the enzyme it acts by inhibiting melanosomal tyrosinase and DHICA (5,6-dihydroxyindole-2-carboxylic acid) polymerase activities at concentrations which is noncytotoxic. In cases of cutaneous hyperpigmentation which is characterized by hyperactive melanocyte activity; arbutin acts as an effective topical treatment [47]. According to a study, stronger inhibitory effect on human tyrosinase activity is shown by α-arbutin than arbutin. In topical skin preparations α-Arbutin has widely replaced arbutin and it is selected as the skin lightening agent as it is effective and stable at producing the desired effects on human skin [48]. Topical treatment with deoxyarbutin conducted in a human clinical trial for 12 weeks had a positive effect as it improved the condition of solar lentigines of both dark-skinned and light-skinned individuals respectively [49].

Flavonoids

Flavonoids are multi-active components having antioxidant and soothing actions and are commonly used in cosmetics. More than 5000 flavonoids have been extracted and identified and they are the largest group among plants with active properties. The best known activity of flavonoid on the skin is because of its antiradical properties. Presence of phenol groups with high reduction potential leads to formation of resonance-stabilized anion radicals. The degree of structure and physicochemical properties determines the scavenging activity of flavonoids.

Flavanoids extract of green tea leaves and seeds, leaves of wine grapes, and the oligomers of these compounds found in the bark of Mediterranean pine are regarded as the most effective protection of the skin against radical stress. Proper synthesis of collagen requires the presence of vitamin C. Free radical activity is one of the main factors which is responsible for depletion of vitamin C concentration in skin. The decomposition of vitamin C is prevented by flavonoids because of their strong anti-radical activity [50].

Aloesin

Aloesin is a compound which is extracted from aloe pant. In human, mushroom and murine sources it has been proven to competitively inhibit tyrosinase. Aloesin inhibits tyrosine hydroxylase and DOPA oxidase activities in a dose dependent manner [51]. It was observed that by using the integrated mechanisms of noncompetitive and competitive inhibitions aloesin along with arbutin can synergistically inhibit melanin production by inhibition of tyrosinase activity [52].

Niacinamide

A biologically active form of niacin (vitamin B3) called niacinamide are mainly found in abundance on many root vegetables and yeasts. Niacinamide is a precursor of both NADH (nicotinamide adenine dinucleotide) and NADPH (nicotinamide adenine dinucleotide phosphate). Participation of these cofactors in a large number of cellular enzyme reactions may form the basis for the benefits of variety of cosmetics. It has been investigated that application of niacinamide in the co-cultures of human melanocytes and keratinocytes have resulted in the inhibition of the relocation of melanosomes to keratinocytes from melanocytes. As shown by the clinical

studies the application of topical niacinamide have resulted in a reversible reduction of hyperpigmented lesions and increase in the skin lightness as compared to the vehicle alone after 4 weeks of use. In another clinical study, use of topical niacinamide has shown decrease in collagen oxidation [53]. According to a study it was found that niacinamide provided significant improvements in fine lines/wrinkles, texture, spots of hyperpigmentation and red blotchiness and also it was well tolerated by the skin along with the refinement in the skin yellowing (sallowness) [54].

Hesperidin

The peel and membranes of citrus fruits contain a bioflavonoid called Hesperidin. Studies have shown the potent ability of Hesperidin to inhibit the synthesis of melanin without cytotoxicity [55]. Protection against UVA-induced damaged of fibroblast along with the prevention of oxidative damage of collagen are some of the notable functions of hesperidin. As hesperidin improves the overall skin tone and has antiyellowing effects, it can be used as a potential skin lightening agent [56].

Mulberry

Mulberry plants belong to Moraceae family. They are usually grown for the purpose of nutrient source for silk worm and also as raw materials for the preparation of jams, marmalades, vinegars, juices, wines, and cosmetics [57]. The leaves of dried mulberry (*Morus alba*) of 85% ethanol extract have shown the inhibition of tyrosinase activity. The active component called Mulberroside F have shown to inhibit tyrosinase activity on the formation of melanin in melan-a cells. In addition to it several phenolic flavonoids are also isolated from its leaves which include quercitin, gallic acid and fatty acid such as palmitic acid and linoleic acid. Because of the superoxide scavenging activity it is used as one of the component in skin lightening agent and even provides protection against auto-oxidation [58].

Liquorice extracts

Liquorice (*Glycyrrhiza glabra* L) is a perennial plant belonging to Fabaceae family which is well known for its sweet-tasting root. A wide range of bioactive natural products are present in liquorice extracts. Glycyrrhizin a triterpine-type saponin has antiviral, anti-inflammatory, antitumor and antimicrobial properties. The extracts of liquorice roots protects the skin

against injuries caused due to oxidative stress [59,60]. In addition to it; it also has the property to accelerate wound epithelization, ameliorate remodeling at the site of the wound and effectively reduce the symptoms of atopic dermatitis (AD) [61]. Studies have shown the benefits of using isoliquiritigenin in the treatment of mice having AD-like skin lesions and thus give us a hope for using it as a potential therapeutic agent in the treatment of AD in humans [62]. The main ingredient present in the hydrophobic portion of liquorice extract is called glabridin and at concentration which ranges from 0.1 to 1.0μg/ml it inhibits the tyrosinase activity in cultured B16 melanoma cells without disturbing the synthesis of DNA. Other active compounds isolated from liquorice extracts that inhibit tyrosinase activity includes glabrene, isoliquiritigenin, licuraside, isoliquiritin and licochalcone. Many properties exhibited by Glabridin are potentially beneficial in cosmetic products because it acts as an antioxidant, estrogenic, anti-inflammatory and skin-whitening agent. It is incorporated in topical products because of the skin depigmentation activity [63,64]. Liquiritin causes depigmenation by other mechanisms as it has no effect on the tyrosinase activity. Studies have shown that application of 20% liquiritin cream at 1g/day for 4 weeks is therapeutically efficacious for melasma [65].

Ginseng

A slow growing perennial plant with fleshy roots named ginseng belongs to the Panax genus of Araliaceae family. Ginseng is commonly used as health supplement and is also used in herbal formulations for the treatment of numerous illness in East Asian countries [66]. Asia, North America and Europe is home to a total of 13 species [67]. Ginseng is commonly referred to the rhizome and dry root of Panax ginseng C.A. Meyer (Araliaceae). It is commonly found in places of cooler climate viz. Northeast China, Korea peninsula and Russia and North America [68]. Evidences suggest the prevention of skin aging with the use of Panax ginseng and ginsenosides. Improvement in facial wrinkling was observed due to the use of ginseng extract in two separate clinical trials. Increase in type I procollagen synthesis contribute to the reduction of wrinkles [69]. Fermented red ginseng is believed to be more efficacious than unfermented red ginseng as it is fruitful in reducing wrinkles and enhance skin whitening [70]. P-coumaric acid is extracted from the fresh leaves of Panax gingseng. In contrast to the inhibition of tyrosinase demonstrated by L-DOPA more stronger inhibition

of the oxidation of L-tyrosine is shown by P-coumaric acid [71]. Treatment of B16 melanoma cells with Radix ginseng in presence of varying concentrations of Radix trichosanthis have resulted in the suppression of the activity of tyrosinase enzyme and melanin content with slightly increase in cell proliferation thereby uplifting the possibility of this combination which can used as an effective skin-lightening agent [72].

Polyphenols

Polyphenols are a large family of naturally occurring plant products and are found to have a wide distribution in plant foods viz. fruits, vegetables, nuts, seeds, flowers and bark [73]. The beneficial health effects of fruits and vegetables are contributed by polyphenols [74]. Phenolic acids, flavonoids, catechins, stilbenes, proanthocyanidins, ellagitannins and anthocyanins constitute the most common polyphenols [75]. These polyphenols exhibit antioxidant capacity. It has been observed that many types of polyphenol plant extracts inhibits melanogenesis. Red wine, cranberry juice and grape seeds are rich source of proanthocyanidins or procyanidins. They exhibit much stronger antioxidant activities than that of vitamin C or E in aqueous systems. Fruits and vegetables are rich in ellagic acid. Around 90% ellagic acid is present in the rinds of pomegranate extract and inhibitory activity is shown by it against mushroom tyrosinase *in vitro*. It may act by the mechanisms that inhibit proliferation of melanocytes and the synthesis of melanin by tyrosinase in melanocytes [76].

Gingko

A potent free radical scavenging activity have been shown by the extracts from the leaves of the gingko tree when they are applied to skin. The tyrosinase activity is inhibited by the gingko flavones glycosides (mainly quercetin and kaempferol derivatives) by chelating copper in the enzyme [77].

Conclusion

Melanin plays an important role in the pigmentation of human skin. Apart from being a pigment it is also a phytoprotective agent that protects the skin from the harmful UV radiation. Since the concentration of melanin is high in darker skin individual, therefore they are prone to less DNA damage than those with lighter skin tone. Disorders of skin pigmentation are mainly due

to the disturbances in the pigment called melanin. Factors ranging from increase and decrease in concentration to abnormal location or distribution of melanin mainly paves the way for skin pigmentation disorders. Middle aged women are more prone to skin hyperpigmentation. In todays world, facial hyperpigmentation has become a major concern and hence the successful treatment of such disorders seems to be challenging because of its inconsistent nature. It is often described as a frustrating problem which affects the patient's quality of life. The active compounds derived from plants are gaining popularity for improving the skin lightness. This is because of several advantages such as having fewer side-effects, better patient tolerance, being relatively less expensive and acceptable due to a long history of use. As a result people prefer the use of herbal or natural skin-lightening agent as they are perceived to be safer than that of synthetics. Herbal treatments are often considered as milder, safer and healthier and hence formulation of herbal products with proven effectiveness is a key concern for the cosmetic industry.

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