

Review on Unveiling the Shadow of Hyperpigmentation

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Abstract

Natural products offer promising solutions for treating skin pigmentation disorders due to their non-toxic properties and effective mechanisms of action. Studies highlight their safety and efficacy through methods, such as cytotoxicity tests, tyrosinase activity assays, and melanogenesis inhibition evaluations. Advanced delivery systems, like liposomes and nanoparticles, further enhance their performance by improving solubility and skin penetration. Skin pigmentation disorders, influenced by factors, such as UV radiation, hormonal changes, and inflammation, result in melanin overproduction and uneven skin tone. Eumelanin and pheomelanin, the two primary pigments, play distinct roles in skin protection and temperature regulation. Historically, pigmentation has been unjustly linked to racial biases, reflecting societal discrimination. Modern treatment options, including hydroquinone and tranexamic acid, provide targeted therapies, though the misuse of corticosteroids remains a concern. The development and application of natural products in pigmentation treatment combine efficacy, safety, and economic benefits, offering a sustainable approach to managing these conditions.

Keywords: Skin pigmentation, tyrosinase inhibitors, hypopigmentation, hyperpigmentation, vitiligo, skin lightening, depigmentation

INTRODUCTION

In this review, the pathophysiology and therapeutic approaches of disorders will be examined while concentrating on the application and mechanism of natural products in the treatment of skin pigmentation. Additionally, a summary of the innovative natural product compositions used to treat skin pigmentation is provided. In conclusion, the traditional pharmacodynamic assessment techniques for researching pigmentation disorders are emphasized as a resource for creating novel formulations of natural products. Natural remedies that have whitening and spot-lightening effects have become more and more popular in recent years because of their great biocompatibility, natural nature, and lack of toxicity [1]. Furthermore, numerous studies have verified the safety and effectiveness of these products based on their cytotoxicity, tyrosinase activity, antioxidant levels, suppression of melanogenesis, as well as the well-established animal pigmentation models [2–3]. Without a doubt, research into natural

items as treatments for pigmentation offers great promise and value in terms of producing positive social and economic effects. Uneven brown to dark brown dots on the skin are a sign of skin pigmentation [4]. Skin injury, acne, cellular inflammation, UV radiation, hormonal changes, and medication effects are all related to the beginning of skin pigmentation [5].

The most used oral medication for treating hyperpigmentation is tranexamic acid, which is regarded as a second-line treatment. Tranexamic acid acts by lowering Sufficient amounts of vitamins and proper growth and efficiency of metabolic processes depend on a human diet that is balanced in terms of macro- and micronutrients. Globally, inadequate food quality or quantity,

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higher dietary needs, higher metabolic losses, or less gastrointestinal absorption are the main causes of vitamin deficiencies. Micronutrients, particularly sufficient vitamin levels, are necessary for the efficient and ideal development of metabolic processes. Globally, inadequate food quality or quantity, higher dietary needs, higher metabolic losses, or less gastrointestinal absorption are the main causes of vitamin deficiencies [6].

TYPES OF SKIN PIGMENTATION

To be pigmented is to be colored. Skin color is impacted by illnesses related to skin pigmentation. Melanin is the pigment that gives your skin its color. Melanin is produced in the skin by certain cells. Melanin production is impacted by the health or injury of these cells. Certain pigmentation abnormalities only impact specific skin areas. People impact your body as a whole. An excess of melanin produced by the body results in darker skin. Your skin can become darker due to sun exposure, Addison's disease, and pregnancy. A deficiency of melanin in the body causes skin lightening. Light-colored patches of skin are a symptom of vitiligo illness. A hereditary disorder affecting the skin is called albinism. A person with albinism may be completely colorless, have skin that is paler than usual, or have patches of missing color. Lighter skin can also result from burns, blisters, and infections.

There are some common types of skin pigmentation.

- Melasma.
- Albinism.
- Vitiligo.
- Addison's Disease.

Melasma

Melasma is a gradual, non-clinging, macular hyper-melanosis of the skin that mostly affects the face and dorsal forearms when exposed to sunlight. It may be idiopathic or commonly linked to pregnancy, oral contraceptives, or anticonvulsants, such as phenytoin (Dilantin). The typical color of dermal melasma is greyish with no enhancement. Dark brown with varying enhancement, mixed types. Combination products that contain topical steroids, glycolic acid, and retinoids along with hydroquinone appear to be slightly more effective. For treatment to remain effective, it is usually necessary to continue it permanently [7–15]. In one study funded by a pharmaceutical company, a triple-combination treatment (TriLuma) consisting of 0.01% fluocinonide, 4% hydroquinone, and 0.05% tretinoin cream demonstrated significantly better efficacy in improving dyspigmentation than treatment with any two of these ingredients combined, with only mild side effects (Figure 1).



Figure 1. Melasma.

However, several modest studies indicate that laser therapy or a combination of intense pulsed light therapy and hydroquinone with sunscreen may be an effective treatment for cutaneous or refractory/mixed-type Melasma [7].

Albinism

A genetic disorder called albinism causes the generation of less melanin, which leaves a person with a fair skin tone, light eyes and hair, and an increased susceptibility to certain skin and eye disorders. The pigment called melanin is what gives your skin and hair their color. It is present in the hair, the eyes, and the epidermis, the skin's outermost layer. Melanin supports the prevention of skin damage and skin cancer by protecting your body from ultraviolet (UV) rays from the sun [8].



Figure 2. Albinism.

Albinism can impact people of any ethnicity. According to estimates, 1 in 20,000 Americans and 1 in 17,000 Australians suffer from this illness. Certain regions of the world have higher prevalence rates of albinism, such as Zimbabwe, Africa, where the frequency is approximately 1 in 1,000 (Figure 2) [9].

Vitiligo

A disfiguring skin condition that causes pigmentation loss is vitiligo. One percent of the general population has vitiligo, which equally affects men and women. About 25–30% of patients have a documented family history of vitiligo. 50% of cases occur before the age of 20, with peak onset happening in the second and third decades of life [10]. Vitiligo lesions are composed of distinct, unpigmented macules that vary in size from 5 to 50 mm. A rim of erythema or hyperpigmentation will appear on some. The face, neck, dorsal hands, genitalia, body folds, and axillae are common locations of involvement (Figure 3).

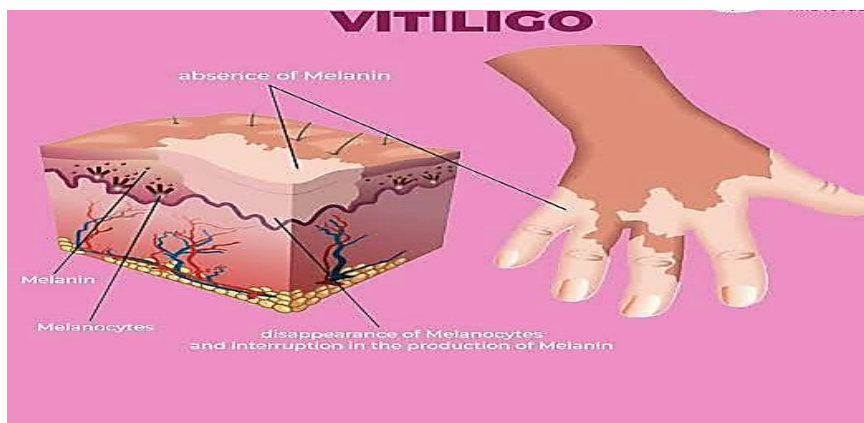


Figure 3. Vitiligo.

Lesions of the perianal, perioral, periorbital, and periumbilical regions can also arise. There are four different kinds of vitiligo: segmental, acral/orofacial, localized, and generalized [10].

Addison's Disease

A rare endocrine illness that affects one in 100,000 people is Addison's disease. It affects both men and women equally and is present in all age groups. This illness bears the name of Thomas Addison, who published the first account of patients with this disorder in the book "On the Constitutional and Local Effects of the Disease of Supra Renal Cap" in 1855. Because Addison's disease is often misdiagnosed in its early stages, it might present as a potentially fatal situation. Since its first description, the underlying cause of Addison's disease has shifted radically from an infectious source to an autoimmune pathology. Still, the most common cause of Addison's disease in poorer nations is tuberculosis (Figure 4) [11].

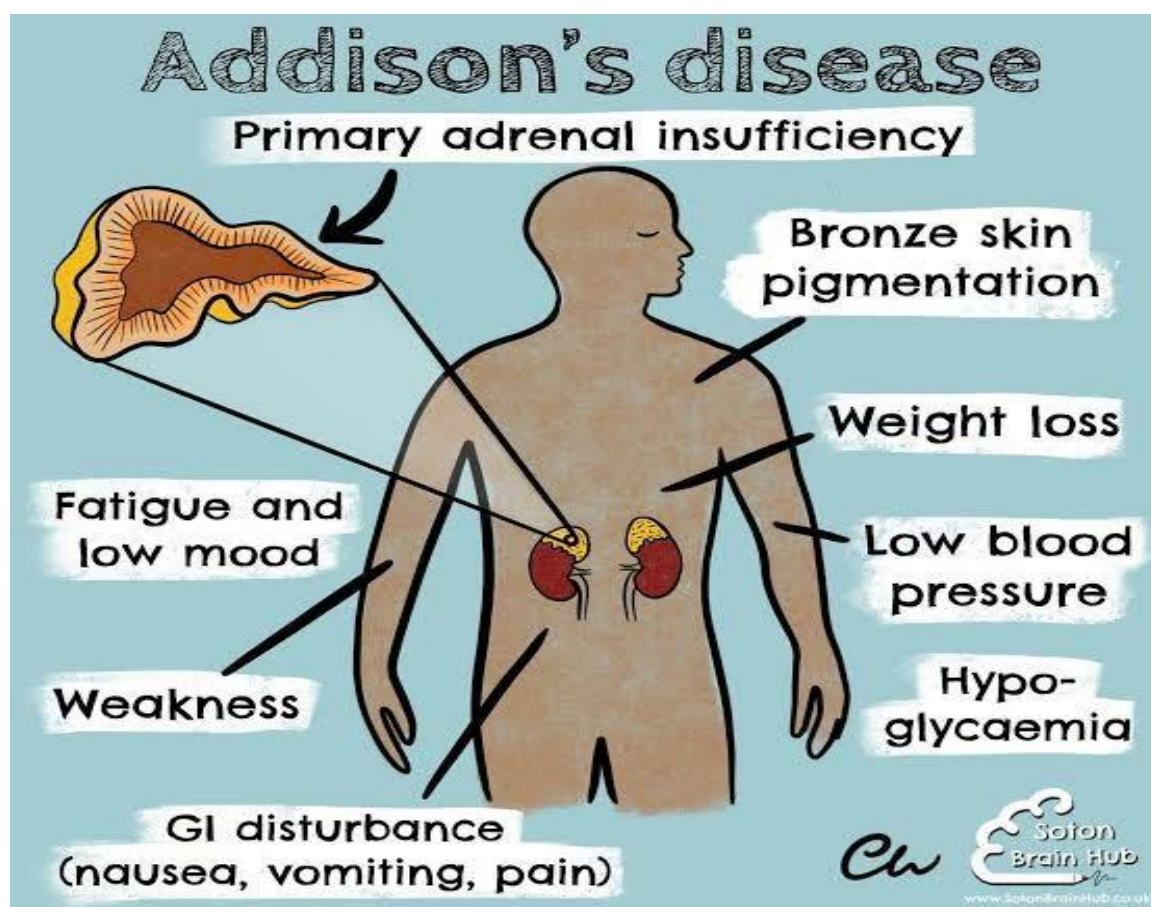


Figure 4. Addison's disease.

CAUSES OF HYPERPIGMENTATION

There are multiple causes of hyperpigmentation. These include endocrinologic factors, such as Addison's disease, Cushing's syndrome, Nelson syndrome, pheochromocytoma, carcinoid, acromegaly, hyperthyroidism, acanthosis Nigricans, and diabetes, as well as external factors, such as these. Factors related to nutrition include tryptophan deficiency, vitamin A deficiency, folic acid deficiency, niacin deficit, and Kwashiorkor. An unwanted side effect of hormonal contraceptive usage is melasma.

Pigmentation is influenced by genetics. Melanocyte development is specialized. These physiological changes demonstrate how aging becomes more noticeable and how specific genes are needed to affect skin color. As per the phrase in individuals over 40 (Figure 5) [12].

CAUSES OF PIGMENTATION

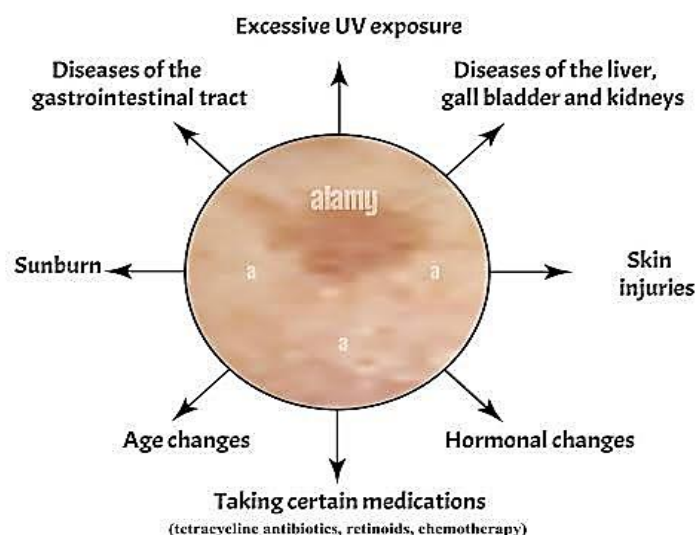


Figure 5. Causes of pigmentation.

Regulation of Skin Pigmentation

Depending on their racial or ethnic heritage, humans might have skin that is exceptionally fair or light or excessively dark, yet all skin types have about the same density of melanocytes in certain areas, including the arms or back [13]. In contrast to dark skin, where the highly pigmented melanosomes are dispersed independently inside keratinocytes to maximize light absorption, fair skin keratinocytes tend to cluster their poorly colored melanosomes above the nucleus. The melanocyte density varies greatly within an individual in different parts of the body, such as the skin. The main factor affecting the pigmentation of human skin is UV light. Immediate pigment darkening, which happens within minutes and lasts for several hours, is a direct result of UV radiation, particularly UVA. Persistent pigment darkening, which happens within hours and lasts for several days, follows immediate pigment darkening [14].

Regulation Function of Skin

Depending on their racial or ethnic history, humans might have skin that is highly pale or light or excessively dark, yet all skin types have almost the same density of melanocytes in certain areas, including the arms or back [15]. Dark skinned keratinocytes have individually distributed intensely colored melanosomes that maximize light absorption, while fair skinned keratinocytes tend to cluster their less pigmented melanosomes above the nuclei. The melanocyte density varies greatly within an individual in different parts of the body, such as the skin on the palms and soles versus other parts of the body. The environment can have an impact on the skin's constitutive melanocyte density. For example, prolonged exposure to UV light can triple or quadruple melanocyte density, and hydroquinone, a poisonous substance, can destroy melanocytes in the skin permanently. Increased melanocyte density, such as freckles, or decreased melanocyte density, such as vitiligo, can also be the outcome of inherited pigmentary illnesses.

Because of their high expression of Bcl2, epidermal melanocytes are highly resistant to apoptosis and multiply slowly, if at all, under normal conditions. Fruit is the most essential and nutritious part of a well-balanced diet. Fruits are low in calories, salt, fat, and cholesterol, but they are also excellent sources of vitamins, minerals, and enzymes. Kiwi fruits are the most important fruit of all [16].

FOOD THAT INFLUENCES SKIN PIGMENTATION

- Melons.
- Tomatoes.
- Oranges.
- Passion Fruit.
- Coffee.
- Green Tea.

Melons

Melons (*Cucumismelo* L) are a good source of beta carotene and vitamin C; cantaloupes have higher levels of these nutrients than honeydews. Dried melon pulp juice concentrate (MPJC) consumption was linked to a reduction in UVR-induced damage in 44 white patients with FSPT II or III, who were between the ages of 18 and 50. For thirty days, participants took either the MPJC or a color-matched control capsule once a day in addition to a control topical cream. The minimum UVR necessary to cause a moderate sunburn or redness is represented by the MED. It is believed that a greater MED corresponds to a lower vulnerability to UVR injury. In another trial, which looked at women with FSPT II to IV between the ages of 40 and 70, participants took a capsule containing the MPJC for eight weeks in addition to grape seed extract, vitamin C, and zinc. Notable improvements were observed in the areas of skin color, brightness, irritation, dark circles beneath the eyes, and overall subjective satisfaction [17].

Tomatoes

The carotenoid lycopene, which has strong antioxidative defense properties, is abundant in tomatoes (*Lycopersicon esculentum*). Among all body tissues, human skin and plasma have the highest concentrations of lycopene. When women with FSPT I or II, ages 21 to 74, received 55 g of tomato paste with 16 mg of lycopene every day for 12 weeks, their erythema threshold rose noticeably in comparison to when they only consumed olive oil [18].

Oranges

It is commonly known that oranges (*Citrus sinensis*) are high in vitamin C. Depending on the variety and environmental conditions during the growth season, different nutritional and polyphenolic profiles are present [19].

Passion Fruits

Beneficial seeds from passion fruits (*Passiflora edulis*) contain polyphenols that are good for the skin. Only the seeds contain piceatannol, and the seeds contain more polyphenols than the pulp or rind. 32 Japanese women with dry skin complaints, ages 35 to 55, who took passion fruit seed extract containing 5 mg piceatannol for 8 weeks showed improved skin barrier function as measured by a significantly higher moisture content and a significantly lower TEWL as opposed to controls. After eight weeks of consuming beverages high in piceatannol, adults also showed increased levels of water content and viscoelasticity on their faces [20].

Coffee

Chlorophyll is one of the several polyphenols found in coffee (*Coffea* L). An observational study that evaluated the amount of chlorogenic acid that 131 Japanese women between the ages of 30 and 60 drank from coffee found a significant correlation between decreased hyperpigmentation and higher coffee consumption (450 mL/d) or coffee polyphenol (900 mg/d). When Japanese women aged 25 to 35 drank a decaffeinated beverage containing 297 mg of coffee polyphenols daily for four weeks, their scaly face and mouth skin improved dramatically in comparison to the control drink [21].

Green Tea

Several flavanols are found in green tea (GT; *Camelliasinensis*), especially epigallocatechin gallant (EGCG). Studies on tea flavanols have revealed anti-allergenic and UVR-protective qualities that may be good for skin health [22]. Moreover, higher levels of skin density, biological elasticity (the capacity to revert to one's initial posture), and serum flavanols were noted.

HERBS AND DRUGS USE IN SKIN PIGMENTATION

Drugs for skin pigmentation have been known for a long time, although they have only recently been more readily accessible. The primary treatments for skin pigmentation are topical creams and oral medicines. To choose which medication is most advantageous, it is best to weigh the benefits and drawbacks of each [23].

- Oral medications.
- Topical creams.

Oral Medication

Treatment for skin conditions and skin tone modification may be accomplished without the use of oral medications. These medications are advantageous since they are more effective than topical creams and do not require as much application or disposal. On the other hand, using oral drugs has some disadvantages. Compared to topical treatments, they can be more costly and have more serious side effects.

Topical Creams

The most popular kind of medication used to treat skin pigmentation is topical cream. They can lighten or darken the skin and are administered directly to the affected area. Topical creams provide the primary benefit of being applied at home without the need for a doctor's visit. Furthermore, their cost is usually lower than that of oral drugs. Applying cream topically, however, has several disadvantages. They may not always be as effective as oral drugs, and their application can be messy and time-consuming [24].

CONCLUSIONS

Natural products have shown considerable promise in treating skin pigmentation disorders due to their natural, non-toxic properties and effective mechanisms. Their use is supported by various studies demonstrating their safety and efficacy through methods, such as cytotoxicity tests, tyrosinase activity assays, and melanogenesis inhibition evaluations. Innovative delivery systems, like liposomes and nanoparticles, further enhance their effectiveness by improving drug solubility and skin penetration.

Skin pigmentation disorders are influenced by factors, such as UV radiation, hormonal changes, and cellular inflammation, leading to the overproduction of melanin and uneven skin coloration. Eumelanin and pheomelanin, the two primary types of skin pigments, play different roles in skin protection and temperature regulation.

Historically, skin pigmentation has been unjustly associated with racial classifications and discrimination, reflecting broader societal biases. Today, various treatment options, including topical agents, like hydroquinone and oral medications like tranexamic acid, offer targeted solutions for hyperpigmentation. However, the misuse of potent corticosteroids remains a concern, potentially exacerbating the condition if not used properly. Overall, the exploration and application of natural products for pigmentation treatment hold significant potential, combining efficacy with safety, and advancing both therapeutic and economic benefits.

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