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Plant-based skin lightening agents: A review

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ABSTRACT

Hyperpigmentation is a skin disorder that occurs widely in the human population in which darkened patches or spots appear on the skin. Cosmetic products containing natural skin lightening agents are regarded as a safe alternative and effective approach to this hyperpigmentation problem. The review paper aims to discuss on some potential plant species with skin lightening properties by focusing on the presence of responsible bioactive compounds and their specific mechanisms of action in minimizing melanin production in hyperpigmentation problem. The finding shows that different bioactive compounds have various modes of action on melanin biosynthesis pathway including tyrosinase inhibition, melanosomes transfer inhibition, anti-oxidant and anti-inflammatory activities. Some plants with skin lightening activity contain several bioactive compounds which contribute to an enhancement of skin lightening effects and inhibition of hyperpigmentation. In conclusion, the screening of potential skin lightening ingredients from natural sources is very crucial process before formulation development for an effective skin lightening product.

Keywords: Hyperpigmentation – Skin lightening – Tyrosinase inhibitor –Melanosomes transfer inhibitor – Antioxidant – Anti-inflammatory

INTRODUCTION

Hyperpigmentation becomes one of the aesthetic problems among humans including the male and female population in which darkened patches or spots appear on the skin. This may probably occur due to an overproduction and accumulation of melanin pigments or an increased amount of melanocytes expressing melanin synthesis within the skin layers^[1,2]. Post inflammatory hyperpigmentation, solar lentigo, melasma, freckles and age spots are examples of hyperpigmentation problems. Melanin is a skin pigment that gives color to the skin, hair and eyes^[3]. The variation in skin color among various races is mainly determined by size and amount of melanosomes and the number, types and distribution of melanin in the suprabasal skin layer. Besides determining human skin color, melanin also plays a crucial protective role in human skin against the deleterious impacts of ultraviolet (UV) radiation, drugs, chemical substances and other environmental factors.

As depicted in Figure 1, epidermal melanin units are arranged within the epidermis which consists of melanocytes surrounded by keratinocytes^[4]. The presence of melanin units is very important for the melanin production. Melanogenesis or melanin biosynthesis is a complex sequential pathway that occurs in the melanosomes, membrane-bound organelles in melanocytes and catalyzed by tyrosinase as a rate limiting enzyme^[5]. However, melanin production can be affected by various internal factors such as hormone regulation and inflammation as well as external factors such as UV exposure and drugs^[1]. Consequently, this will lead to increased melanin production and hyperpigmentation.

Therefore, cosmetic products containing skin lightening agents are considered as an effective approach towards this problem. Currently most cosmetic products contain various types of skin lightening ingredients either found in natural, semi-synthetic or synthetic form^[6]. In addition to resulting in a brighter and even complexion skin tone, it is claimed that skin lightening agents are used to prevent hyperpigmentation by reducing melanin production^[2]. Different skin lightening agents possess distinct mechanisms of action on the melanin biosynthesis pathway.

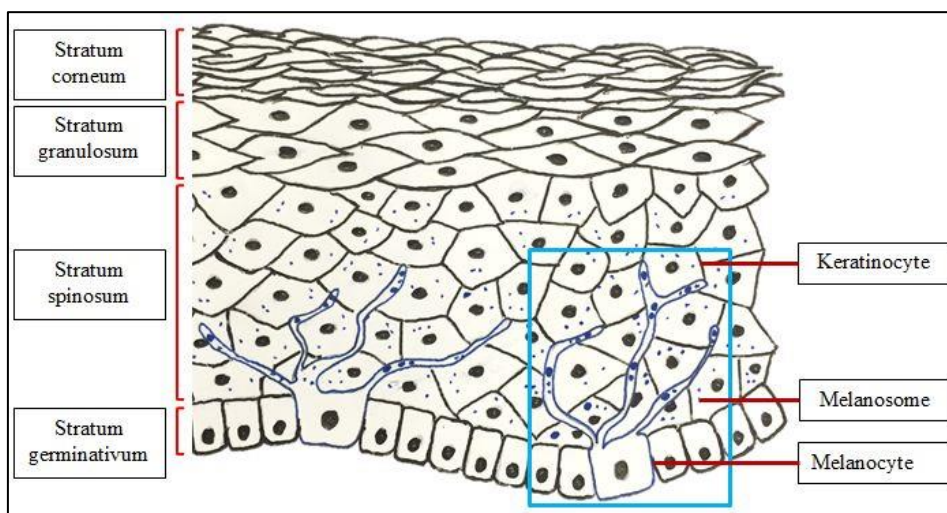


Figure 1: Layers of epidermis and an epidermal melanin unit (Represented by a blue box) ^[4].

However, the use of available skin lightening products commercialized in a market has some controversial and doubtful safety issues to the users. This is due to the incorporation of harmful whitening chemicals in the cosmetic products such as hydroquinone ^[7] and mercury ^[8] for an instant and greater lightening effect. It was reported that these chemical substances have serious safety concern among consumers as they exert many adverse effects to the skin and body health such as skin irritation, contact dermatitis, depigmentation, ochronosis ^[9] and organ toxicity ^[8]. As a result, the use of these toxic substances as skin lightening agents in cosmetic products is strictly banned by the Ministry of Health Malaysia to ensure consumer safety.

Therefore, natural origin skin lightening products are preferable alternative over those chemical substances due to safely and cost effective and fewer side effects ^[10]. Natural skin lightening agents refers to biologically active constituents that are extracted and derived from natural sources such as plants, animals and minerals ^[11]. At the present time, many research studies have found various plant extracts known to have skin lightening activity due to the presence of particular bioactive compounds ^[12]. Hence, this review highlights several natural skin lightening agents and their mechanisms of action in altering melanin biosynthesis pathway. In addition, some potential plants

having skin lightening effects and their bioactive compounds that are responsible for lightening activity are also highlighted in this review.

Mechanisms of action of natural skin lightening agents

Currently, most cosmetic products contain various kinds of skin lightening ingredients which are extracted from natural sources of plant materials as well as microorganisms. The natural skin lightening ingredients such as arbutin, licorice and niacinamide are capable of preventing hyperpigmentation without initiating other skin problems ^[11]. Therefore, the incorporation of natural ingredients into cosmetic formulations is often preferable over synthetic substances.

Generally, the induction of pigmentation can be controlled through many ways such as the inhibition of tyrosinase activity, inhibition of melanosome transfer, acceleration of epidermal turnover as well as the effect of antioxidant and anti-inflammatory agents ^[13]. However, among all targets, tyrosinase inhibition is one of the most important targets in minimizing melanin production and it is considered as the best approach in preventing hyperpigmentation ^[14]. There are many processes involved in melanin biosynthesis in which different skin lightening agents act at various targets and levels of the pigmentation process as illustrated in Figure 2.

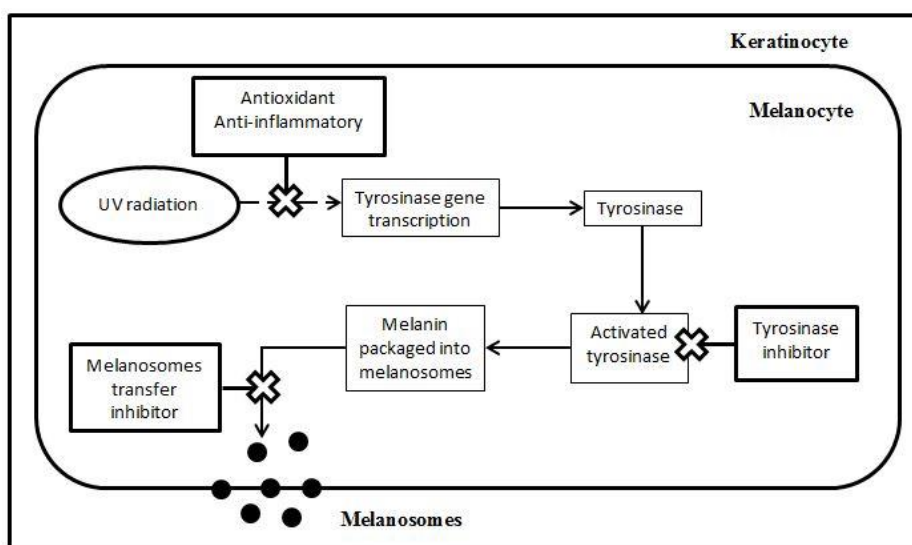


Figure 2: Mechanisms of action of skin lightening agents on melanin biosynthesis.

Inhibition of tyrosinase activity

Inhibition of tyrosinase enzyme activity in the melanogenesis process is an effective way of overcoming skin hyperpigmentation. Tyrosinase is known as a copper-containing and rate-limiting enzyme in the synthesis of melanin pigment which primarily utilizes tyrosine as a substrate [9]. It plays a vital role in catalyzing the hydroxylation of L-tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA) as well as

oxidizing L-DOPA to L-DOPA quinone during melanin biosynthesis as shown in Figure 3 [9]. However, blocking this key enzyme at an initial step of process will result in the interruption of the whole melanin biosynthesis pathway. As a result, melanin production will be eventually minimized. There are various chemical compounds found to have an inhibitory activity against tyrosinase. Most compounds are naturally isolated and derived from natural sources such as arbutin and glabridin.

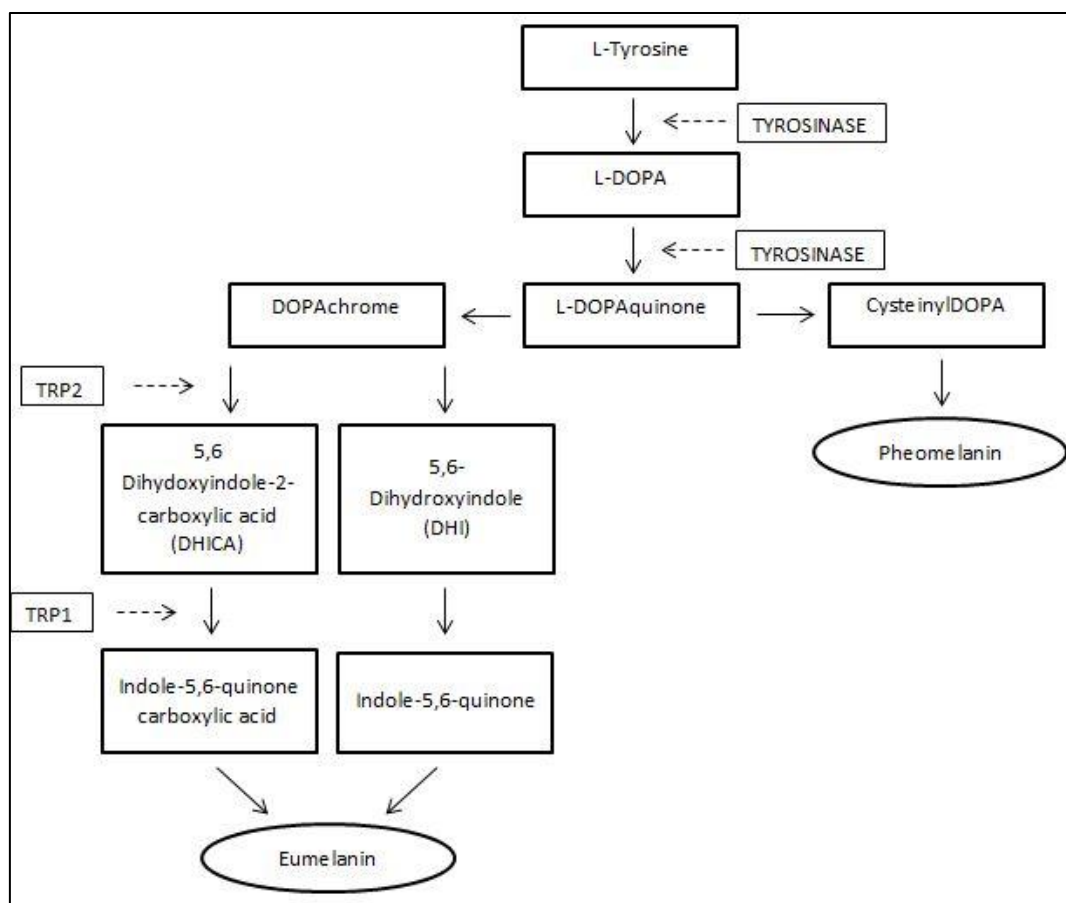


Figure 3: Melanin biosynthesis pathway and production of eumelanin and pheomelanin

Arbutin

Arbutin is known as a naturally occurring substance, β -D-glucopyranoside [15] which is derived from hydroquinone in a glycosylated form [2]. It is found in plant extracts of several species such as bearberry, blueberry, cranberry, pear and wheat [2, 12]. Although arbutin is a derivative of hydroquinone, it inhibits melanogenesis without causing the melanocytotoxicity effect of [15].

According to a study done by Seo *et al.* [16], arbutin is a phytoconstituent that possess skin lightening activity which can prevent the occurrence of hyperpigmentation. This can be proven by the potent inhibition of tyrosinase enzyme activity in the synthesis of melanin without interfering with mRNA gene expression [2, 13]. As a result, melanin biosynthesis will be affected and melanin production will be eventually minimized.

In addition, arbutin also suppresses melanogenesis by inhibiting the activity of 5,6-dihydroxyindole-2-carboxylic acid (DHICA) polymerase which is responsible for the polymerization of 5,6-DHICA [12]. Consequently, this action will affect the melanin biosynthesis pathway and reduce eumelanin production based on Figure 3. The reduction of skin pigmentation was proven by a randomized single-blind placebo study which demonstrated that the topical formulation

containing 1% arbutin exhibited a significant response without any side effects reported [3].

Glabridin

Licorice extract is widely used as commercialized skin lightener in current cosmetic products on the market. One of the important active compounds responsible for skin lightening activity is glabridin [1]. Glabridin is a phytoconstituent derived from licorice root of *Glycyrrhiza glabra* and it is known as a main substance of the hydrophobic part of licorice extract [11, 12].

It has been shown that glabridin is effective in reducing hyperpigmentation by inhibiting tyrosinase enzyme activity in B16 murine melanoma cells without interfering with DNA expression [1, 12]. As a result, the inhibition of tyrosinase activity during melanin biosynthesis will reduce melanin production and its deposition within the skin layers. Therefore, skin hyperpigmentation can be controlled and minimized.

Suppression of melanosomes transfer

The formation of melanosomes in melanocytes is a crucial step which completes the melanogenesis process [13]. According to Figure 2, after

melanins are produced and packaged into melanosomes within melanocytes, they are then transported out into adjacent keratinocytes. Thus, the distribution and accumulation of melanin pigment within keratinocytes will contribute to skin pigmentation. Therefore, the inhibition of melanosomes transfer from melanocytes into keratinocytes will lead to a reduction of melanin deposition within skin layers. One of the biologically active compounds that inhibit the melanosomes translocation process is niacinamide^[9, 12].

Niacinamide

Niacinamide is another common natural skin lightening ingredient incorporated into cosmetic formulations. Niacinamide is recognized as a naturally active form of niacin (Vitamin B) which is abundantly found in yeast and the roots of some vegetables^[12]. It is believed that niacinamide is safely effective skin lightener for hyperpigmentation condition^[3].

Niacinamide possess a great potential in reducing skin hyperpigmentation by inhibiting melanosomes transfer from melanocytes to keratinocytes^[12]. Therefore, a minimal amount of melanosomes-containing melanin will be distributed and deposited in keratinocytes. Thus, hyperpigmentation problem can be controlled and reduced. The effectiveness of niacinamide in overcoming this problem is strongly supported by a study by Gruber and Holtz^[17] who revealed that niacinamide significantly suppresses melanosomes transfer to adjacent keratinocytes instead of directly inhibits melanin biosynthesis. This can be proven by a clinical study in which topical niacinamide showed a significant improvement in hyperpigmentation and greater skin lightness compared with vehicle alone after 4 weeks of use^[18].

Antioxidant

Antioxidants are one of mechanisms that can help to minimize hyperpigmentation problem. This is due to an activation of melanogenesis process which is easily induced by oxidative stress from prolonged UV radiation. Based on a study demonstrated by Huang *et al.*^[19], an oxidative cellular stress is gradually developed due to the formation of harmful hydrogen peroxide (H₂O₂) as well as reactive oxygen species (ROS) in the skin. As a result, the formed ROS will be accumulated and will trigger the melanogenesis process by interacting with tyrosinase enzyme^[11]. Therefore, antioxidants are very crucial in controlling and minimizing the formation of free radicals in the skin by scavenging and neutralizing these harmful radicals as well as stimulating free radical degradation^[11]. Further, antioxidants also have potential in reducing hyperpigmentation conditions by interacting with o-quinones within the melanin intermediates and chelating copper ions in an active site of tyrosinase enzyme^[13].

As illustrated in Figure 2, antioxidants may inhibit hyperpigmentation by down regulating UV induced melanogenesis prior to further tyrosinase gene transcription. The most common phytochemicals that exhibit antioxidant properties in the prevention of melanogenesis are flavonoids, vitamin C and vitamin E.

Flavonoids

Flavonoids are known as naturally occurring compounds that classified under polyphenolic compounds. These compounds can be categorized into several sub-groups such as flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins and chalcones^[12, 20]. Moreover, flavonoids are recognized as secondary plant metabolites which abundantly distributed in various plant species such as green tea, grape seed, mulberry and soy bean^[2].

According to Kumar and Pandey^[21], flavonoids exhibit antioxidant properties by scavenging free radicals formation induced by UV radiation in the melanin biosynthesis pathway. In addition, they also revealed that flavonoids act as metal chelators in the active site of tyrosinase, thus inactivating tyrosinase activity during melanogenesis. Many research studies have proven significant antioxidant potential of

bioactive compounds from the flavonoid group. Quercetin is one of the flavonol members which proven to have a potent antioxidant activity. Based on *in vivo* study done by Casagrande *et al.*^[22], the application of formulations containing quercetin on the UVB-exposed hairless mice at a dose of 5mg was proven to inhibit the UVB radiation-induced depletion glutathione. This experiment highlighted the antioxidant properties of quercetin through the detection of reduced glutathione before and after UVB exposure and without and with quercetin treatment.

Vitamin C

Vitamin C or ascorbic acid is another natural antioxidant that benefits in preventing skin hyperpigmentation problem via regulation of signaling factors such as UV radiation as illustrated in Figure 2. Most cosmetic products frequently contain this naturally occurring vitamin C as a safe and effective antioxidant agent for skin lightening purposes^[3, 17].

As mentioned by Ali *et al.*^[1], the antioxidant effect of vitamin C can be highlighted through a reduction of melanin intermediates in the oxidation process in melanogenesis such as L-DOPA. By referring to Figure 2, tyrosinase will oxidize L-DOPA to L-DOPAquinone. However, the conversion of melanin intermediates into melanin will be inhibited through an interference of crucial oxidation process in melanin biosynthesis. Thus, melanin production will be minimized. The vitamin C is also beneficial in scavenging harmful ROS generated in the skin following UV exposure by chelating copper ions in the tyrosinase active site of action^[13]. As a result, the activation of tyrosinase enzyme will be suppressed and melanin production will be inhibited. Based on a study demonstrated by Humbert *et al.*^[23], the topical cream formulation of 5% vitamin C significantly showed improvement in photoaged skin among healthy female volunteers for six month-period.

Potential plants with skin lightening effect

There are large number of plant species reported to have skin lightening effect due to the presence of phytochemicals which derived and isolated from various parts of plant such as flowers, fruits, seeds, leaves, bark, stems, rhizomes, roots and even the whole plant. As summarized in Table 1, some potential plant species are found to have skin lightening properties due to principle bioactive compounds present which have been described as melanogenesis inhibitor.

Aloe vera

Aloe vera is a commonly used plant in cosmetic industry which exhibits countless skin care benefits such as for relief of skin burns, eczema, wound and other skin inflammatory conditions. It is reported that the aloe species has a great potential of skin lightening activity due to the presence of aloesin as a responsible bioactive compound isolated from the leaves of this plant^[12].

The skin lightening effect of aloesin can be demonstrated mainly through the inhibition of several enzymes' activity in the melanin biosynthesis pathway. It has been shown that aloesin acts as a non-competitive natural tyrosinase inhibitor^(1, 11, 12) and DOPA polymerase inhibitor^[12] during the melanogenesis process. As shown in Figure 3, tyrosinase plays a crucial role in catalyzing the hydroxylation of L-tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA) and followed by the oxidization L-DOPA to L-DOPAquinone. The inhibitory activity of aloesin was proven by a study conducted Choi *et al.*^[24] who reported that the topical treatment of aloesin on the UV-irradiated on the inner forearm resulted in the suppression of skin pigmentation in a dose-dependent manner.

Based on articles reviewed by Sarkar *et al.*^[25] and Katiyar *et al.*^[12], it has been stated that aloesin inhibits the melanin biosynthesis pathway by impeding tyrosine hydroxylase activity, non-competitively and DOPA oxidase activity, competitively. By inhibiting these crucial

enzymes, this modulate the melanin biosynthesis pathway and eventually limit melanin production, resulting in a significant lightening effect and the hyperpigmentation problem may be resolved.

Arctostaphylos uva-ursi

Arctostaphylos uva-ursi or more commonly known as bearberry is other plant species having skin lightening properties. This can be understood by the presence of principle bioactive compounds found in the leaf extracts of this plant, including arbutin which act as skin lightening agent^[12].

As explained before, arbutin acts as a skin lightening agent by having an inhibitory effect towards two types of enzymes involved in melanin production which are tyrosinase^[2, 13, 16] as well as 5,6-DHICA polymerase^[12]. As a result, this inhibitory effect will disrupt melanin synthesis and eventually minimize melanin production within skin layer.

Camellia sinensis

Camellia sinensis or commonly known as green tea is widely used in cosmetic products especially for skin lightening purposes. The leaf extract of green tea contains polyphenolic compounds including epigallocatechin-3-gallate which is a main bioactive compound in green tea extract^[2]. Furthermore, epigallocatechin-3-gallate (ECGC) is also shown to have skin lightening properties by exhibiting various mechanisms of action in melanin biosynthesis pathway such as tyrosinase inhibitor^[1, 2], antioxidant^[25] as well as anti-inflammatory activities^[2, 25].

According to a review article done by Sarkar *et al.*^[25] and Ali *et al.*^[1], it has been revealed that green tea extract has competitive inhibitory activity against tyrosinase enzyme based on *in vitro* mushroom tyrosinase inhibition assay. Besides that, these polyphenolic compounds, mainly ECGC which derived from green leaf extract, are reported to have an antioxidant effect on the melanin biosynthesis pathway^[25]. As illustrated in Figure 2, antioxidants are responsible in preventing stimulating factors of melanogenesis process such as UV radiation. Based on a study demonstrated by Katiyar *et al.*^[26], the topical application of ECGC to human skin was proven to contribute to a potent inhibitory effect against UV-induced ROS production.

On the other hand, it also has been shown that ECGC of polyphenolic groups exerts anti-inflammatory properties by minimizing superoxide anion formation and cyclooxygenase activity as shown in Figure 2^[2, 25, 9]. In brief, all of these mechanisms of action on melanin biosynthesis pathway can lead to a reduced melanin production.

Citrus limon linn

Lemon or its scientific name called as *Citrus limon linn* shows a significant antioxidant activity that is responsible in preventing melanin biosynthesis^[12, 27]. This is due to the presence of principle bioactive compounds including hesperidin and ascorbic acid which are abundantly found in the peel of lemon fruits^[12].

Hesperidin is considered as a major flavonoid compound in lemon which exerts antioxidant activity by scavenging the formed free radicals. According to study done by Lee *et al.*^[27], hesperidin also has a significant ability in diminishing tyrosinase activity in normal human melanocytes as well as B16F10 cells after a hesperidin treatment in a dose-dependent manner. The result of the study also proved an effectiveness of hesperidin in minimizing melanin production. On the other hand, ascorbic acid contained in the peel of lemon fruits also exhibits similar antioxidant effects as hesperidin. As stated previously by Kim *et al.*^[13], ascorbic acid demonstrates its antioxidant effect by scavenging of harmful ROS through chelation action on tyrosinase active site. As a result, tyrosinase will be inactivated and melanin production will be disrupted.

Coffea arabica

Coffeeberry or scientifically recognized as *Coffea arabica* is reported to have skin lightening properties. The fruit extract of coffeeberry plant becomes a main source of polyphenolic compounds including proanthocyanidins^[2], quinic acid, caffeic acid and chlorogenic acid. Due to a high amount of polyphenolic compounds contained in the fruit extract, it has been shown that coffeeberry contributes to an effective antioxidant activity compared to vitamin C and E and green tea extract^[28].

The antioxidant effect of coffeeberry as skin lightening agent can be demonstrated through the inhibition of ROS formation^[2]. Due to reduced formation of ROS within skin layers, melanin synthesis will be suppressed since ROS are responsible in stimulating the process through the activation of tyrosinase^[11, 27]. According to clinical trials on 30 patients with actinic damage, the combination uses of 0.1% coffeeberry cleanser with 1% coffeeberry day and night creams exhibited a significant improvement in fine line, wrinkle, pigmentation and overall appearance after six-week treatment period^[29]. Thus, this finding correlates to the antioxidant activity of coffeeberry.

Glycine max

Glycine max or commonly known as soy bean has a variety of important bioactive compounds which greatly contribute to cosmeceutical and dermatological benefits^[30]. Based on article reviews done by Fisk *et al.*^[2], it has been shown that soy bean extract contains naturally serine protease inhibitors which are important in inhibiting melanosomes transfer from melanocyte into keratinocyte through suppression of protease-activated-receptor 2 (PAR2). As proven *in vivo* study, the topical application of serine protease inhibitor promoted the skin lightening effect of the dark skin Yucatan swine^[31].

Moreover, a review done by Fisk *et al.*^[2] also revealed a similar finding on antioxidant activity of soy bean extract during melanogenesis. It is reported that genistein, a potent soy isoflavones has an ability to protect the skin against an oxidative stress of DNA cellular induced by UV radiation. As a result, melanin biosynthesis pathway will be modulated and this will lead to minimal melanin production. Based on a clinical study, it revealed that the topical treatment of genistein potentially inhibited UVB-induced skin photodamage in human skin before and after UVB exposure^[32].

Morus alba

Morus alba or called as mulberry plant is widely used in folk medicine in China, Korea and Japan as it possesses various medicinal benefits of antioxidant, antidiabetic, antihyperlipidemic, antiatherogenic, antitumor, immunomodulatory as well as neuroprotective^[33]. This plant also acts as skin lightening agent which is important for preventing melanogenesis process.

It has been reported that Mulberroside F, an active compound isolated from mulberry leaves, has a great potential in inhibiting tyrosinase activity^[1, 2] and demonstrating an antioxidant effect^[2, 12] during the melanin biosynthesis pathway. As a result, both mechanisms of action of mulberry plant will modulate the melanin biosynthesis pathway and ultimately decrease melanin amount within the skin layers. According to *in vitro* study done by Lee *et al.*^[34], it manifested that Mulberroside F effectively suppresses tyrosinase activity and melanin production in melan-a cells.

Piper betle Linn.

Piper betle Linn. is a plant species of the Piperaceae family, evergreen and perennial plant with glossy heart-shaped leaves. It is recognized as an aromatic plant which has a characteristic odor and pungent taste. This plant is generally found in India and other South-East countries such as Vietnam and China^[35].

It has been reported that *Piper betle* possess inhibitory activity against tyrosinase [35]. Based on a patent by Majeed *et al.* [36], it has been shown that hydroxychavicol or 1-allyl-3, 4-dihydroxybenzene present in *Piper betle* leaves is found to be an important major phenolic compound that contributes to anti-tyrosinase properties [35]. In addition, Majeed *et al.* also manifested that the inhibitory concentration (IC₅₀) value of tyrosinase inhibition activity of 90% hydroxychavicol content was 8 µg/mL.

Vitis vinifera

Grape seed which extracted from *Vitis vinifera* plant species has a great potential in exhibiting skin lightening properties besides its common uses in food and beverages industry. The skin lightening activity of grape seed extract can be highlighted through a rich source of polyphenolic compounds contained in the extract such as proanthocyanidins [37] and procyanidins [2, 37].

Based on an article reviewed by Sarkar *et al.* [25], it has been agreed that proanthocyanidins which specified under flavonoid group, are considered to have an effective antioxidant effect. The antioxidant effect of protoanthocyanidins can be established by the inhibition of harmful ROS [2] as well as scavenging of generated free radicals [37]. The lightening mechanism exhibited by proanthocyanidins has been discussed previously. Moreover, it also has been suggested that the antioxidant potency of grape seed extract is greater than other phytoconstituents such as vitamin C, vitamin E as well as β-carotene [37]. Therefore, by exerting antioxidant effect on melanin biosynthesis pathway, the production of melanin will be reduced. It has been proven that the oral intake of proanthocyanidin-rich grape seed extract effectively improves the hyperpigmentation of Japanese women having chloasma [37].

Table 1: Overview of plant species containing skin lightening phytoconstituents and mechanisms of actions.

Plant species	Common name	Plant parts	Phytoconstituents	Lightening effect mechanism
<i>Aloe barbedensis</i>	Aloe	Leaves	Aloesin	i. Non-competitive tyrosinase inhibitor ii. DOPA polymerase inhibitor iii. Non-competitive tyrosine hydroxylase inhibitor Competitive DOPA oxidase inhibitor
<i>Arctostaphylos uva-ursi</i>	Bearberry	Leaf extract	Polyphenols, Arbutin	i. Tyrosinase inhibitor ii. DHICA polymerase inhibitor
<i>Camellia sinensis</i>	Green tea	Leaf extract	Polyphenols (ECGC)	i. Tyrosinase inhibitor ii. Antioxidant iii. Anti-inflammatory
<i>Citrus limon linn</i>	Lemon	Peel	Hesperidin, Ascorbic acid	i. Antioxidant
<i>Coffea arabica</i>	Coffeeberry	Fruit	Polyphenols (Proanthocyanidins, quinic acid, caffeic acid and chlorogenic acid)	i. Antioxidant
<i>Glycine max</i>	Soy bean	Whole plant	Serine protease inhibitor, Isoflavones (genistein)	i. Melanosomes transfer inhibitor ii. Antioxidant
<i>Morus alba</i>	Mulberry	Leaves	Mulberroside F	i. Tyrosinase inhibitor Antioxidant
<i>Piper betle</i>	Betle	Leaf extract	Hydroxychavicol	i. Tyrosinase inhibitor
<i>Vitis vinifera</i>	Grapes	Seeds	Polyphenols (Proanthocyanidins)	i. Antioxidant

CONCLUSION

In conclusion, the identification and determination of potential skin lightening ingredients to be incorporated in cosmetic products are very crucial part before formulation development level. From this literature review, various plant species are discussed and proven to have skin lightening activity in correspond to their bioactive compounds which derived and extracted from plant parts. These bioactive compounds are regarded as a safe and effective alternative skin lightening agents compared to other harmful whitening chemicals such as hydroquinone and tretinoin. In addition to that, various mechanisms of action of particular skin lightening agents are emphasized in this review since different agents act distinctly on various levels of pigmentation process. Based on findings obtained, among all modes of action, tyrosinase activity inhibition becomes the most common target in altering melanin biosynthesis pathway to reduce melanin production within skin layers.

Hence, this literature review can be considered as a platform for future study to explore and reveal other plant species with potential skin lightening properties through an identification of similar bioactive compounds. Furthermore, this review assists in developing an effective skin lightening cosmetic products to overcome a critical hyperpigmentation concern among human population. Besides an efficacy of natural skin lightening agents, a safety feature on the use of bioactive compounds from plant species also have to be emphasized and further studied to avoid any undesired and harmful effect towards the skin.

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