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Review Article

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Antityrosinase effect of botanicals: A review of medicinal plants cosmetic

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ABSTRACT

Antityrosinase as skin whitening agents commercially available for cosmetic to helping people to get lighter skin appearance. Besides as whitening agents, antityrosinase can be used to treat over pigmentation of skin pigmentation disorder in clinical treatment. This agent can inhibit tyrosinase activity in melanogenesis proses. In this review we present an overview of antityrosinase from botanicals as a review of medicinal plants cosmetic.

Keywords: antityrosinase, melanin, medicinal plants, cosmetic

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INTRODUCTION

The skin is a fundamentally important organ of the body, protecting it from damage caused by direct contact with the outside environment it is the first line of defense from external factors [1, 2]. Environmental factors that injure the skin such as: ultraviolet radiation, dehydration, bacterial invasion, mechanical trauma or physical injuries but ultraviolet irradiation is the most common and pernicious [3, 4]. Epidemiological and clinical studies have identified excessive sun exposure as a primary causal factor in various skin diseases including: premature aging, inflammatory conditions, melanoma and non-melanoma skin cancers [5, 6].

In recent days, skin whitening agents bring the attention of researchers to find the solution for skin pigmentation disorders. Inhibition of tyrosinase and antioxidant agents as a way of preventing overproduction of melanin in epidermal layers.

UV RADIATION

UV is part of the electromagnetic spectrum including of two types: visible and X-ray regions. Ozone layer in atmosphere as an ultraviolet radiation (UV-R) barrier and absorbed it with result only 5–10% of the total radiant energy received at the surface of the Earth and the rest is divided between the visible (40%) and the infrared (50%) [7]. According to it wavelengths, UV-R is divided in UV-A (320–400 nm), UV-B (280–320 nm), and UV-C (200–280 nm) but only wavelengths under 280 nm can reach the Earth's surface [8].

Losing of ozone layer causes UV-R can reach the earth's surface. However, UV-B excessive penetration leading to a higher risk for UV-induced carcinogenesis [9]. UV-R is responsible for a wide variety of different acute and chronic effects on the skin. Process referred to deleterious biochemical reactions occur within the skin when it is exposed to excess UV-R called photoaging [10]. Photoaging is premature aging of the skin process caused by repeated exposure to UV primarily from the sun, but also from artificial UV-R sources [11-13].

The adverse role of UV-A in this regard is less well studied, and currently there is a great deal of controversy regarding the relationship between UV-A exposure and the development of melanoma. UV-A causes DNA damage via photosensitized reactions that result in the production of oxygen radical species. UV-A can induce mutations in various cultured cell lines [14]. UV-B causes sunburn reaction within the skin and is absorbed mainly by the epidermis and upper dermis; stimulates the production of melanin and induce erythema [15]. Our bodies manufacture vitamin D when the sun's UV-B rays interact with 7-dehydrocholesterol (7-DHC) present in the skin. However, we can produce only a limited amount of vitamin D from UV-B [16].

Two defensive barriers as a skin responds to UV-R exposure: thickening of the stratum corneum and increasing melanin production in epidermis cells. Acute responses of human skin to UV-R include photodamage, erythema, mutation, immunosuppression, synthesis of vitamin D and tanning. Chronic UV-R effects include photoaging and photocarcinogenesis, which is considered to be induced by mutation and immunosuppression [17].

UV-R leads to alterations in the composition of the skin, including the accumulation of elastic fibres [18, 19]; collagen reduction and degeneration; [20] and glycosaminoglycans (GAGs) deposition [21]. UV-R modulates secondary metabolism in the skin for the formation and delivery of melanin [22]. Melanin can filters out UV-R, but the melanin in hair follicles, particularly in light hair, actually increases the sun damaging effects of UV-R and causes cell death in the hair follicle [23].

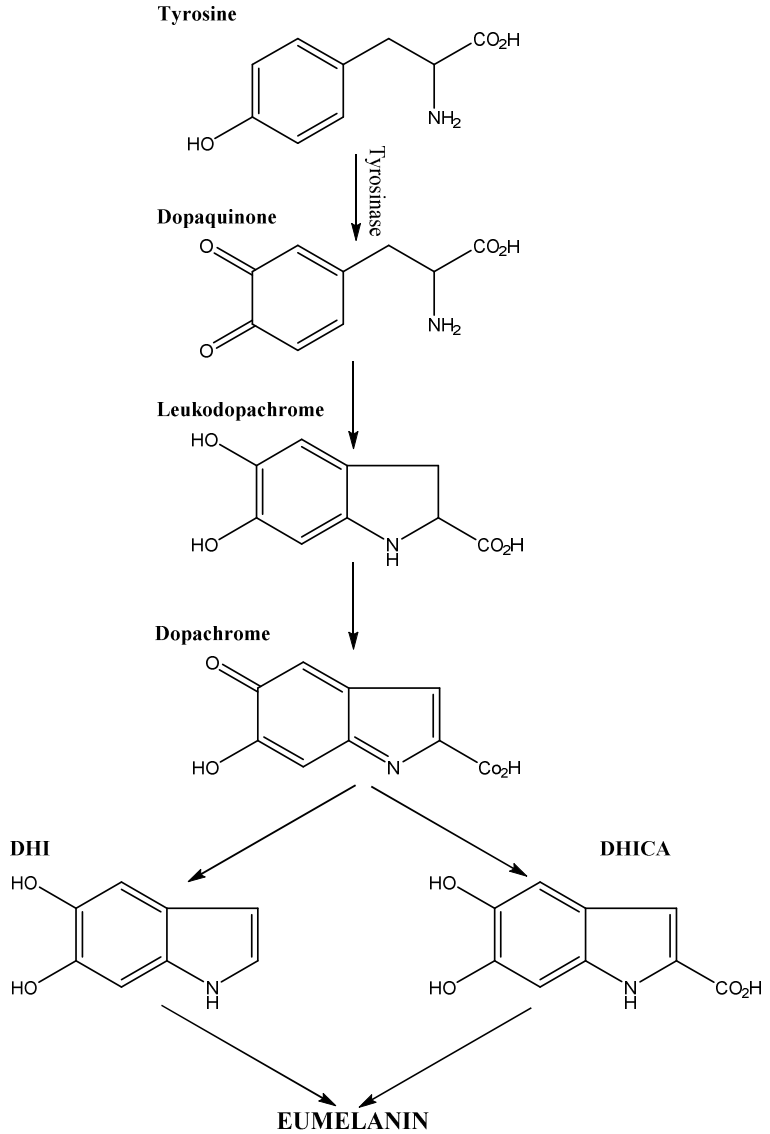

Figure 1.Schematic of a melanocyte: the engine for melanin production. Melanin synthesis begins in the liver where phenylalanine is converted to tyrosine by the action of phenylalanine hydroxylase. The oxidation of L-Tyrosine to L-DOPA is then catalysed by the action of tyrosinase enzymes within the melanocyte's melanosome. In the next step L-DOPA is oxidized to DOPA-quinone and become pheomelanins by cysteine. Than L-DOPA is oxidized to DHICA and DHI. DHI is a precursor of DHI-melanins. DHI, 5,6-dihydroxyindole; DHICA, 5,6-dihydroxyindole-2-carboxylic acid (Adopted from *J of Invest Dermatology, 2010:130 pp 645–647* and *The FASEB J, 2007:21;4 pp 976-994*) [22, 27]

SKIN PIGMENTATION DISORDERS

Melanosome is an enzyme which located in dendritic melanocytes of epidermal cells responsibility to product melanin. Melanin gives coloring in the skin and it effective absorb the UV-R (able to dissipate over 99.9% of absorbed UV-R). Melanin also is thought to protect skin cells from UV-B radiation damage, reducing the risk of cancer [24].

Melanin synthetize begins with DOPA-quinone is converted to leuco-DOPA-chrome and then DOPA-chrome through auto-oxidation, and subsequently in the presence of DOPA-chrome tautomerase and dihydroxyindole-2-carboxylic acid oxidase, DOPA-chrome is converted to 5,6-dihydroxyindole. Finally, the oxidation of 5,6-dihydroxyindole (DHI) to indole-5,6-quinone by tyrosinase leads to the formation of eumelanin (brown-black pigment. In the presence of cysteine or glutathione, DOPA-quinone is converted to cysteinyl-DOPA Subsequently, pheomelanin, a yellow-red pigment, is formed through the oxidative polymerization of cysteinyl-DOPA via 1,4-benzothiazinylalanine intermediates [25, 26].

ANTITYROSINASE

The most target for skin whitening is direct inhibition of tyrosinase (antityrosinase) activity. Antityrosinase can find in clinical application in cosmetics and pharmaceutical formula [28]. Antityrosinase has a few side effects because only targeting to melanogenesis in the cell but there are some inhibitor can inhibit tyrosinase gene expressions that cause hypopigmentation. So, searching for new melanogenesis inhibitors based on direct inhibition of tyrosinase catalytic activity seems to still be the major field of interest for further study [29].

Tyrosinase (phenol-oxidase activity) which catalyzes the transformation of L-tyrosine into L-DOPA by hydroxylation and further into DOPA-quinone by oxidation. Then, through a series of non-enzymatic reactions, DOPA-quinone is rapidly transformed into melanins, which is measured at 492 nm in a spectrophotometer.

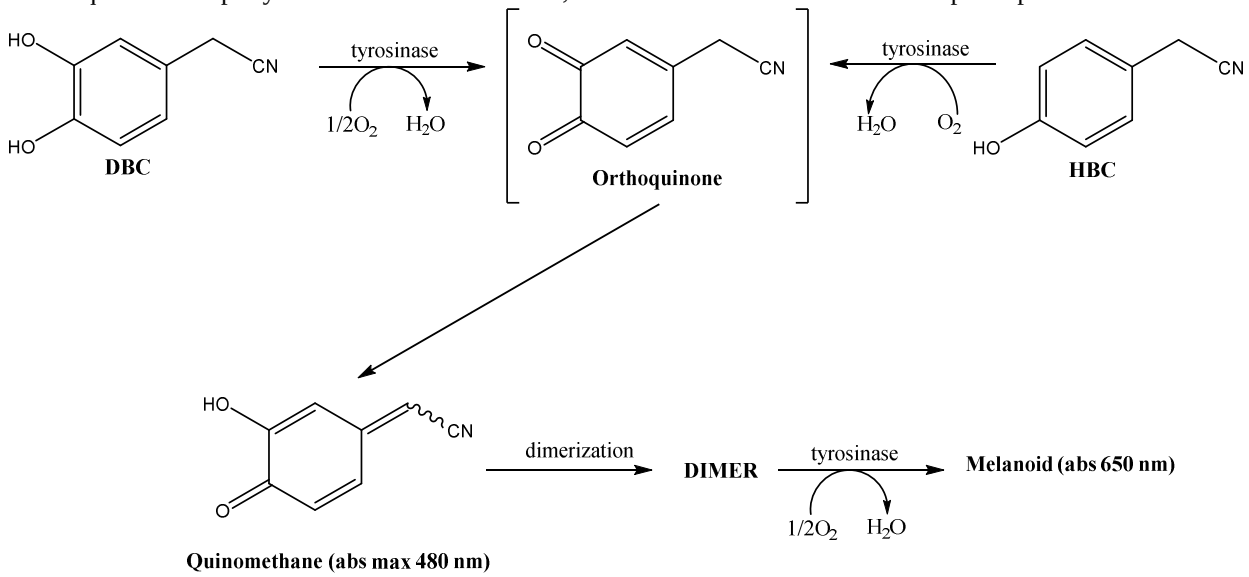

Figure 1.Diagrammatic outline when 3,4-dihydroxybenzylcyanide (DBC) is oxidized by mushroom tyrosinase become quinomethane, exhibits an absorption maximum at 480 nm. The monohydric phenol, 4-hydroxybenzylcyanide (HBC), was not oxidized by tyrosinase unless the enzyme was pre-exposed to DBC, the maximum acceleration of HBC oxidation being obtained by approximately equimolar addition of DBC. This reaction with subsequent decay, possibly to a dimer, which is oxidized by tyrosinase to a melanoid product absorbing at 650 nm [30]

HERBAL IN ANTITYROSINASE

Many plants in traditional Ayurvedic knowledge have been described to be useful in skin pigmentation disorders including antityrosinase [31]. The use of medicinal plants and natural products increased dramatically in the last two decades in all over the world. More than hundred medicinal plant species have been used ethnopharmacologically and traditionally to treat skin pigmentation disorder [32].

This review was undertaken to discuss medicinal plants cosmetic with antityrosinase activities, to serve as a guide for further research and also to persuade the conservation of such plants with due consideration and proper planning.

Tabel 1.Plant extracts and compounds selected as tyrosinase inhibitors by extraction from natural sources and the (possible) isolation and characterization of the active ingredients. Using plant as antityrosinase have been used ethnopharmacologically and traditionally to treat skin pigmentation disorder

Plant Name	Family	Plant part or compounds	Reference
Amberboa ramosa	Compositeae	3beta, 21, 22, 23-tetrahydroxy-cycloart-24 (31), 25 (26)-diene	[33]
Anacardium occidentale	Anacardiaceae	Anacardic acids, 2-methylcardols, and cardols	[34]
Arbutus andrachne	Ericaceae	Arbutin, hydroquinone, β-sitosterol and ursolic acid	[35]
Artocarpus gomezianus	Moraceae	Norartocarpetin and resveratrol	[36]
Artocarpus heterophyllus	Moraceae	Dihydromorin, steppogenin, norartocarpetin, artocarpanone, artocarpesin and isoartocarpesin	[37, 38]
Artocarpus incisus	Moraceae	Flavonoids, stilbenes and related 4-substituted resorcinols	[39]
Broussonetia kazinoki	Moraceae	Kazinol C, kazinol F, broussonin C and kazinol S	[40]
Buddleja coriacea	Scrophulariaceae	Phenolic compounds	[41]
Cassia fistula	Fabaceae	Pods (methanol 70%)	[42]
Castanea sativa Mill.	Fagaceae	Stem bark (methanol 80%)	[43]
Cariniana brasiliensis	Lecythidaceae	Bark [(Propylene glycol: deionized water (50/50, %)]	[44]
Ecklonia stolonifera, an edible brown alga	Laminariaceae	Phloroglucinol, eckstolonol, eckol, phlorofucofuroeckol A and dieckol	[45]
Entada Africana	Mimosaceae	Bark [(propylene glycol: deionized water (50/50, %)]	[44]
Eucalyptus camaldulensis	Myrtaceae	Leaves (methanol 80%)	[43]
Flemingia macrophylla	Fabaceae	Roots (water)	[46]
Garcinia kola	Guttiferae	Biflavanones (BG-2)	[47]
Gnaphalium cheiranthifolia	Asteraceae	Phenolic compounds	[41]
Glycine tomentella	Fabaceae	Roots (water)	[46]
Glycyrrhiza inflata B.	Fabaceae	Licochalcone A	[48]
Glycyrrhiza uralensis F.	Fabaceae	Liquiritin, licuraside, isoliquiritin and liquiritigenin	[48]
Graphina glaucorufa	Graphidaceae	Methanol	[49]
Graphina multistriata	Graphidaceae	Methanol	[49]
Graphina salacinilabiata	Graphidaceae	Methanol	[49]
Graphis assamensis	Graphidaceae	Methanol	[49]
Graphis nakanishiana	Graphidaceae	Methanol	[49]
Guioa villosa	Sapindaceae	Betulin, lupeol and soyacerebroside I	[50]
Hippophae rhamnoide	Elaeagnaceae	Berries (methanol 70%)	[42]
Juglans regia L.	Juglandaceae	Leaves (methanol 80%)	[43]
Lonicera japonica T.	Caprifoliaceae	Herb (ethanol)	[51]
Marrubium cylleneum	Lamiaceae	Flavonoids and phenylethanoid glycosides	[52]
Marrubium velutinum	Lamiaceae	Flavonoids and phenylethanoid glycosides	[52]
Momordica charantia	Cucurbitaceae	Whole plant (methanol)	[53]
Morus alba	Moraceae	Root bark (ethanol)	[54, 55]
Muntingia calbura L.	Elaeocarpaceae	Leaves (hydro-ethanol)	[56]
Paeonia suffruticosa	Paeoniaceae	Kaempferol, quercetin, mudanpioside B, benzoyloxypaeoniflorin, mudanpioside H and pentagalloyl-beta-(D)-glucose	[57]
Phaeographopsis indica	Graphidaceae	Methanol	[49]
Phaleria macrocarpa	Thymelaeaceae	Fruits, leaves and stems (ethanol)	[58]
Phellinus linteus	Hymenochaetaceae	Protocatechualdehyde and 5-hydroxymethyl-2-furaldehyde (HMF)	[59]
Prosopis africana	Mimosaceae	Bark [(propylene glycol: deionized water (50/50, %)]	[44]
Pulsatilla cernua	Ranunculaceae	3,4-dihydroxycinnamic acid and 4-hydroxy-3-methoxycinnamic acid	[60]
Portulaca pilosa	Portulaceae	Leaves	[44]
Rapanea parviflora	Asteraceae	Leaves and stem [(dichloromethane and methanol (1:1)]	[61]
Raphanus sativus	Brassicaceae	Whole plant (50% propylene glycol)	[53]
Rhodiola rosea	Crassulaceae	Herb (ethanol)	[51]
Rhus javanica	Anacardiaceae	Tannic acid	[62]
Ruprechtia sp.	Polygonaceae	Aerial organs [dichloromethane and methanol (1:1)]	[61]
Scheelea princeps	Arecaceae	Phenolic compounds	[41]
Sesamum indicum L.	Pedaliacae	Sesamol	[63]
Sophora flavescens	Fabaceae	Kuraridin, kurarinone and norkurarinol, sophoraflavanone G, kuraridin and kurarinone	[64, 65]
Stryphnodendron barbatimao	Fabaceae	Bark [propylene glycol: deionized water (50/50, %)]	[44]
Trifolium balansae	Leguminosae	Phytyl-1-hexanoate, stigmast-5-ene-3 beta,26-diol and stigmast-5-ene-3-ol, campesterol and pentacosanol	[66]
Veratrum patulum L.	Melanthiaceae	Resveratrol, oxyresveratrol and their analogs	[67]
Xanthoceras Sorbifolia	Sapindaceae	Saponins isolate	[68]

COSMETIC USE OF HERB FOR SKIN PIGMENTATION DISORDERS

Hydroquinone contain in cosmetic formulation has been widely used as an effective whitening agent but it has serious safety concerns. Hydroquinone has been connected with mutagenicity and the increased incidence of ochronosis [69-71]. Other compounds often used likes kojic acid, arbutin and azelaic acid (Table 1).

Nowadays, large variety of whitening products commercially available in the market using herb extracts or isolated active compounds as raw materials [72]. Although the information on the exact formulations for all the whitening products is not easily accessible on the internet, we made an attempt to summarize the active whitening ingredients for some of them. Some companies still use single synthetic compounds Table 2).

Table 2. Limited selection of whitening products available on the market with some information on active ingredients

Company	Product	Ingredients	Documentations
Civant Skin Care	Meladerm	Alpha arbutin, tego cosmo C, gigawhite, kojic acid, licorice extract, mulberry extract, bearberry extract, lemon juice extract and emblica extract	http://www.civantskincare.com/ingredients/
Holland & Barrett	Dr. Organic Royal Jelly Light & Bright Cream	Royal jelly, *Aloe barbadensis* leaf extract, *Prunus amygdalus* Dulcis (sweet almond) and *Ascophyllum nodosum* extract	http://www.hollandandbarrett.com/shop/product/dr-organic-royal-jelly-body-skin-whitening-cream-60086386
Paula's Choice	Resist Pure Radiance Skin Brightening Treatment	Mulberry extract, licorice extract and *Vitis vinifera*	*Journal of the European Academy of Dermatology and Venereology*, October 2011, pages 1,140–1,405 [73] *American Journal of Clinical Dermatology*, April 2011, pages 87–99 [74]
St. Dalfour	Dalfour Beauty Whitening Creams	Bearberry extract and seaweed extract	http://www.flawlessbeautyandskinph.com/Authentic-Dalfour-Beauty-Gold-Seal-Beauty-Whitening-Cream-Steamed-Cream--For-Acne-Prone-or-Sensitive-Skin_p_145.html
STIFA Makassar	Nadivayesha	*Curculigo orchioides* extract	http://stifamks.ac.id/
Swiss botany	Swiss botany whitening mask	*Simmondsia chinensis* (jojoba) seed oil, *Morus alba* root extract and papaya Extract	http://www.amazon.com/Whitening-Whiten-Removing-Blemishes-Competitors/dp/B00H5BDX7Y
Whitenicious by Dencia	Facial radiance daytime cream	*Glycyrrhiza glabra* (licorice) root extract, arbutin, *Morus alba* root extract, *Daucus carota sativa* extract, *Lilium candidum* flower extract, *Citrus aurantium dulcis* fruit extract	http://whitenicious.com/products/facial-radiance-daytime-cream

CONCLUSION

Some herbal alternatives employed in these traditions are proven to protect skin pigmentation disorder and to develop polyherbal formulations which contain various herbs acting to supported the main effect. Efficacy and safety aspect have regained herbal popularity and supported by controlled clinical research. Ongoing research worldwide has provided valuable clues regarding the precise mechanism of action of these herbal alternatives and these herbs, have shown interesting results in various target specific biological activities.

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