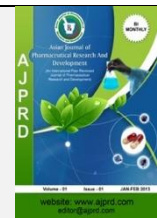


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Review Article

## Review on Advancement in Cosmetic Science For Melasma

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### ABSTRACT

Melasma, a common hyperpigmentation disorder, poses a significant challenge in the field of dermatology and cosmetic science. Characterized by symmetrical, brownish facial pigmentation, melasma primarily affects women of reproductive age, with a notable impact on quality of life. Despite its prevalence, effective and long-lasting treatments remain elusive. This review explores the latest developments in cosmetic science aimed at addressing melasma, focusing on innovative formulations, ingredients, and technologies. Traditional and contemporary cosmetic approaches to melasma, including the use of topical agents such as hydroquinone, retinoids, and corticosteroids. Additionally, the review discusses emerging ingredients like tranexamic acid, niacinamide, kojic acid, and botanical extracts known for their skin-lightening properties.

The review concludes by emphasizing the need for a multifaceted approach in cosmetic science to effectively manage melasma. By combining traditional and novel ingredients, optimizing delivery systems, and integrating advanced technologies, cosmetic formulations can offer improved efficacy and patient satisfaction in the management of melasma. Future directions for research and development are also discussed, with an emphasis on personalized skincare regimens tailored to individual patient characteristics.

**Key word:** Melasma, cosmetic approach, topical applications, effective management.

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### INTRODUCTION:

The word cosmetic is derived from the Greek word “kosmtikos” meaning having the power, arrange, skill in decorating. The origin of cosmetics forms a continuous narrative throughout the history of man as they developed in prehistoric times 3000BC. The word cosmetics defined as “Substances of diverse origin, scientifically compounded and used to i) cleanse, ii) allay skin troubles, iii) cover up imperfections and iv) beautify”. Cosmetic science is a multidisciplinary field that combines elements of chemistry, biology, pharmacology, and engineering to develop and enhance cosmetic products. It involves researching and creating formulations for items like skincare, hair care, makeup, and fragrances, with a focus on improving appearance and promoting overall well-being. Cosmetic scientists work to understand the interactions between various ingredients and their effects on the skin and hair, ensuring the safety, efficacy, and quality of cosmetic products. Cosmetic

science is a dynamic discipline that unites scientific principles with artistic flair to formulate products aimed at enhancing beauty and promoting skin and hair health. It is any substance used to clean, improve or change the complexion, skin, hair, nails or teeth. Melasma is a common hypermelanotic disorder affecting the face that is associated with considerable psychological impacts. The management of melasma is challenging and requires a long-term treatment plan. The search for safer alternatives has given rise to the development of many newer agents, several of them from natural sources. Well-designed controlled clinical trials are needed to clarify their role in the routine management of melasma. Melasma (from the Greek word, ‘melas’ meaning black) is a common, acquired, circumscribed hypermelanosis of sun-exposed skin. It presents as symmetric, hyperpigmented macules having irregular, serrated, and geographic borders. The most common locations are the cheeks, upper lips, the chin, and the forehead, but other sun-exposed areas may also occasionally

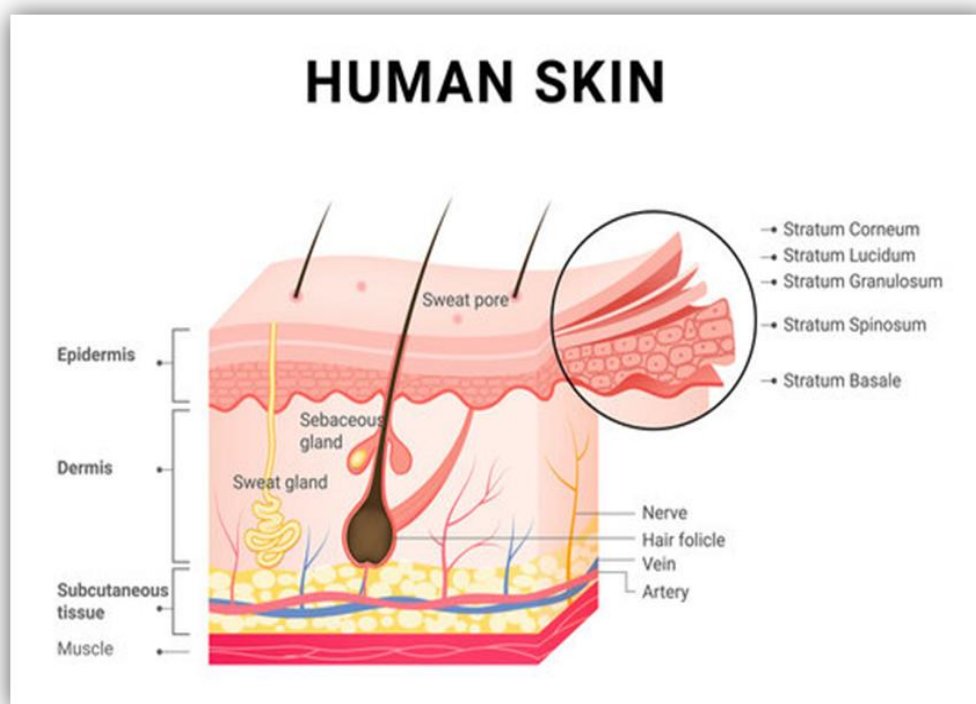
be involved. Melasma is the most common pigmentary disorder among Indians.(1)

Melasma, formerly known as chloasma, is an acquired pigmentary condition, occurring most commonly on the face. This disorder, which is more prevalent in females and darker skin types, is predominantly attributed to ultraviolet (UV) exposure and hormonal influences. Melasma is generally a clinical diagnosis consisting of symmetricreticulated hypermelanosis in three predominant facial patterns: centrofacial, malar, and mandibular.(2)The major clinical pattern in 50–80% of cases is the centrofacial pattern, which affects the forehead, nose, and upper lip, excluding the philtrum, cheeks, and chin (3). Though common, the management of this disorder remains challenging given the incomplete understanding of the pathogenesis, its chronicity, and recurrence rates. This review will provide an up-to-date overview of the current literature on melasma, including clinical diagnosis, pathogenesis, and treatments including discussion of new topical therapies.

## STRUCTURE OF SKIN

The skin, also known as the cutaneous membrane, covers the outer surface of body and is the biggest organ of body in weight. In grown-ups, the skin covers part of around 2 sq. m. (22 sq. ft) and weighs 4.5-5 kg (10-11 lb), about 7% of whole-body weight. It goes in thickness from 0.5 mm on eyelids to 4.0 mm on the heels. Over a large portion of the body it is 1-2 mm thick, pH of the skin fluctuates from 4 to 5.6 and refers to the pH of film of water and other dissolvable materials present on the outside of the skin. Sweat and Fatty acids emitted from sebum impact pH of the skin surface. It is recommended that Causticity of the skin helps in constraining or forestalling the development of pathogens and other organisms. The skin consists of three functional layers-

1. Epidermis
2. Dermis
3. Hypodermis



## FUNCTION OF SKIN :

Some of the many roles of skin include:

- Protecting against pathogens. Langerhans cells in the skin are part of the immune system.
- Storing lipids (fats) and water.
- Creating sensation through nerve endings that detect temperature, pressure, and injury.
- Controlling water loss by preventing water from escaping by evaporation.
- Providing water resistance by preventing nutrients from being washed from the skin.
- Helping with thermoregulation by producing sweat and dilating blood vessels, which helps keep the body cool. “Goosebumps” and blood vessel constriction help peoplretain heat.

### Pathophysiology of Melasma:



Figure 1: Melasma Skin

- The pathophysiology of melasma remains indefinable, but multiple factors have been implicated. The role of female hormonal activity has been suggested by the increased frequency of occurrence of melasma in pregnancy and in those on oral contraceptive pills. The mechanism of induction of melasma by estrogen may be related to the presence of estrogen receptors on the melanocytes that stimulate the cells to produce more melanin.
- Genetic factors are indicated by familial occurrence of melasma and its increased incidence in people of Asian and Hispanic origins.
- Other factors implicated in the etiopathogenesis of melasma are photosensitizing and anticonvulsant medications, mild ovarian or thyroid dysfunction, and certain cosmetics.
- One of the most important factors in the development of melasma is ultraviolet exposure from sunlight or other sources.
- Melasma results in an increased deposition of melanin in the epidermis, in the dermis within melanophages, or both. The number of melanocytes in the lesions has been variably reported to be normal.(4)

### Types of Melasma:

The lesions range in color from light brown to dark brownish-black and affect the regions of the face in different patterns. Three clinical patterns of distribution of the pigmentation may be recognized: Centrofacial, malar, and mandibular. (5)

**1. Centrofacial pattern:** It is most common and involves the cheeks, nose, forehead, upper lip, and chin.



Figure 2: Centrofacial pattern

**2. Malar pattern:** It involves the cheeks and nose.



Figure 3: Malar pattern

**3. Mandibular pattern:** The ramus of the mandible is involved in this pattern.



**Figure 4:** Mandibular pattern

Melasma does not involve the mucous membrane.

It is also classified into four histological types according to the depth of pigment deposition (6)-

- 1. Epidermal type:** It is the most common in which the pigmentation appears more intense. Melanin is distributed throughout the epidermis; topical treatment may work best in this type of melasma.
- 2. Dermal type:** The pigmentation is due to plenty of melanophages in the dermis.
- 3. Mixed type:** The pigmentation is due to increased epidermal melanin as well as dermal melanophages.
- 4. Indeterminate type:** No benefit in very dark individuals. This classification may partly work in lighter skin types but not in brown or black skin types.

Depending on the natural history of the lesions, melasma may also be classified into *transient* and *persistent* types. (7)

- 1. Transient type:** It disappears within one year of cessation of hormonal stimuli like pregnancy or oral contraceptive pills.
- 2. Persistent type:** It continues to be present more than one year after the hormonal stimulus is removed and is caused by the action of UV rays and other factors, highlighting the role of sun-avoidance in the management of melasma.

Morphologically, melasma presents as symmetric reticulated hyperpigmented patches with irregular borders on the centrofacial region, malar cheeks, mandible, and rarely upper chest and extremities. While melasma is known to more commonly affect darker skin types, it can occur in all skin types. (8)

#### Topical treatment:

By causing cosmetic blemish of the face, melasma is frequently associated with a significant emotional

effect. There is no universally effective specific therapy for the disease—existing agents have varying degrees of effectiveness, and the condition, more often than not, relapses.(9)Most cases are treated with topical agents, used alone, or in combinations.

Recurrence of melasma occurs on exposure to sunlight and other sources of ultraviolet rays. Photoprotective measures like the avoidance of direct sun-exposure and the regular use of a broad-spectrum sunscreen are always advised, although clinical studies on their role are lacking. Treatment with demelanizing agents must be continued for several months before significant clinical benefits become noticeable. Topical agents are much more effective in the epidermal type of melasma.

#### 1. Hydroquinone :

Hydroquinone (HQ), it is also known as dihydroxybenzene. It is a hydroxyphenolic compound that is structurally similar to precursors of melanin. HQ is the most frequently prescribed depigmenting agent worldwide and it has remained the gold standard for the treatment of melasma, particularly of the epidermal type. HQ preparations are commonly used in the treatment of melasma at concentrations varying from 2 to 5% applied once daily. Treatment should be continued for at least three months, up to one year(10). Adverse reactions of HQ are related to its dose and the duration of treatment. Irritation is the most common complication; other adverse effects include erythema, stinging, colloid milium, irritant and allergic contact dermatitis, nail discoloration, transient hypochromia, and paradoxical postinflammatory hypermelanosis.(11)HQ is also formulated in combination with other agents like sunscreens, topical steroids, retinoids, and glycolic acids for added benefits. HQ is an oxidizing agent that can oxidize in tubes or bottles, turning the color of formulations from white to brown. Products that have undergone this color change are ineffective and should be discarded. Regulatory agencies in Japan, Europe, and most recently the USA, have raised

questions about the safety of HQ (12) and it has been banned in cosmetic preparations in many countries. This has encouraged research into alternative agents for the topical management of melasma.

## 2. Azelaic acid:

Azelaic acid is a naturally occurring, nonphenolic, saturated, nine-carbon dicarboxylic acid that competitively inhibits tyrosinase. Azelaic acid was initially developed as a topical anti-acne agent but because of its effect on tyrosinase, it has also been used to treat hyperpigmentary disorders like melasma. Its mechanisms of action include the inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects toward the melanocyte(13). A combination of azelaic acid with 0.05% tretinoin or 15-20% glycolic acid may produce earlier, more pronounced skin lightening. Adverse effects of azelaic acid include pruritus, mild erythema, and burning (14).

## 3. Kojic acid:

Kojic acid (5-hydroxy-2-hydroxymethyl-4-pyrone) is a naturally occurring, hydrophilic fungal product derived from certain species of *Acetobacter*, *Aspergillus*, and *Penicillium*(15). It is generally univalent to other therapies but may be more irritating. Kojic (KA) acid is used at concentrations ranging from 1 to 4%. KA may be effective if a patient has difficulty tolerating other first-line therapies. It may cause contact dermatitis and erythema(16).

## 4. Retinoids:

Retinoids, such as tretinoin, were first used in combination with HQ as penetration enhancers, but were later recognized to have their own effect on melanogenesis (17). Retinoic acid (RA) suppresses UVB-induced pigmentation by reducing tyrosinase activity. Compared with phenolic compounds like HQ, RA takes a much longer time to act; clinically significant lightening becomes evident after 24 weeks. Tretinoin monotherapy has produced a good therapeutic response in clinical trials but better results are obtained in combination with other agents like HQ and corticosteroids. The most common side effects include erythema, burning, stinging, dryness, and scaling. Patients must be advised to use sunscreens during treatment with retinoic acid. Adapalene, a naphthoic acid derivative with retinoid activity, was found to be equally efficacious in a randomized trial in Indian patients but with significantly less untoward effects than tretinoin (18).

## 5. Glycolic acid:

Glycolic acid is an alpha-hydroxy acid that is usually combined with other agents at a concentration of 5-10% for its skin-lightening property. The mechanism of its effect might be due to epidermal remodeling and accelerated desquamation, which would result in quick pigment dispersion on pigmentary lesions. It also directly reduces melanin formation in melanocytes by tyrosinase inhibition (19). Irritation was a common side effect which resolved with the temporary cessation of application and application of moisturizers (20).

## 6. Arbutin:

Arbutin, the beta-D-glucopyranoside derivative of hydroquinone, is a naturally occurring plant product which

has been used successfully in the treatment of hyperpigmentary disorders. Arbutin acts by the inhibition of tyrosinase, thereby decreasing melanin formation. The normal skin microflora may also hydrolyze arbutin; the hydrolyzed hydroquinone shows more potent free-radical scavenging activity and tyrosinase inhibition than arbutin.(21)

## Other New and Experimental Agents:

A number of agents, both synthetic and those derived from natural sources like plants, have been investigated for their potential role in reducing melanin pigmentation. Although experimental evidence suggests their possible benefits, dependable controlled clinical trials are mostly lacking. Some of the compounds are formulated in combination products and marketed by pharmaceutical companies; many are available as ingredients of over-the-counter preparations.

- **Ascorbic acid:** Ascorbic acid has antioxidant properties and affects melanogenesis by reducing dopaquinone to DOPA and preventing free-radical production and absorption of ultraviolet radiation.(22)
- **Niacinamide:** Niacinamide (nicotinamide), the biologically active amide form of niacin (vitamin B<sub>3</sub>), can reduce pigmentation by reversibly preventing the transfer of melanosomes from melanocytes to the keratinocytes. In clinical studies, niacinamide significantly decreased hyperpigmentation and increased skin lightness compared with vehicle alone after four weeks of use. (23)
- **Liquorice derivatives:** Liquorice is the root of the perennial herb *Glycyrrhiza glabra*. *Glabridin* is an oil-soluble derivative of liquorice extract. *Glabridin* has been shown to have tyrosinase inhibitory as well as anti-inflammatory properties in experimental studies.(24)
- **Flavonoids:** Flavonoids are naturally occurring polyphenolic compounds that have well-known anti-inflammatory, antioxidant, antiviral, and anticarcinogenic properties. Many plant-derived flavonoid compounds have hypopigmentary effects and their roles are still under investigation.
- These include *catechin* conjugated with *gallic acid* (from green tea leaves), *ellagic acid* (from green tea, strawberry, eucalyptus etc), and *aloesin* (from aloe tree).(25)
- Other agents known to affect melanin pigmentation and sometimes used in formulations are *N-acetyl glucosamine*, *thiotic acid* (alpha-lipoic acid), *gentisic acid*, *soybean extract*, and *paper mulberry extract*.

## Indian laws and acts related to cosmetics

1. The main aim of The Drugs and Cosmetics Act, 1940 and Rules 1945 is to maintain the import, manufacture, distribution, and sale of drugs and cosmetics.
2. Continuous use of cosmetics in luxury items prove to be harmful as they may contain harmful ingredients. Therefore, there is a need to control the cosmetics.
3. This Act verifies that the drugs and cosmetics should be manufactured, distributed, and sold only by qualified persons having a license
4. For this purpose, The Central and State Drugs Control

authorities are also recognised to control these actions in 1940 government of India, drug and cosmetics act and rules implemented in 1945.

#### Aim of drug and cosmetics act :

1. Verify standard and quality of drug and cosmetics manufactured in India
2. Regulate their manufacture, sale, distribution
3. Maintain high standard of medical treatment

#### Exemptions of this act :

- For preventing substandard in drugs, probably for treatment and preserving high medical standards.
- For controlling the import, manufacture, distribution, and sale of drugs and cosmetics by licensing.
- For ensuring that manufacture, distribution, and sale of drugs and cosmetics is done by qualified persons only.
- For controlling the manufacture and sale of Ayurvedic, Siddha, and Unani drugs.
- For establishing Drugs Technical Advisory Board (DTAB)

and Drugs Consultative Committees (DCC) for Allopathic and Allied drugs and Cosmetics.

#### Amendments of the act :

The act has been amended several times.

The following are a list of amending acts:

1. The Drugs (Amendment) Act, 1960
2. The Drugs (Amendment) Act, 1962
3. The Drugs and Cosmetics (Amendment) Act, 1964
4. The Drugs and Cosmetics (Amendment) Act, 1972
5. The Drugs and Cosmetics (Amendment) Act, 1982
6. The Drugs and Cosmetics (Amendment) Act, 1986
7. The Drugs and Cosmetics (Amendment) Act, 1995
8. The Drugs and Cosmetics (Amendment) Act, 2008
9. The Drugs and Cosmetics (Amendment) Act, 2016
10. The Drugs and Cosmetics (Amendment) Act, 2022

#### Comparison of Cosmetic act 1940 and 2022

Chapters	Drug and Cosmetic Act 1940	Chapters	New drug, medical device and cosmetic bill, 2022
I	Introductory	I	Introductory
II	The drugs technical advisory board, the central drugs laboratory and the drugs consultative committee	II	Technical advisory boards, drugs laboratory, medical devices testing centres and consultative committee
III	Import of drugs and cosmetics	III	Import of drugs and cosmetics
IV	Manufacture, sale and distribution of drugs and cosmetics	IV	Manufacture, sale and distribution of drugs and cosmetics and clinical trials of drugs
IV A	Provisions relating to ayurvedic siddha and unani drugs	V	Provisions relating to ayurvedic siddha and unani drugs and homeopathic drugs
V	Miscellaneous	VI	Import, manufacture, sale, distribution and clinical investigation of medical devices
VI	Miscellaneous	VII	Miscellaneous

#### CONCLUSION:

Management of melasma can be challenging and requires long-term treatment with topical agents. The results are often unsatisfactory and topical agents may sometimes cause significant adverse reactions. Hydroquinone has remained the gold standard of topical treatment but concerns regarding its side effects remain. A triple combination of hydroquinone, retinoic acid, and corticosteroids has been suggested to be the first-line topical treatment for this pigmentary disorder. Many new agents that inhibit melanogenesis have been developed. Although *in vivo* and *in vitro* experimental studies have suggested their potential role in the management of melasma, controlled clinical trials are mostly lacking and are urgently needed in the future.

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