EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 12
Issue: 1
Year: 2025

AN EMPIRICAL CHARACTERIZATION OF HYPERPIGMENTATION

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Article Received on 08/11/2024 **Article Revised on 29/11/2024** **Article Accepted on 19/12/2024**

ABSTRACT
The kind, quantity and distribution of melanin mostly influence pigmentation, which is an unusual trait that varies greatly among human cultures. Skin pigmentation is a common disorder that can be caused by many factors. Increased melanin production and accumulation characterize several skin disorders, such as acquired hyperpigmentation like melasma, post-inflammatory melanoderma, solar lentigo. Hyperpigmentation is a common cosmetic concern for people with a variety of skin types, but it is more common in middle-aged women and people with skin types III–VI. During skin hyperpigmentation, the body produces an abundant amount of melanin through the process of melanogenesis. The three main variables that cause skin pigmentation are genetics, sun exposure and certain medication. Hyperpigmentation can be treated by natural substances like aloevera, cinnamic acid, green tea extract, mulberry extract, etc, .and synthetic substances like arbutin, vitamin c, niacinamide, etc,. Furthermore, this research lays the groundwork for future studies exploring innovative treatments and therapies to address hyperpigmentation, ultimately improving patient outcomes and quality of life.

KEYWORDS: Pigmentation, Hyperpigmentation, Melasma, Postinflammatory hyperpigmentation, solar lentigo.

1. INTRODUCTION

1.1. SKIN PIGMENTATION

A person‘s ethnicity, genetics and physiology significantly influence human pigmentation.[1] The kind, quantity and distribution of melanin mostly influence pigmentation, which is an unusual trait that varies greatly among human cultures.[2] The two types of pigmentary disorders consist of those that show up as hypopigmentation, or decreased pigment, and hyperpigmentation, or apparent excess pigment.[1] Skin pigmentation, or the amount of melanin the body produces, is what gives skin its color. Pheomelanin and eumelanin are the two main types of melanin that are produced by melanocytes in the epidermal layer of the skin. Lighter skin tones are produced by pheomelanin, and darker skin tones are produced by eumelanin. Sunlight is absorbed by the dark brown pigment eumelanin, which protects the skin from sunburn. Darker skin tones are associated with higher levels of eumelanin, whilst lighter skin tones are associated with lower levels. The ability of eumelanin to prevent skin cancer is one of its extra advantages.[3]

Table 1.

Skin type	*Skin color*	*Characteristics*
I	very fair; white ; red or blond hair; blue eyes; freckles ;	Burns always, never tans
II	White; fair; red or blond hair; blue, green or hazel eyes	Usually burns, tans with difficulty
III	Creamy white; fair with any eye or hair color; very common	occasionally mild burn, gradually tans
IV	Brown color ; typically Mediterranean skin	Rarely burns, tans with easily
V	Dark brown skin color; Middle-Eastern skin types	Tans very easily, Very rarely burns
VI	Black color skin	Never burns, tans more easily

2. HYPERPIGMENTATION

Increased melanin production and accumulation characterize several skin disorders, such as acquired hyperpigmentation like melesma, post-inflammatory melanoderma, solar lentigo and others.[4] Melanocytes produce or distribute melanin unevenly, resulting in skin hyperpigmentation. Under the general term "hyperpigmentation," numerous pigmentation, darkening, and skin discoloration problems are included.

It primarily affects women and mainly affects the face and neck areas. Hyperpigmentation is a common cosmetic concern for people with a variety of skin types, but it is more common in middle-aged women and people with skin types III–VI.[6] Post-inflammatory hyperpigmentation (PIHP) and melasma are two frequently acquired pigmentary disorders that cause hyperpigmentation.[7] A condition known as skin hyperpigmentation occurs when certain areas of skin turn darker than the surrounding normal skin tone. This happens when the skin's melanin production is excessive in some areas. During skin hyperpigmentation, the body produces an abundant amount of melanin through the process of melanogenesis. Melanosis is the term for increased melanin pigment in epithelial cells.[8]

2. TYPES

2.1. POST-INFLAMMATORY HYPERPIGM-ENTATION

An injury or inflammation to dark skin (Fitzpatrick types IV to VI) usually results in post-inflammatory hyperpigmentation, which can lead to lesions that last for months or even years. After laser therapy for various pigmented skin lesions, post-inflammatory hyperpigmentation may also develop. At the locations of prior injury or inflammation, uneven, darkly pigmented macules and patches are an indicator of post-inflammatory hyperpigmentation.[9] From mosquito bites, psoriasis, hypersensitivity reactions from medicine, harm from irritants, and cosmetic activities can all cause it. Post-inflammatory hyperpigmentation (PIH) does in fact, tend to follow acne in patients with darker skin. There might be an increase in melanocytes activity, which reactive oxygen species and inflammatory mediators may both boost.[10]

2.2. MELASMA

Melasma is a progressive, macular, no scaling hyper melanosis of the skin in areas exposed to sunlight. It may not have a known cause or be associated with oral contraceptives, pregnancy, or anticonvulsants (such as phenytoin). People with skin types IV to VI including middle easterners, south America and Asians, are more likely to develop melasma nine times more frequently in women than in men. Though it is mostly asymptomatic, the patient frequently experiences cosmetic stress. Three patterns of distribution are commonly observed in cases with melasma: mandibular (16%), malar (21%) and Centro facial (63%). The typical appearance of dermal melasma is grayish and non-enhancing. The best sunblocks are opaque ones that contain zinc oxide or titanium dioxide. The condition usually clears upon its own a few months after delivery or when the medicine is stopped.[9] Sebocytes have been reported to facilitate the formation of melasma. Estrogen significantly influences pigmentation as one of the physiological and pathological states of the skin.[10]

2.3. SOLAR LENTIGINES

On sun-exposed skin surfaces, macular, hyperpigmented, well-circumscribed lesions of one to three centimeters are known as solar lentigines, also known as liver spots. Their color ranges from pale yellow to deep brown, and they frequently have a scattered look. The most common areas, which appear following either acute or chronic UV exposure, are the face, hands, forearms, chest, back, and shins. The majority of people with solar lentigines are white or Asian, particularly if they have skin types I to III and have a tendency for freckles.[9] Because of the lipofuscin bodies of the basal cells, age spots are brown. The lipid and protein combination seen in lysosomes that binds to protein fragments via malondialdehyde is called lipofuscin. Age spots differ in shape, size, color, and level of skin protrusion. The basal cells in the epidermis that attach to the basement membrane are responsible for the age spots on the skin. An aged cell thus exposes its neighboring cells at greater risk of damage and malfunctions. Neighboring cells age as a result of this process.

3. ETIOLOGY OF HYPERPIGMENTATION

Skin pigmentation is a common disorder that can be caused by many factors.

3.1. GENETICS

Unexpectedly, skin tone can be influenced by 125 genes. Hormones and genes control the synthesis of melanin. An individual can regulate the quantity of pheomelanin or eumelanin produced by their skin by making choices about how much sun exposure they get, how much medication and cosmetics they use, and other factors. Over time, these factors may change the skin's tone. Therefore, genetics is one of the most common causes of skin color. It is possible to predict the number of melanocytes in an individual with genetics. Skin cells called melanocytes are responsible for producing melanin. However, melanosomes, the organelles that contain melanin, must be transported during hyperpigmentation and tanning.[1]

3.2. SUN EXPOSURE

To protect the skin from prolonged sunlight exposure, the body creates more melanin. This may result in dark patches or areas of skin known as sun spots or age spots. Skin pigmentation is frequently caused by exposure to sunlight. The body makes more melanin to protect itself from the sun's UV radiation. In order to protect the skin from the sun's rays, this could make the skin more pigmented. The development of pigmentation is a result of continuous UV exposure.

The formation mechanism is composed of the following stages.
(1) Free radicals are produced by UV light.
(2) The biological agents that affect melanocytes, the cells that produce pigment, are activated by UV radiation and free radicals.
(3) Tyrosine is changed into an amino acid by the enzyme tyrosinase.[1]

3.3. SKIN INFLAMMATION

Post-inflammatory hyperpigmentation (PIH) is the term for dark, flattened patches that can range in color from brown to black, depending on the extent of inflammation and skin tone. Uneven skin tone is caused by elevated melanin synthesis and deposition in skin cells increased UVR and sun exposure frequently worsen these abnormalities. Inflammatory skin conditions may also be the cause of PIH. Topical retinoid is the best choice for PIH associated to acne because of its anti- inflammatory and bleaching qualities.[13]

3.4. HORMONAL CHANGES (MELESMA)

For certain people, the development of melasma may be influenced by hormones. Hormonal fluctuations may result in the appearance of darker skin patches. This type of hyperpigmentation is common during pregnancy. In contrast to other types of hyperpigmentation, obstetric patients have been observed to have the mask of pregnancy. The normal rise in progesterone, estrogen, and melanocyte-stimulating hormone levels that takes place in the third trimester of pregnancy is one possible contributing cause. Nulliparous melasma patients exhibit greater numbers of estrogen receptors within the lesions but no increased amounts of MSH or estrogen. Furthermore, melasma associated with oral contraceptives including progesterone and estrogen as well as diethylstilbestrol treatment for prostate cancer have been documented.[12]

3.5. AGE

Melanocytes, or the cells that produce melanin, become fewer in number as skin ages, but the ones that remain grow larger and are more concentrated in their distribution. Age spots in people over 40 have increased, which can be explained by these physiological changes. Further information regarding skin aging can be found at skin aging.[14]

4. MANAGEMENT OF HYPERPIGMENTAION

4.1. SYNTHETIC SOURCES

4.1.1. ARBUTIN

One of the most often prescribed skin-lightening and depigmentation medications in world is arbutin. Dried leaves of a variety of plant species, including pear, blueberry, blackberry(Arctostaphylosuva-ursi), and blueberry, contain arbutin, a naturally occurring plant chemical that is derived from hydroquinone b-D-glucopyranoside. In cultured melanocytes, arbutin dose dependently and competitively inhibits tyrosinase activity at non-cytotoxic doses.[18] Moreover, it is less cytotoxic to melanocytes than hydroquinone and prevents the maturation of melanosomes. Higher concentrations may work better, but there is a higher chance of paradoxical hyperpigmentation.

4.1.2. VITAMIN C

Tyrosinase's active site interacts with copper ions through the action of vitamin C, a naturally occurring antioxidant. Melanogenesis is inhibited by vitamin C because it functions as a reducing agent during the several oxidative stages of melanin production. Research indicates that the decrease in tyrosinase activity produced by vitamin C might be attributed to antioxidant activity instead of tyrosinase activity being directly inhibited. Fruits and vegetables are unstable sources of topical vitamin C, which raises concerns about their efficacy.[11]

4.1.3. NIACINAMIDE

The niacinamide is the physiologically active amide of niacin, or vitamin B3, is also referred to as nicotinamide (3-pyridinecarboxamide). The synthesis of the enzymes required for cellular metabolism, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), is aided by niacin. Niacinamide suppresses melanogenesis by blocking the contact between keratinocytes and melanocytes, as demonstrated by a study using pigmented rebuilt epidermis (PREP). Additionally, it affects the protease-activated receptor (PAR) surround them. After four weeks of therapy, 2% niacinamide dramatically lowers the overall area of hyperpigmentation and improves skin brightness, according to clinical research. The therapy has reached a plateau in its efficacy, which could be the result of a delicate balance between the hyperpigmented area's increased melanogenesis and the niacinamide-induced slowing. The primary component of Fair and Lovely, the most well-liked hyperpigmentation cosmetic on the Indian market, is niacinamide, which is also mixed with sunscreen for added advantages.

4.1.4. SUNSCREEN

Using a variety of sunscreen creams is the first step in treating hyperpigmentation. UVA light is absorbed by avobenzone. It is fragile, though. When oxybenzone and avobenzone are mixed, the stability of the former is increased. For further benefits, physical sunscreens like zinc oxide and titanium dioxide are frequently used in cosmetic goods' formulations.

4.2. NATURAL SOURCES

4.2.1. ALOEVERA EXTRACT

In animal studies, A. Vera leaf extract and its active ingredient aloe have been shown to have a strong, dose-dependent, physiologically relevant melanin-aggregating effect, leading to skin lightening by stimulating adrenergic receptors. Aloe Vera extract is an ingredient in several different marketed preparations.

4.2.2. CINNAMIC ACID

This is a phenylpropanoid derivatives found in plants that inhibits tyrosinase activity as shown by studies in human and guinea pig melanocytes. Tan et al. found that cinnamic acid (2 mmol/l; 0.5 mmol/l) inhibited tyrosinase activity more than hydroquinone (0.5 mmol/l).

4.2.3. GREEN TEA EXTRACT

Polyphenolic chemicals found in green tea extracts have anti-inflammatory, antioxidant, and anti-carcinogenic properties by influencing different biochemical pathways. Green tea's primary active component is epigallocatechin-3-gallate. Research by Nu et al. has demonstrated that in vitro inhibition of fungal tyrosinase by green tea extracts may be responsible for the depigmentation effect.

4.2.4. MULBERRY EXTRACT

Plants of the Moraceae family, such as Morus Alba L, are the source of mulberry extract. Its root bark derivatives have been shown to brighten skin tone. Tyrosinase's superoxide scavenging action and dopa oxidase inhibition may be the cause of this. In comparison to 5.5% hydroquinone and 10.0% kojic acid, the IC50 (concentration that inhibits tyrosinase activity by 50%) is incredibly low (0.396%). Using 1% paper mulberry extract, a patch test revealed no appreciable skin irritation after 24 and 28 hours.

4.2.5. LICORICE EXTRACT

Extract of licorice is made from Glycyrrhiza Glabra Linn roots. In India, it is widely grown. By reducing the amount of free radicals produced, cyclooxygenase activity, melanin biosynthesis, and melanin breakdown, licorice extract improves hyperpigmentation. The primary component of licorice extract is the polyphenolic flavonoid called glaciridin. Research has demonstrated that glabridin inhibits superoxide anion and cyclooxygenase activity, which reduces pigmentation brought on by ultraviolet B (UVB) radiation and has anti-inflammatory properties. Nevertheless, additional research is required to validate this depigmentation impact.

Figure 2.1: Post inflammatory Hyperpigmentation.

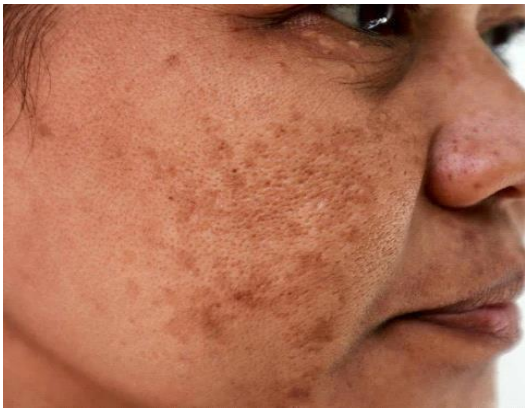

Figure 2.2: Melasma.

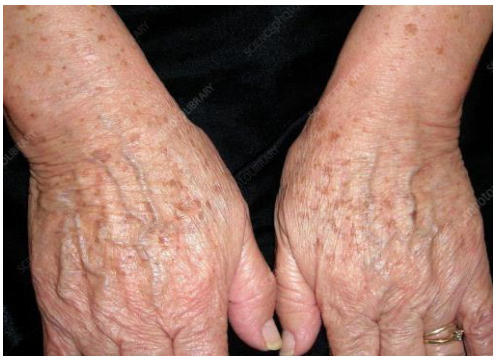

Figure 2.3: Solar Lentigines.

Figure 3: Etiology of Hyperpigmentation.

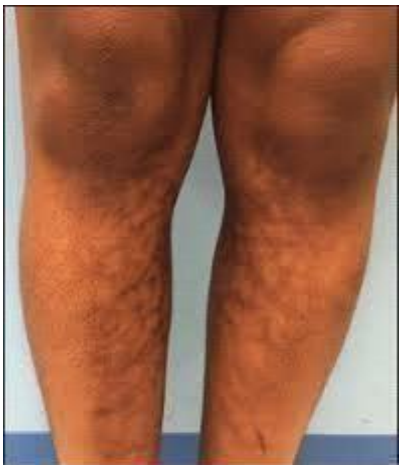

Figure 3.3: Skin Inflammation.

Figure 3.5: Age.

Figure 4.1.4: Sunscreen.

Figure 4.1.1: Arbutin.

Figure 4.2.1: Aloevera extract.

Figure 4.1.2: Vitamin C.

Figure 4.2.3 Green tea extact.

Figure 4.1.3: Niacinamide.

Figure 4.2.4: Mulberry extract.

Figure 4.2.5: Licorice extract.

5. CONCLUSION

This project provides a comprehensive empirical characterization of hyperpigmentation, shedding light on its prevalence, clinical characteristics, and underlying factors. The findings of this study contribute significantly to our understanding of hyperpigmentation, highlighting the need for personalized treatment approaches and further research into its causes and consequences. The results have implications for dermatological practice, emphasizing the importance of tailored interventions and patient education. Furthermore, this research lays the groundwork for future studies exploring innovative treatments and therapies to address hyperpigmentation, ultimately improving patient outcomes and quality of life.

BIBILOGRAPHY

1. Meys R Skin Pigmentation, Medicine, 2017 Jul 1; 45(7): 438-43.
2. Parra EJ. Human pigmentation variation: Evolution, genetic basis, and implications for public health. American Journal of Physical Anthropology: The official publication of the American Association of Physical Anthropologists, 2007; 13(S45): 85-105.
3. Thawabteh AM, Jibreen A, Karaman D, Thawabteh A, Karaman R. Skin Pigmentation Types, Causes and Treatment—A Review Molecules, 2023 Jun 18; 28(12): 4839.
4. Briganti S, Camera E, Picardo M. Chemical and Instrumental Approaches to Treat Hyperpigmentation. Pigment cell research, 2003 Apr; 16(2): 101-10.
5. Woolery-Lloyd, H, Kammer JN Treatment of Hyperpigmentation. InSeminars in cutaneous medicine and Surgery, 2011 Sep; 30(Vol.30.No.3): pp171—175, WB Saunders.
6. Nautiyal A, Wairkar S, Management of hyperpigmentation: Current treatments and emerging therapies. Pigment cell & melanoma research, 2021 Nov; 34(6): 1000-14.
7. S. Schalka New data on hyperpigmentation disorders. Journal of the European Academy of Dermatology & venereology, 2017 Sep; 31: 18—21.
8. Rathee, P., Kumar, S., Kumar, D. Skin hyperpigmentation and its treatment with herbs: an alternative an alternative method. Future Journal of Pharmaceutical Sciences, 2021 Dec; 7: 1-4.
9. Plens dorf S, Livieratos M, Dada N. Pigmentation Disorders: Diagnosis and Management. American family physician, 2017 Dec 15; 96(12): 797-804.
10. Thawabteh AM, Jibreen A, Karaman D, Thawabteh A, Karaman R. Skin pigmentation types, causes and treatment – a review. Molecules, 2023 Jun 18: 28(12): 4839.
11. Nieuweboer-Krobotova L. Hyperpigmentation types, diagnostics and targeted treatment options.
12. HajiraBasit; Kiran V. Godse; Ahmad M. Al Aboud. Melasma.
13. Postinflammatory hyperpigmentation: A comprehensive overview: Treatment optionsand prevention S.Suteeraporn Chaowattanapanit MD a b, Narumol Silpa-archa MD a c, Indermeet Kohli PhD a, HenryW. Lim MD a, Iltefat Hamzavi MD.
14. Rashmisankar, Pooja Arora1, and K Vijay Garg. Cosmeceuticals for Hyperpigmentation: What is Available?