

A Review: Skin hyperpigmentation and its treatment with herbs

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ABSTRACT

A frequent dermatological disorder called hyperpigmentation is defined by an excess of melanin produced on the skin, which results in dark areas or spots. Numerous things, including sun exposure, hormone fluctuations, inflammation, and skin traumas, can cause it. Antihyperpigmentation agents are essential for the management of this condition because they either promote the breakdown of melanin or restrict its creation, so preventing it from reaching the skin's surface. An overview of the workings and uses of antihyperpigmentation drugs is given in this abstract. Alpha hydroxy acids (AHAs) and retinoids are examples of agents that promote skin cell turnover, which helps remove pigmented cells from the skin and encourages the appearance of new, uniformly colored skin. Furthermore, components with antioxidant qualities like niacinamide and vitamin C might lessen oxidative stress on melanocytes, which helps to mitigate hyperpigmentation. In addition, preventing melanin from being transferred from melanocytes to nearby keratinocytes is a potential therapy for hyperpigmentation. Substances that disrupt this process, such as tranexamic acid and N-acetylglucosamine, significantly lessen the visibility of black patches on the skin. Combination treatments or formulations frequently increase the effectiveness of antihyperpigmentation medications. For example, synergistic benefits can be achieved in the treatment of hyperpigmentation by combining a tyrosinase inhibitor with a retinoid or an exfoliating agent. Incorporating components that target other aggravating causes like as inflammation or UV damage might also improve the treatment regimen's overall effectiveness.

Key Words: Melanin, Hyperpigmentation, treatment with herbs.

INTRODUCTION:

Herbal anti-pigmentation creams are skincare products formulated with natural ingredients derived from plants, herbs, and botanical extracts. These creams aim to address skin discoloration issues, offering an alternative to synthetic or chemical-based treatments. ^[1] Common herbal ingredients include licorice extract, mulberry extract, turmeric, aloe Vera, and green tea, known for their skin-brightening and anti-inflammatory properties. Licorice extract, containing glabridin, has demonstrated tyrosinase inhibition, effectively reducing melanin production. ^[2] Mulberry extract is rich in arbutin, which contributes to skin lightening. Turmeric, with its anti-inflammatory and antioxidant qualities, helps alleviate pigmentation concerns. Aloe vera soothes and hydrates the skin, while green tea polyphenols provide antioxidant protection. These herbal formulations often prioritize gentle yet effective solutions for hyperpigmentation, making them suitable for individuals with sensitive skin. ^[3] The creams are applied topically, targeting specific areas with dark spots or uneven pigmentation. While herbal anti-pigmentation creams are generally considered safer due to their natural origins, it's essential for users to patch-test new products to ensure compatibility and avoid potential allergic reactions. ^[4] Dermatologist consultation remains valuable for personalized skincare advice. Pigmentation refers to the coloration of the skin, resulting from the production of melanin, the pigment responsible for its tone. Conditions like hyperpigmentation involve excess melanin, leading to dark spots or uneven skin tone. Hypopigmentation, on the other hand, involves a lack of melanin, resulting in lighter areas. Various factors, including sun exposure and genetics, influence pigmentation. ^[5]

Topical Preparations: A Brief Overview

Pharmaceutical formulations applied to the skin or mucous membranes for localized therapeutic effects are known as topical medications. They include a wide variety of formulations, such as pastes, lotions, oils, gels, creams, and transdermal patches. The kinds, formulation considerations, uses, and new developments in topical medicines will all be covered in this succinct review.

Types of Topical Preparations:

- 1. Lotions and Creams:** While ointments are semisolid treatments usually comprising petrolatum or lanolin, creams are emulsions of oil and water. They are frequently used to treat dermatological disorders and offer moisturization ⁽⁶⁾.
- 2. Gels:** Gels are semisolid materials with a liquid phase scattered within a solid phase. They have benefits including better drug release kinetics and simplicity of application ⁽⁷⁾.
- 3. Lotions:** Liquid treatments called lotions include active chemicals either dissolved or suspended in them. They are indicated for situations that require quick absorption and have a lighter viscosity than creams ⁽⁸⁾.
- 4. Paste:** Pastes are thick, semisolid mixtures with a high solids content. They serve as a barrier of defense and are applied to ailments like wound healing ⁽⁹⁾.
- 5. Transdermal Patches:** Drugs are applied topically via transdermal patches to achieve systemic effects. They are practical for patients and provide regulated release ⁽¹⁰⁾.

Formulation Points to Remember:

Selection of Base: The choice of base affects patient acceptance, stability, and medication release. It is necessary to take into account variables including permeability, irritation potential, and solubility ⁽¹¹⁾.

Solubility of Drugs: The release and absorption of the active substance are influenced by its solubility. Drug bioavailability can be increased by using solubility enhancers ⁽¹²⁾.

Stability and pH: Stability and reducing irritation depend on having an ideal PH To guarantee formulation stability, modifications could be performed ⁽¹³⁾.

Viscosity: Spread ability and skin adhesion are impacted by viscosity. To get the right consistency, thickeners or viscosity modifiers are added ⁽¹⁴⁾.

Uses for Topical Preparations:

- 1. Conditions Dermatological:** Topical treatments are frequently used to treat ailments including acne, psoriasis, and eczema. They offer focused treatment with a lower risk of systemic adverse effects ⁽¹⁵⁾.
- 2. Pain Management:** Topical analgesics provide targeted pain treatment for injuries including sprains and arthritis. Commonly utilized ingredients include capsaicin and lidocaine ⁽¹⁶⁾.
- 3. Wound Healing:** By lowering inflammation and avoiding infection, topical medicines aid in the healing of wounds. Formulations frequently include growth factors and antiseptics ⁽¹⁷⁾.
- 4. Cosmetic Use:** Cosmetics with topical formulations are used for anti-aging and skincare. Antioxidants and

retinoids, among other ingredients, enhance the look of skin (18).

SKIN

The skin, the biggest organ in the human body, acts as a protective barrier against external forces, regulates temperature, and aids in sensory awareness. This quick study will look at the structure and functions of the skin.

The Skin's Structure:

The skin is composed of three major layers:

- 1. Epidermis:** The outermost layer of the skin, known as the epidermis, is mostly composed of keratinocytes, which produce the protein keratin and provide the skin its structural integrity. Skin color is caused by melanin, which is produced by melanocytes; on the other hand, immune response is facilitated by Langerhans cells (22).
- 2) Dermis:** Beneath the epidermis, the dermis is home to nerves, blood vessels, connective tissue, and anatomical features like sweat glands and hair follicles. Collagen and elastin, which provide the skin strength and suppleness, are produced by fibroblasts (23).
- 3. Hypodermis:** The hypodermis, sometimes referred to as the subcutaneous tissue, is a layer of adipose tissue that acts as a cushion, offering insulation and storing energy (24).

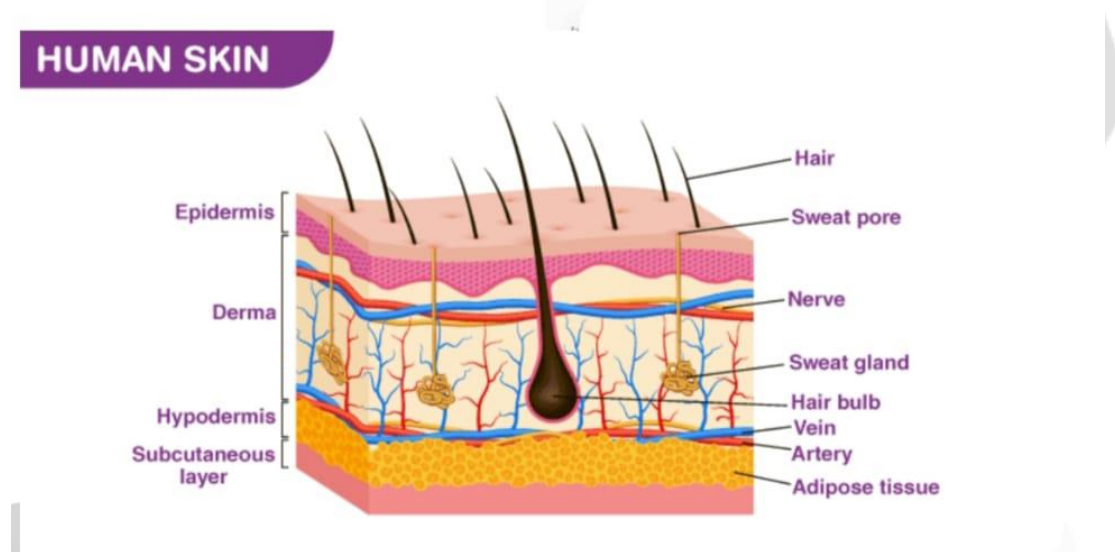


Figure 1: Structure of Skin

The skin's functions include:

- 1. Barrier Function:** The skin serves as a physical barrier that keeps infections, allergies, and dangerous substances out of the body. By preventing water loss and preserving hydration, lipids in the stratum corneum support the barrier's ability to function (25).
- 2. Temperature Regulation:** Through vasodilation and vasoconstriction, blood vessels in the dermis control the exchange of heat with the surroundings. When the body temperature rises, perspiration produced by sweat glands

evaporates off the skin's surface and aids in cooling the body ⁽²⁶⁾.

3. Sensory Perception: The skin's specialized nerve endings provide sensory input by detecting a range of stimuli, such as pressure, temperature, touch, and pain. ⁽²⁷⁾

4. Reaction Immune: Langerhans cells and other immune cells in the skin function as an organ of defense, identifying and reacting to pathogens and antigens that cross the epidermal barrier. The immunological response is triggered by the production of inflammatory mediators ⁽²⁸⁾.

PIGMENTATION CREAM

Skin lightening or brightening creams, often referred to as pigmentation creams, are topical solutions intended to treat dark patches, uneven skin tone, and hyperpigmentation. The active components in these creams target the synthesis of melanin, block tyrosinase activity, and encourage skin rejuvenation. We will examine the characteristics, uses, and benefits and drawbacks of pigmentation creams in this in-depth discussion.

Features of Creams for Pigmentation:

1. Ingredients Active: Several active compounds used in pigmentation creams target distinct pathways involved in the generation of melanin and skin coloring. Hydroquinone, kojic acid, arbutin, azelaic acid, retinoids, vitamin C, niacinamide, and plant extracts such as bearberry and licorice are common constituents

2. Type of Emulation: There are many different formulas of pigmentation creams, including creams, lotions, gels, serums, and masks. The formulation used will rely on a number of variables, including skin type, pigmentation severity, and personal taste. Because of their moisturizing qualities, creams and lotions are frequently chosen for everyday usage, while gels and serums may have lighter textures and quicker absorption ⁽²⁹⁾.

3. Sunscreen: Sunscreen ingredients are incorporated in many pigmentation treatments to shield the skin from additional sun damage, as UV rays can intensify hyperpigmentation. It is advised to use broad-spectrum sunscreens with SPF 30 or higher to avoid pigmentation caused by UVA and UVB rays.

4. Support for Skin Barrier: Certain pigmentation creams contain components that hydrate the skin and assist the function of the skin barrier. • Hyaluronic acid, ceramides, and glycerin are commonly included for their moisturizing properties.

5. pH Balance: The pH of pigmentation creams is critical for maximum effectiveness and skin compatibility. To reduce irritation and enhance active ingredient penetration, formulations with pH values similar to the skin's natural pH (~5.5) are recommended ⁽³⁰⁾.

Application of Pigmentation Creams:

1. Skin Lightening: Pigmentation creams are widely used to lighten hyperpigmented regions, such as black patches, melasma, or freckles, resulting in a more even skin tone. ⁽³¹⁾

2. Treatment of Post-Inflammatory Hyperpigmentation: Pigmentation treatments can help diminish dark patches left behind by acne, eczema, or other inflammatory skin diseases by blocking melanin formation. ⁽³²⁾

3. Sun Damage Repair: Pigmentation creams containing ingredients like retinoids or hydroquinone can help repair sun damage by fading sunspots and preventing further melanin production. ⁽³³⁾

4. Treatment of Vitiligo: In some cases, pigmentation creams may be used to repigment areas affected by vitiligo by stimulating melanocyte production ⁽³⁴⁾

5. Prevention of Post-Surgical Hyperpigmentation: Pigmentation creams can be applied post-surgery to prevent or minimize the risk of hyperpigmentation at incision sites, particularly in individuals with a predisposition to develop dark scars⁽³⁵⁾

Advantages of Pigmentation Creams:

1. Targeted Treatment: Pigmentation creams provide focused therapy for particular areas of hyperpigmentation, enabling precise application and localized results.⁽³⁶⁾

2. Non-invasive: In contrast to invasive procedures such as chemical peels or laser therapy, pigmentation creams are non-invasive and may be used at home without physician supervision.⁽³⁷⁾

3. Convenience: Pigmentation creams are simple to use and may be included into regular skincare procedures. They provide a simple remedy for pigmentation issues that does not require visits to a doctor or aesthetician.⁽³⁸⁾

4. Cost Effective: Pigmentation creams are typically less expensive than professional treatments, making them available to a wider spectrum of people seeking therapy for hyperpigmentation.⁽³⁹⁾

5. Hydrating Formulations: Many pigmentation creams include moisturizing chemicals that help hydrate the skin, enhancing overall texture and look while treating pigmentation issues.⁽⁴⁰⁾

Disadvantages of Pigmentation Creams:

1. Skin Irritation: People with sensitive skin or sensitivities to specific components are more susceptible to experiencing skin irritation, redness, or itching from some pigmentation treatments.⁽⁴¹⁾

2. Temporary Results: Long-term or continuous treatment is necessary for sustained effects because stopping the usage of pigmentation creams may cause hyperpigmentation to reappear.⁽⁴²⁾

3. Uneven Lightening: If pigmentation creams are not used regularly or according to instructions, they may occasionally lighten the skin unevenly, resulting in blotchiness or regions of lighter and darker skin tone.⁽⁴³⁾

4. Photosensitivity: If appropriate sun protection measures are not performed, some components in pigmentation creams, such as retinoids or alpha hydroxy acids (AHAs), can enhance the skin's sensitivity to sunlight, potentially resulting in sunburn or worsening of pigmentation.⁽⁴⁴⁾

Pathogenesis of hyperpigmentation

Another important factor in hyperpigmentation is inflammation. Inflammatory mediators such as interleukins, prostaglandins, and growth factors can stimulate melanocytes directly or indirectly by promoting the release of melanogenic cytokines like endothelin-1 (ET-1) from neighbouring cells. ET-1, in particular, plays a crucial role in melanogenesis by upregulating the expression of enzymes involved in melanin production.⁽⁴⁵⁾ One well-known cause of hyperpigmentation is UV exposure. Oxidative stress is brought on by UV exposure producing reactive oxygen species (ROS) in the skin. In order to increase the synthesis of melanin, ROS can directly activate melanocytes and cause the release of pro-inflammatory cytokines. Furthermore, UV radiation stimulates signalling pathways that increase the transcription of genes involved in melanogenesis, such as the mitogen-activated protein kinase (MAPK) pathway.⁽⁴⁶⁾ The pigmentation can also be a consequence of hormonal changes, particularly those brought on by hormone therapy or during pregnancy. Melasma, or pregnancy-induced hyperpigmentation, is believed to be caused by changes in hormone levels, including elevated progesterone and estrogen, which stimulate melanocytes and improve melanin formation. Similarly, in sensitive people, hormonal therapies like progesterone or estrogen may increase hyperpigmentation.⁽⁴⁷⁾ The main culprit is UV light, which increases the creation of melanin by inducing oxidative stress and activating signalling pathways like MAPK. Melanocytes are stimulated either directly or through the production of melanogenic cytokines by inflammatory mediators like TNF- α and interleukins.⁽⁴⁸⁾ Additionally,

melanogenesis is further enhanced by endothelin-1, which is elevated in response to inflammation and UV exposure.⁽⁴⁹⁾ In short, the development of hyperpigmentation is the result of a complex interaction between molecular and cellular processes. The dysregulation of melanin synthesis and deposition in the skin is caused by a number of factors, including inflammation, UV radiation-induced oxidative stress, hormonal fluctuations, genetic predisposition, and stimulation of melanocytes by different signalling pathways. Creating efficient hyperpigmentation treatment plans requires an understanding of these processes.⁽⁵⁰⁾

Treatment of skin pigmentation by herbs

In furtherance of photo safety, a number of drugs and therapies can safely and effectively treat darker skin patients' hyperpigmentation, however they may have unfavourable side effects.^[51] Therefore, using herbs and phytoconstituents to treat skin conditions is a superior option. excessive pigmentation. Table 1 lists a few herbs along with their mode of action for treating skin hyperpigmentation. Certain medications, such as hydroquinone, azelaic acid, kojic acid, liquorice extract, retinoids, etc., as well as therapies like laser therapy and chemexfoliation, may be beneficial whether used alone or in conjunction with other medications.^[52]

Skin whitening drugs

Because the herbs contain phenolic component, the skin-whitening chemicals are potent. With an IC₅₀ value of 3.0 mM in HEMn, arbutin is a naturally occurring tyrosinase inhibitor with skin-whitening properties cells. Hydroquinone [HQ], arbutin, kojic acid, liquid nitrogen, laser treatment, chemical skinning, and supernatural dermabrasion are the chemical agents that are most frequently utilized.^[53]

Glycyrrhiza glabra

The primary reason glycyrrhiza glabra extracts are important for skin health is because of their potent antioxidants, particularly glycyrrhizin, triterpene saponins, and flavonoids. The principal characteristics are skin lightening, skin whitening, skin depigmentation, anti-aging, antiarrhythmic, emollient, anti-acne, and photo protective properties.^[54]



Figure 2: Glycyrrhiza glabra

Aloe

Aloe vera leaf gel is used to treat small burns and sunburns. Its primary properties include antifungal, anti-inflammatory, and hepatoprotective. Barbaloin, aloesin, aglycone of aloesin, 2''-O-feruloyl aloesin, isoaloeresin D, and aloe resin E are the isolates of Aloe vera that exhibit strong tyrosinase inhibitory qualities. The lyophilized gel displays an IC₅₀ of 10.53 and a methanolic extract of 6.08 mg mL⁻¹. Among the compounds derived from aloe, aloesin has the highest level of inhibition.^[55]



Figure 3:Aloe

Ginkgo biloba

The Ginkgoaceae family includes Ginkgo biloba. The majority of the G. biloba extract (EGb761) is made up of derivatives of quercetin and kaempferol. Terpenes [6%] from tree leaves, which include flavone glycosides [33%], have been found to have the ability to reduce sunburn cells in mice exposed to ultraviolet B (UVB) light. Ginkgo possesses tyrosinase, antioxidant, anti-inflammatory, and anti-vasculature qualities.^[56]



Figure 4:Ginkgo biloba

Muntingia calabura

Calabura extracts are prepared in different solvents such as ethanol, aqueous, hydro Muntingia -ethanol, petroleum ether using decoction methods with various parts of plant including leaves, flora, and fruits. This results in optimum anti-tyrosinase and antioxidant activity in the leaf extract of Muntingia calabura in hydro ethanol. Plant extracts have an inhibitory effect on melanogenesis. The human body's reactive oxygen species increases the damage done to DNA, the melanin biosynthesis, and the melanocyte proliferation. M. calabura leaf hydro ethanol shows $94.00 \pm 1.97\%$ inhibition of tyrosinase enzyme.^[57]



Figure 5: Muntingia calabura

Blumea balsamifera

Blumea balsamifera is a medicinal plant that belongs to the Asteraceae family. The leaves are used for certain conditions such as rheumatism and high blood pressure. As part of the plant with different physiological activities, its leaves have attracted attention, including plasmin inhibitory, antifungal, and heatproof, antidiabetic, wound cure, antigenic. In addition, antibacterium, free radical scavenging, inhibitory activity of lipid peroxidation, xanthine oxidase inhibition, superoxide scavenging activities, and ant tyrosinase activity were identified in the methanol extracts of the leaves.^[58]



Figure 6: Blumea balsamifera

Preparation of herbal pigmentation cream

Two distinct stages can be added to the formulation, and they are as follows.

Phase 1: In a China dish over a hot plate, melt the beeswax.

Phase 2: Next, borax was dissolved and cooked in a 100 ml beaker along with rose water on a hot plate at 70°C. All of the oils are then added to this and heated at this temperature.

At 70°C, keep stirring continuously for 5 minutes. Then, turn off the heat and continue stirring until the mixture cools down and a semi-solid mass is achieved.⁽⁵⁹⁾



Figure 7:Preparation of herbal pigmentation cream

EMERGING TECHNOLOGY IN HYPERPIGMENTATION

Dark patches or spots on the skin are a common dermatological condition known as hyperpigmentation, which is caused by an overabundance of melanin production. Although topical medications, chemical peels, and laser therapy are examples of established treatment techniques that have demonstrated some degree of effectiveness, new technologies present innovative approaches that may offer enhanced safety and efficacy profiles. By examining new developments in the field of hyperpigmentation therapy, this review seeks to provide light on their mechanisms of action, clinical effectiveness, and potential future developments.^[60]

1.Picosecond Lasers:

When it comes to treating hyperpigmentation, picosecond lasers mark a major breakthrough in laser technology. These lasers produce picosecond-long, ultra-short pulses that photomechanically destroy melanin particles without seriously heating up the tissues around them. With fewer side effects than conventional nanosecond lasers, picosecond lasers have demonstrated encouraging results in the treatment of a variety of pigmentary illnesses, including melasma and post-inflammatory hyperpigmentation.^[61]

2.Topical agents based on nanotechnology:

Topical agents aimed at treating hyperpigmentation can be more effectively delivered and effective because to the novel approaches provided by nanotechnology. Active compounds can be encapsulated in nanoparticles for more effective penetration through the stratum corneum and targeted distribution to the skin's deeper layers. Nanocarriers can also improve the stability of delicate substances and shield them against deterioration. Ingredients including hydroquinone, kojic acid, and vitamin C have been shown in nano formulations to be more effective at reducing the generation of melanin and enhancing skin tone.^[62]

3.Light-Emitting Diode (LED) treatment:

Also referred to as photo biomodulation, LED treatment stimulates skin cellular processes by using particular light wavelengths. In the treatment of hyperpigmentation, LEDs producing visible spectrum wavelengths like red (620–700 nm) and blue (400–470 nm) have demonstrated potential. Red light increases skin renewal and collagen formation, which improves skin tone and texture, while blue light targets germs and inflammation that cause acne.^[63]

4.Fractional Radiofrequency Microneedle

This technique combines the advantages of radiofrequency energy's thermal effects with microneedling's benefits. Using controlled thermal damage to the dermis, this method preserves the epidermis while promoting collagen remodelling and synthesis. Fractional radiofrequency microneedling is a viable treatment option for hyperpigmentation because of its demonstrated effectiveness in encouraging general skin regeneration, decreasing pigmentation, and enhancing skin texture.^[64]

List of some anti pigmentation cream:

Brand Name	Price (MRP)	Photo
Detoxie	747 Rs.	
Mamaearth	471 Rs.	

Himalaya	237 Rs.	
Khadi	247 Rs.	

Figure 8:List of some anti pigmentation cream

CONCLUSION

Antihyperpigmentation treatments include a wide range of techniques, each with specific mechanisms and factors to take into account. Even though understanding and treating hyperpigmentation has advanced significantly, further research is still needed to solve unresolved issues and improve treatment results. Dermatology is moving toward more individualized and efficient methods of treating hyperpigmentation and boosting everyone's confidence and skin health by welcoming innovation, encouraging diversity, and emphasizing patient-centred treatment.

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