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Evaluation and Formulation of Polyherbes for The Treatment of Melasma

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Abstract:
Melasma is a common acquired hypermelanosis of tne face, the treatment of which is challenging. that is more common in female gender, although melisma is a multifactorial skin disorder, however, sun-exposure and genetic predisposition are considered as the main etiologic factors in melisma occurrence. Although numerous topical and systemic therapeutic agents and also non-pharmacologic procedural treatments have been considered in melisma management, however, the commonly available therapeutic options have several limitations including the lack of sufficient clinical effectiveness, risk of relapse, and high rate of unwanted adverse drug reactions. Now-a-days melisma is a common pigmentary condition, particularly among Asians, and its treatment is challenging for dermatologists because of unsatisfactory responses and high recurrence rates in many patients. Objectives: This dissertation provides an overview of the aetiology and pathogenesis of melisma, followed by a focus on its current management.

Keywords: Formulation of Gel, Pathophysiology, Evaluation Test.

1.1 INTRODUCTION: Melasma is a common skin disorder . Loosely translated, the word means "black spot." If you have melisma you're probably experiencing light brown ,dark brown &/or blue-gray patches on your skin .They can appear as flat patches or freckle-like spots. Commonly affected areas include your face including the cheeks ,upper lip and forehead , as well as the forearms .Melasma is sometimes called the "mask of pregnancy" because it frequently affects pregnant women . Melasma typically darkens and lightens over time, often getting worse in the summer and better in the winter.
Another, less common name for melisma is chloasma. Although this disorder is completely harmless ,it understandably makes some people feel self-conscious.
More research is needed to fully answer this question. Researchers have discovered that when someone has melasma, the cells that give skin its color (melanocytes) tend to be more active. Exactly why this happens isn't well understood.It may be that melasma develops when something triggers these skin cells, causing them to go into overdrive.

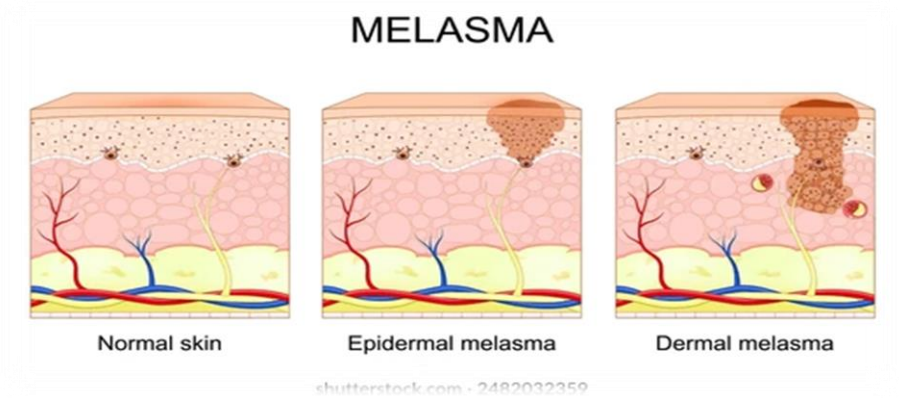

FIG: 1

The list of possible melasma triggers includes:
Sunlight: When sunlight hits our skin, it triggers the body to produce more melanin. This seems to explain why melasma develops on skin that gets the most sunlight like skin on the face, neck, and arms.
Pregnancy: An increase in the hormones estrogen and progesterone, which occurs during pregnancy, is thought to trigger melasma.

FIG : 2

1.2 Key Indicators of Melasma:

- **Symmetry:** Patches frequently appear identically on both sides of the face. **Appearance:** They look like darker patches of skin that may blend together, sometimes appearing as freckle-like spots.
- **Location:** Most common on the cheeks, forehead, chin, bridge of the nose, and above the upper lip.
- **Trigger:** Patches darken, become more noticeable, or appear after sun exposure.
- **Population:** Affects all skin types, but 90% of cases occur in women.

1.3 PATHOPHYSIOLOGY:

The pathophysiology of melasma is multifactorial [3] and has not been fully elucidated. It appears to be directly related to female hormonal activity, in that melasma occurs more frequently in females than in males and commonly develops or worsens during pregnancy and with the use of oral contraceptive pills. Indeed, one half of melasma cases present initially during pregnancy. Additionally, the expression of estrogen receptors appears to be upregulated in melasma lesions. [4] Progesterone has also been found to increase melanogenesis. [5] Whether hormone levels play a role in the development of melasma in males remains a subject of debate.Other factors implicated in the pathogenesis of melasma are photosensitizing medications, mild ovarian dysfunction, and certain cosmetics. An exogenous form of melasma known as ochronosis is occasionally caused by specific implicated medications. Genetic predisposition clearly plays a role as well, in that a family history of melasma is known to be an important risk factor for its development. Between 55% and 64% of patients with melasma have a family history of this condition. [6]
The most important factor in the development of melasma is exposure to sunlight. Ultraviolet (UV) radiation induces production of reactive oxygen species (ROS) in the skin, which subsequently promotes melanogenesis. [7] UV radiation is also known to induce increased production of alpha-melanocyte–stimulating hormone and corticotropin, as well as interleukin (IL)-1 and endothelin (ET)-1, all of which contribute to increased melanin production by intraepidermal melanocytes.Fibroblasts located in the dermal layer of the skin may also contribute to the development of melasma; overexpression of the

tyrosine kinase receptor c-kit and certain stem cell factors have been identified in melasma lesions, and these are believed to increase melanogenesis. [8]A growing body of evidence supports the view that melasma is not purely a condition of enhanced melanocyte activity but, rather, a chronic inflammatory condition of the skin microenvironment. A 2025 review by Miao et al described melasma as a disorder of epidermal-dermal crosstalk and immune modulation .

1.4 EPIDIMIOLOGY :

Melasma is a common dyschromia that often motivates the search for dermatological care. Its populational prevalence varies according to ethnic composition, skin phototype, and intensity of sun exposure.

In a 2010 population-based study, 1500 adults from several Brazilian states were surveyed. Pigmentation disorders were reported as the main cause of demand for dermatological care by 23.6% of men and 29.9% of women.7

According to a survey of 57,343 diagnoses performed at dermatological consultations in Brazil that was conducted by the Brazilian Society of Dermatology (BSD) in 2006, melanodermias (among them, melasma) represented the third largest group of diseases in dermatological practice, accounting for 8.4% of all complaints. This prevalence varied from 5.9% to 9.1% in the different regions of the country.8

A study conducted in Nepal in 2008 with 546 dermatological patients evidenced melasma as the fourth most frequent diagnosis and the first most commonly reported pigmentary dermatosis.

1.5 CLINICALLY PRESENTATION :

Clinically, melasma presents as a symmetrically di-stributed macular pigmentation□with irregular borders, which can vary in colour ranging from a light to dark brown or brown–gravy. □e number hyper pigmented lesions may range from one single lesion to multiple patches located on the forehead, cheeks, dorsum of the nose, upper lip, chin, occasionally on the V-neck area and forearms. Pigmentation may be gestate or confetti-like, linear, or con□uent; it evolves slowly over weeks or years. □e hyper pigmented patches often fade in winter and get worse in the summer.□

According to the distribution of lesions, there
are three clinical patterns of melisma: Centro facial(65%), malar (20%), and mandibular (15%). Centro facial pattern involves the forehead, cheeks, upper lip, nose, and chin; the malar pattern involves the cheeks and nose, and mandibular the ramus of the
mandible . Wood's lamp (320–400□nm) is used to determine the depth of melanin in the skin. Wood's light may also serve as a prognostic guide in the treatment of melisma, as the epidermal type of melisma is more likely to respond favourably to topical DE pigmenting agents. Common reasons for diagnostic failure are topical petrolatum and salicylic acid, lint and soap.

1.6 MECHANISTIC INSIGHTS OF MELASMA:

According to recent research, a number of factors, such as genetic predisposition, UV radiation, Photo aging, Hormonal factors etc. can cause or worsen the condition of Melisma,

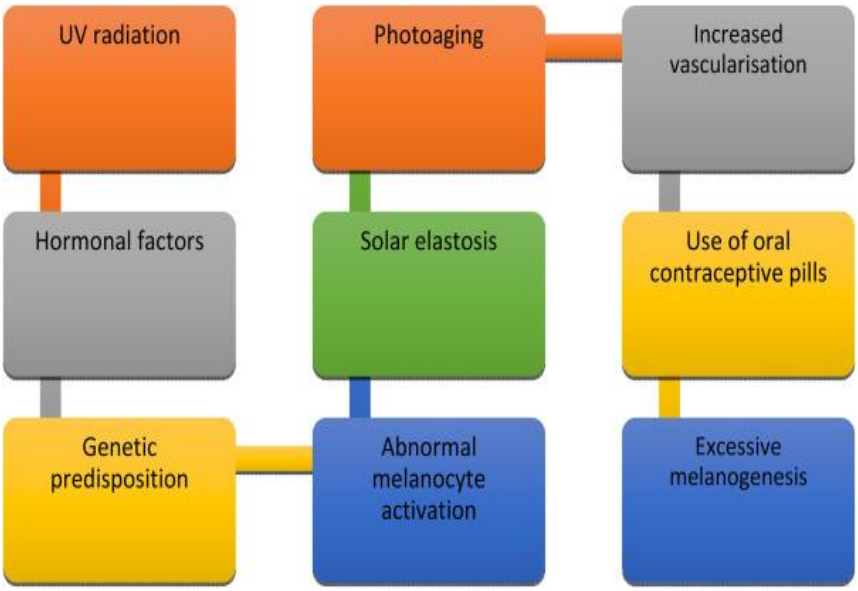

FIG : 3

Recent research suggests that melisma is a multifactorial disorder involving complex interactions between genetic, environmental, hormonal, vascular, and inflammatory pathways. Several factors can initiate or aggravate the condition, including genetic predisposition, ultraviolet (UV) radiation, photo aging, hormonal influences, and other external triggers,

1.7 MAJOR MECHANISMS INVOLVED IN MELASMA :

1. **Genetic Predisposition**
   - A positive family history is commonly observed in patients with melasma.
   - Genetic susceptibility may influence melanocyte activity and skin response to UV exposure.
2. **Ultraviolet (UV) Radiation**
   - UV-A and UV-B radiation stimulate melanocyte proliferation and melanin synthesis.
   - UV exposure increases reactive oxygen species (ROS) and activates tyrosinase, leading to hyperpigmentation.
3. **Visible Light and Infrared Radiation**
   - Visible light, especially blue light, can induce persistent pigmentation in darker skin types.
   - Infrared radiation contributes to oxidative stress and dermal inflammation.
4. **Photo aging**
   - Chronic sun exposure causes dermal damage, basement membrane disruption, and solar elastics.
   - Photo aged skin shows increased melanogenic signaling and abnormal melanocyte distribution.
5. **Hormonal Factors**
   - Estrogen and progesterone influence melanocyte stimulation.
   - Pregnancy, oral contraceptive pills, and hormone replacement therapy are commonly associated with melasma development.
6. **Vascular Factors**
   - Increased dermal vascularization and elevated vascular endothelial growth factor (VEGF) have been identified in melasma lesions.

- Vascular changes may enhance melanocyte activity.

7. **Inflammatory Pathways**

- Inflammatory mediators such as cytokines, prostaglandins, and nitric oxide contribute to melanogenesis.
- Chronic low-grade inflammation may sustain pigmentation.

8. **Oxidative Stress**

- Increased oxidative damage and reduced antioxidant defense mechanisms are observed in melasma patients.
- Reactive oxygen species stimulate melanocyte activity and pigment production.

9. **Skin Barrier Dysfunction**

Altered epidermal barrier function may increase skin sensitivity and susceptibility to external triggers.

10. **Drugs and Cosmetics**

- Certain medications and photosensitizing cosmetics can precipitate or worsen melasma. Overall, melasma is now considered not merely a pigmentary disorder but a chronic photoaging-associated condition involving melanocytes, keratinocytes, fibroblasts, vascular structures, and inflammatory mediators.

1.8 DRUG PROFILE RELATED TREATMENT OF MELASMA:

DIAGNOSIS:

The diagnosis of melisma is essentially clinical, and poses no greater difficulties to the dermatologist.
The main differential diagnoses of melisma are freckles, solar lent go, toxic melanodermia, Riehl's melanosis, post-inflammatory hyperpigmentation, friction melanosis, ochronosis (endogenous and exogenous), cutaneous erythematosus lupus. We can also cite: phytophotodermatosis, pellagra, endogenous photo toxicity, nevus of Ota, *café au laity* macules, seborrhoea keratosis, Cuvette's poikiloderma, acquired bilateral nevus of Ota-like macules (Hori's nevus), periorbital hyperpigmentation, erythrose pigmentaire peribuccale of Brocq, erythromelanosis follicularis faciei, facial acanthosis nigricans, drug-induced pigmentation (e.g.: amiodarone) and actinic lichen planus

1.9 DRUG PROFILE RELATED TREATMENT OF MELASMA:

MECHANISM OF ACTION OF INGREDIENTS IN POLYHERBAL ANTI-MELASMA GEL

Sr. No.	INGREDIENT	MECHANISM OF ACTION	ROLE IN GEL
1.	Aloe vera gel	Contains aloin, aloe-emodin and polysaccharides that reduce inflammation, hydrate the skin and promote wound healing. It also inhibits tyrosinase enzyme to reduce melanin production.	Soothing agent, moisturizer, depigmenting aid
2.	Neem extract (*Azadirachta indica*)	Rich in nimbidin and quercetin, which exhibit anti-inflammatory, antibacterial and antioxidant effects. Helps reduce oxidative stress involved in melasma.	Anti-inflammatory and antioxidant agent
3.	Green tea extract	Contains epigallocatechin gallate (EGCG), a potent antioxidant that inhibits tyrosinase and suppresses UV-induced pigmentation.	Skin-lightening and antioxidant agent
4.	Turmeric extract (Curcumin)	Curcumin inhibits tyrosinase activity and decreases melanin synthesis. It also reduces inflammation by blocking NF-κB and COX-2 pathways.	Depigmenting and anti-inflammatory agent
5.	Carbopol 934	Cross-linked polyacrylic acid polymer that swells in water and forms a gel when neutralized with triethanolamine.	Gelling agent
6.	Glycerin	Attracts water to the skin by humectant action, maintaining hydration and improving skin softness.	Humectant and moisturizer
7.	Propylene glycol	Enhances penetration of active ingredients into the skin and also acts as a humectant.	Penetration enhancer and solvent
8.	Methyl paraben	Inhibits growth of bacteria and fungi by disrupting microbial enzyme systems.	Preservative
9.	Propyl paraben	Provides antifungal and antibacterial preservation, especially against molds and yeasts.	Preservative
10.	Triethanolamine (TEA)	Neutralizes Carbopol and adjusts pH, converting the dispersion into a clear gel.	pH adjuster and gel activator
11.	Purified Water (q.s.)	Serves as the vehicle to dissolve and disperse all ingredients uniformly.	Solvent / Vehicle

FIG : 4

1.10 METHOD & MATERRIAL :

TABLE NO : 1 Formulation Table

INGREDIENT	BATCH 1 (25ml)	BATCH 2 (35ml)	BATCH 3 (45ml)
1)Aloe Vera.	2.5g	3.5g	4.5g
2)Neem Extract	0.5g	0.7g	0.9g
3)Green tea extract	0.25g	0.35g	0.45g
4)Licorice Extract	0.125g	0.175g	0.225g
5)Carbopol 934	0.25g	0.35g	0.45g
6)Glycerin	1.25ml	1.75ml	2.25ml
7)Propylene Glycol	1.25ml	1.75ml	2.25ml
8)Methyl parable	0.05g	0.07g	0.09g
9)Propyl Paraben	0.025ml	0.035ml	0.045ml
10)Triethanolamine	q.s	q.s	q.s
11)Distilled Water	q.s	q.s	q.s

1.11 PROCEDURE:

The required quantity of Carbopol 934 was dispersed in a small amount of distilled water and allowed to swell for proper gel formation. Glycerin and propylene glycol were then added with continuous stirring to obtain a smooth mixture. After that, neem extract, aloe vera gel, green tea extract, and turmeric extract were added slowly and mixed uniformly. Methyl paraben was incorporated as a preservative. Finally, triethanolamine was added dropwise to adjust the pH and convert the dispersion into a gel. The final volume was made up to 45 mL using distilled water, and the preparation was stirred continuously until a homogeneous gel was obtained.

1.12 RESULT:

IDENTIFICATION TEST FOR CRUDE DRUGS

TEST	**COLOUR**	**RESULT**
1)MOLISH TEST	Violet Ring forms	+
2)ALKOLOIDE TEST	Purrple Colour Observed	+
3)FOAM TEST	Foam particle form	+
4)PROTEINE TEST	Light purple	+
5)FLAVONOIDE TEST	Yellow Colour pot	+
6)SAPONIFICATION TEST	Fatty Acid present	+
7)GLUCOSE TEST	NO COLOUR	-

TABLE NO : 2

1.13 EVALATION TEST FOR MELASMA GEL

1)PHYSICAL APPEARANCE :

I.COLOUR : Brown in colour.

II.CLARITY : Clarity may be present , gel showed smooth texture.

III.HOMOGENEITY : Good homogeneity

IV.Presence of lumps or grittiness : No visible parcles or phase .

2)PH Determination :

Test : The pH of the gel is measured using a digital pH meter by dispersing the gel in distilled water.

Result : The pH of the gel was found to be between 5.5 – 6.8, which is suitable for skin application.

3)Viscosity Test

Test :

Viscosity is measured using a Brookfield viscometer at room temperature.

Result :

The gel showed optimum viscosity, indicating good consistency and easy spread ability.

4) Spread ability Test :

Test : A small amount of gel is placed between two glass slides and the spreading time is observed.

Result : The gel spread uniformly with good spreadability and required less time for spreading.

5) Extrudability Test

Test : The gel is filled into a collapsible tube and pressed to check ease of extrusion.

Result : The gel was easily extruded from the tube with slight pressure.

6) Washability Test :

Test: The applied gel is washed with water to observe removal.

Result : The gel was easily washable and left no sticky residue.

7) Drug Content Uniformity spectrophotometrically.

Result : The drug content was found to be uniform and within acceptable limits (95–100%).

8)Skin Irritation Test :

Test : The gel is applied on skin and observed for redness or irritation.

Result : No redness, itching, or irritation was observed, indicating the formulation is safe for topical use.

9) Stability Study:

Test : The gel is stored at room temperature and observed for changes in color, door, and consistency.

Result : No significant change in physical appearance or consistency was observed during storage.

1.14 CONCLUSION:

The prepared gel formulation showed satisfactory physicochemical properties, good stability, proper spread ability, and was suitable for topical application.The formulated topical gel successfully demonstrated optimal physicochemical and mechanical characteristics required for effective dermatological delivery. The evaluation parameters, including pH, viscosity, and drug content uniformity, remained within the ideal therapeutic range, ensuring both compatibility with the skin barrier and consistent dosing. Furthermore, stability studies confirmed that the formulation maintains its structural integrity, appearance, and active ingredient potency over time under various environmental conditions, without showing signs of phase separation or degradation. The gel also exhibited excellent spreadability, allowing for smooth, uniform, and effortless application across the skin surface without causing mechanical irritation. Collectively, these favorable attributes confirm that the prepared gel is a stable, consumer-acceptable, and highly suitable vehicle for topical therapeutic administration.

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