

Melasma update

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ABSTRACT

Melasma is an acquired pigmentary disorder characterized by symmetrical hyperpigmented macules on the face. Its pathogenesis is complex and involves the interplay of various factors such as genetic predisposition, ultraviolet radiation, hormonal factors, and drugs. An insight into the pathogenesis is important to devise treatment modalities that accurately target the disease process and prevent relapses. Hydroquinone remains the gold standard of treatment though many newer drugs, especially plant extracts, have been developed in the last few years. In this article, we review the pathogenetic factors involved in melasma. We also describe the newer treatment options available and their efficacy. We carried out a PubMed search using the following terms “melasma, pathogenesis, etiology, diagnosis, treatment” and have included data of the last few years.

Key words: Etiology, hydroquinone, lasers, melasma, pathogenesis, peeling, treatment

INTRODUCTION

Melasma is a common pigmentary disorder that manifests as symmetric hyperpigmented macules and patches on the face. It typically affects women of reproductive age with Fitzpatrick skin type IV-VI, though the condition can occur in men also. Genetic predisposition, ultraviolet (UV) radiation exposure, hormonal factors such as female sex hormones and thyroid disease, pregnancy and drugs like phenytoin are the known risk factors.

In recent times, there have been studies throwing light on other factors that could be involved in the pathogenesis of melasma. These include various vascular growth factors, genetic factors, and the role of H19, inducible nitric oxide synthase (iNOS), and Wnt pathway modulator genes. Identifying these factors could facilitate the development of newer treatment options for melasma.

Hydroquinone (HQ) and triple combination creams (TCCs) remain the gold standard of treatment. There have been concerns about the side effects and long term safety of HQ; hence the need to develop alternate treatment options. Current treatment modalities include kojic acid, azelaic acid, arbutin, ascorbic acid, chemical peels and lasers. Newer formulations that are being tried include tranexamic acid (TA),

rucinol (4-n-butylresorcinol), oligopeptides silymarin and orchid extracts. Various botanical extracts that have been tried in melasma are grape seed extract, pycnogenol, aloesin, green tea extracts, coffee berry, soy, and licorice extract.

EPIDEMIOLOGY

The prevalence of melasma varies between 1.5% and 33.3% depending on the population.^[1,2] Its prevalence in pregnancy is around 50-70%.^[3,4] Melasma can also occur in men, though less common. Sarkar *et al.* conducted an etiological and histological study in Indian males with melasma and found that men represent 20.5-25.83% of the cases.^[5,6] In men, the malar pattern is more common than the centrofacial and mandibular patterns [Figures 1 and 2].^[5-7]

A study conducted in male patients with melasma has shown that the levels of testosterone were low indicating a role of subtle testicular resistance in the pathogenesis of melasma.^[8] Other etiological factors that have been described in men with melasma include the use of vegetable oil especially mustard oil on the face^[5,7] and diethylstilboestrol therapy for prostate cancer.^[8]

ETIOLOGY

Several factors have been implicated in the etiology of melasma. These are genetic

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Figure 1: Centrifacial melasma

predisposition, UV radiation, thyroid disease, pregnancy, oral contraceptive pills (OCPs) and drugs such as phenytoin.^[9-12]

Hormonal influences

Various studies evaluating the hormonal profile in patients with melasma have found significantly increased levels of luteinizing hormone and lower levels of serum estradiol suggesting subclinical evidence of a mild ovarian dysfunction. Significant association has been reported between thyroid autoimmunity and melasma, mainly in women whose condition developed during pregnancy, or after ingestion of OCPs.

Ortonne *et al.* carried out a large survey in 12 centers of nine countries involving 324 patients to study the impact of UV radiation and hormonal influences in the development of melasma.^[13] They found that only 20% of patients developed melasma in the peripregnancy period. The risk of onset during pregnancy was more with greater outdoor activity. An interesting finding in this study was the weak impact of OCPs on the evolution of melasma, especially in patients with a family history of melasma, supporting the view that hormonal contraceptives need not be changed in such patients.

Drugs

Pigmentation resembling chloasma develops in 10% of patients receiving phenytoin. The drug exerts direct action on melanocytes causing dispersion of melanin granules and also induces increased pigmentation in the basal epidermis. Pigmentation disappears in a few months after withdrawal of the drug.

Role of visible light

Mahmoud *et al.* studied the impact of long-wavelength ultraviolet A (UVA) and visible light on melanocompetent skin.^[14] They found that both UVA and visible light were able to



Figure 2: Malar melasma

increase pigmentation especially in patients with dark skin (skin type IV-VI). Furthermore, pigmentation was more intense and stable after visible light compared to UVA. The study shows that visible light can also induce skin hyperpigmentation, emphasizing the need to use physical sunscreens to prevent melasma relapses.

Pathogenesis

Studies have confirmed that both melanocytosis (increased number of melanocytes) as well as increased melanogenesis (increased production of melanin) are responsible for the hyperpigmentation in melasma. Kim *et al.* carried out a histological study to evaluate the vascular characteristics of melasma.^[15] They found that vascular endothelial growth factor was increased in lesional skin in melasma signifying increased vascularization. This has clinical implications and indicates the need to devise treatment options to target the vascular component in melasma. In a prospective comparative split-face randomized study carried out by Passeron *et al.*, it was found that combination of TCC and pulsed dye laser (PDL) was more effective than TCC alone.^[16] The combination treatment also prevented the relapses.

Kang *et al.* performed a transcriptional analysis in melasma skin samples and found that 279 genes were stimulated and 152 were found to be downregulated. Many melanin biosynthesis related genes as well as melanocyte markers such as TYR, MITF, SILV, and TYRP1 were found to be upregulated in melasma skin.^[17]

Several other genes involved in other biological pathways were found to be affected. These include Wnt pathway modulation genes, genes involved in prostaglandin synthesis and fatty acid metabolism.^[17]

Another interesting finding was the role of H19 gene in melasma pathogenesis as studied by Kim *et al.*^[18] H19 gene

transcribes a noncoding ribonucleic acid (RNA) and is found to be downregulated in melasma lesions. This induces stimulation of melanogenesis and increased transfer of melanin from melanocytes to keratinocytes.

iNOS and nuclear factor-kappa B pathways have also been found to be implicated in melasma pathogenesis. In a study by Jo *et al.*, iNOS expression was found to be increased in melasma lesions.^[19]

The most affected biological process in melasma is lipid metabolism.^[17] Lipid metabolism genes, such as peroxisome proliferator-activated receptor alpha (PPAR), arachidonate 15- lipoxygenase, PPAR gamma coactivator 1 alpha, type B (ALXO 15B), diacylglycerol o-acyltransferase 2-like 3 were found to be downregulated. This downregulation is caused by chronic UV exposure.^[20] Another change seen in melasma skin is thinning of the stratum corneum (SC) as found in skin biopsies that show rete ridge flattening and epidermal thinning. SC thinning coupled with disturbed lipid synthesis is responsible for the impaired SC integrity and a delayed barrier recovery rate seen in melasma skin.^[21]

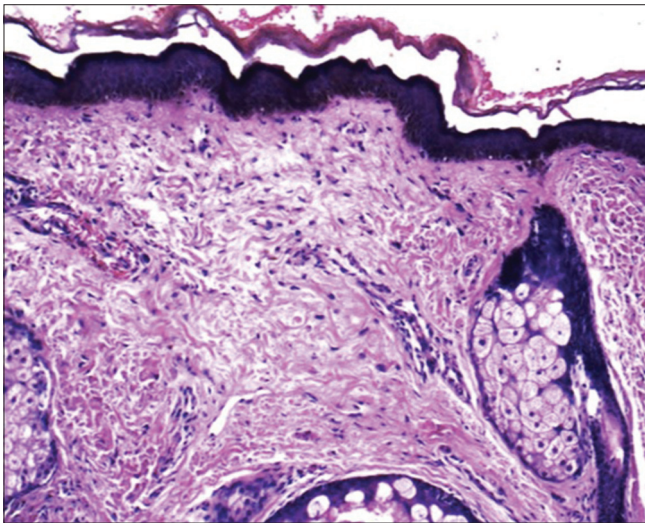


Figure 3: H and E, x200 epidermis shows increased melanin concentration in basal keratinocytes and underlying solar elastosis along with dermal melanophages (Courtesy of Dr. Uday Khopkar, Mumbai, India)

In a study by Lee *et al.*, melanin index, erythema index, and SC hydration were found to be significantly higher in lesional melasma skin as compared to perilesional normal skin. This proves that prominent vascularization accompanies hyperpigmentation.^[21]

Prolonged UV exposure-induced dermal inflammation and fibroblast activation may upregulate stem cell factors in the melasma dermis, causing increased melanogenesis.

The above findings emphasize the need for devising treatment options targeting these pathogenetic factors in melasma.

Classification of melasma

Table 1 shows the traditional classification^[22] being used for melasma. It is based on the depth of melanin pigment and helps in predicting the therapeutic outcome. However, Wood's light examination may not be accurate in determining the depth of pigment.^[23,24] There is poor correlation between the classification based on Wood's light examination and histopathology [Figure 3].

Dermoscopy can be used for the diagnosis of melasma. Lesions of melasma show diffuse reticular pigmentation in various shades of brown with sparing of follicular openings. Figures 4-9 depict the dermoscopic appearance of a patient with epidermal melasma. Dermal melasma shows diffuse dark brown to grayish pseudoreticular pigmentation. Annular, honeycomb and arcuate structures may be seen.

Reflectance confocal microscopy (RCM) is a noninvasive tool for the evaluation of the skin up to the papillary dermis.^[25] This technique can provide real-time *en face* images that have a resolution that matches that of histopathological examination. Kang *et al.* carried out a study to investigate the role of RCM in melasma and provide a set of morphological criteria with histological correlations.^[26] These are depicted in Figures 10 and 11. These are shown in Table 2.

RCM showed significant solar elastosis and increase of blood vessels in the dermis. It was also seen that the topographic distribution of melanophages was heterogenous within and

Table 1: Classification of melasma based on the depth of melanin pigment

Type	Normal light	Wood's light	Histology	Response to t/t
Epidermal	Light brown	Enhancement of contrast	Melanin deposition in basal and suprabasal layers of epidermis [Figure 3]	Good
Dermal	Bluish gray	No enhancement	Melanin laden melanophages seen in superficial and mid-dermis	Poor
Mixed	Dark brown	Some areas show contrast enhancement	Melanin deposition found in the epidermis and dermis	Partial
Wood's light not apparent in patients with dark skin types V and VI	Bluish gray/ unrecognized	Not evident under Wood's light	Melanin deposition in the dermis	Unpredictable



Figure 4: Dermoscopy from left cheek melasma showing dispersed brownish spots. White hairs are due to bleaching



Figure 5: Dermoscopy from right cheek melasma showing dispersed brownish spots



Figure 6: Dermoscopy from right cheek melasma showing dispersed pigment and depigmentation



Figure 7: Dermoscopy from nasal melasma showing larger dispersed brownish spots



Figure 8: Dermoscopy from the surrounding skin revealing more steroid induced telangiectasias



Figure 9: Dermoscopy from surrounding normal skin revealing mild steroid abuse-induced telangiectasias

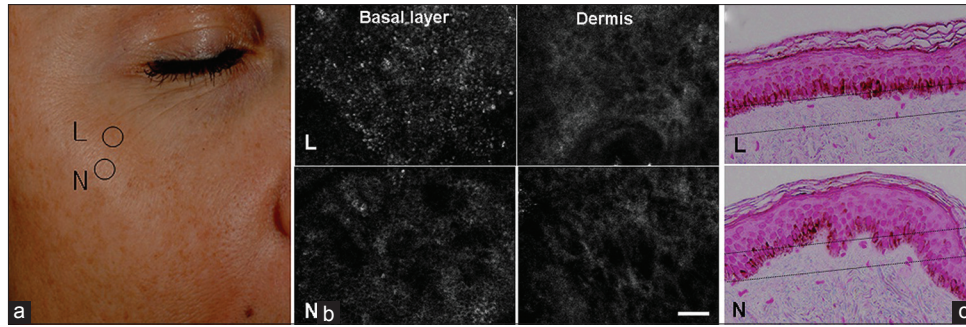


Figure 10: Confocal microscope images of melasma showing epidermal pigmentation: (a) Melasma on the cheek. L is for lesional skin and N is for normal perilesional skin. (b) Confocal images depict cobblestoning and loss of dermal papillary rings at the basal layer of the melasma lesion (L) compared to perilesional normal skin (N). Scale bar: 50 um. (c) Histopathology from same lesion showing greater epidermal hyperpigmentation and flattened rete ridges in lesion compared to perilesional normal skin Fontana-Masson staining, horizontal line indicates where reflectance confocal microscopy image is taken from (source acknowledged: Kang HY, Bahadoran P, Ortonne JP. Reflectance confocal microscopy for pigmentary disorders. *Exp Dermatol* 2010;19:233-9)

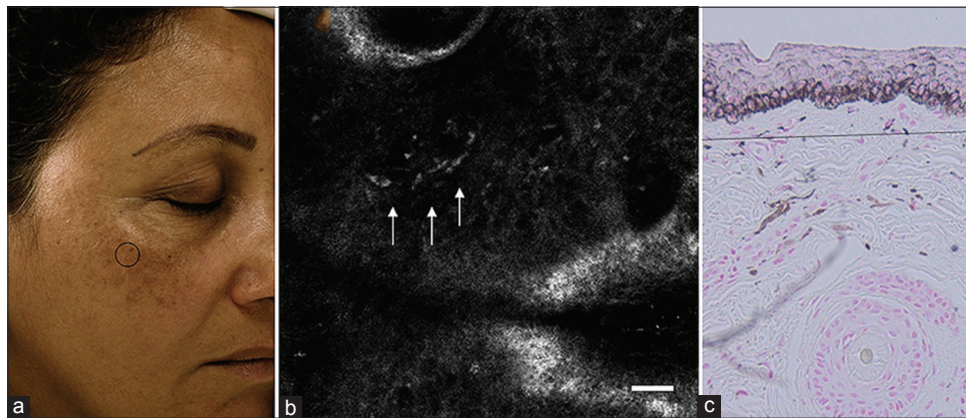


Figure 11: Confocal microscopy image of melasma showing dermal pigmentation: (a) Clinical picture of melasma. (b) Confocal microscopy showing bright plump cells in dermis. (c) Histopathology picture showing melanophages in the dermis (source acknowledged: Kang HY, Bahadoran P, Ortonne JP. Reflectance confocal microscopy for pigmentary disorders. *Exp Dermatol* 2010;19:233-9)

Table 2: Morphological criteria along with histological correlation seen in patients with melasma using RCM

Depth	RCM	Histology
Epidermis	Hyperrefractile cobblestone cells	Hyperpigmented basal keratinocytes
	Dendritic cells	Activated melanocytes
Dermis	Plump bright cells	Melanophages
	Ragged, less refractile lacy structures	Solar elastosis
	Dark round to tubular structures	Blood vessels

RCM: Reflectance confocal microscopy

among different regions. RCM offers an innovative way of classifying melasma by pigment changes. This can help us in refining the prognosis of melasma. It can also help in monitoring response to therapy.

THERAPEUTIC MODALITIES

Current role of HQ

HQ is a dihydric phenol that inhibits the conversion of dopa to melanin by inhibiting the tyrosinase enzyme. Other proposed

mechanisms of action include the inhibition of RNA and deoxyribonucleic acid synthesis and destruction of melanocytes.

HQ is considered the gold standard of treatment for melasma. It is used at a concentration of 2-4%. Its efficacy is enhanced when used in combination with other agents. These combinations include the Kligman formula (5% HQ, 0.1% tretinoin, and 0.1% dexamethasone), modified Kligman's formula (4% HQ, 0.05% tretinoin and 1% hydrocortisone acetate), Pathak's (2% HQ and 0.05-0.1% tretinoin) and Westerhof's formula (4.7% N-acetylcysteine, 2% HQ and 0.1% triamcinolone acetonide).^[27] Combination of microencapsulated HQ 4% with retinol 0.15% and antioxidants has also been tried in melasma with studies showing improvement in disease severity, pigmentation intensity, lesion area and colorimetry assessments.^[28]

In a randomized, split-face study, Monheit and Dreher compared the safety and efficacy of skin lightening cream (containing HQ 4% and four skin brightening actives) with a TCC (containing 4% HQ, 0.05% tretinoin, and 0.01% fluocinolone acetonide) in 20 Caucasian female patients with melasma.^[29] They found that after 4 weeks once daily treatment, the skin lightening

cream SLC was comparable in both efficacy and safety to the well-established TCC treatment for melasma. One-third of patients experienced local side effects in the form of erythema, peeling of skin and dryness with both the creams.

In a randomized, controlled study Arellano *et al.* compared the clinical efficacy and safety of two 6-month triple combination (containing HQ, fluocinolone acetonide and tretinoin) maintenance regimens in 242 Brazilian and Mexican patients with moderate-to-severe melasma.^[30] Global severity score, melasma area severity index (MASI), and quality of life questionnaire were used to assess the efficacy of treatment. After eight weeks of daily TCC application, subjects were randomized to receive TCC in a twice weekly or tapering regimen (3/week [1st month], 2/week [2nd month], 1/week [4th month]) for 6 months. They found that twice-weekly regimen showed better effectiveness on postponing relapse in patients with severe melasma. About 53% of patients were relapse-free after 6 months.

Tranexamic acid

Tranexamic Acid (TA) is trans-4-(aminomethyl) cyclohexane carboxylic acid, a lysine analog that is in use as an antifibrinolytic agent for over 30 years. It inhibits UV-induced plasmin activity in keratinocytes by preventing the binding of plasminogen to the keratinocytes. This results in less free arachidonic acid and a diminished ability to produce prostaglandins, and this decreases melanocyte tyrosinase activity. Zhang *et al.* demonstrated that TA can interfere with the catalytic reaction of tyrosinase and inhibit melanogenesis.^[31] In the treatment of melasma, TA can be used orally, topically or by intradermal microinjection. As a hemostatic, TA is prescribed in a dose of 1000 mg 3 times daily, whereas in the treatment of melasma, it is used in a dose of 250 mg twice daily.^[32]

In a study conducted by Wu *et al.*, 74 Chinese patients with melasma were treated with TA 250 mg twice daily for 6 months. The effects of treatment were evaluated by two physicians and by the patients based on the reduction in melasma size and improvement of pigmentation. The results were excellent in 10.8%, good in 54%, fair in 31.1% and poor in 4.1%. Side effects seen were gastrointestinal discomfort and hypomenorrhea. Recurrence was seen in 9.5% patients.^[33]

TA can also be used topically. In a recent double-blind randomized prospective study by Kanechorn *et al.*, 5% TA incorporated in a liposome gel formulation was used in 23 Asian women with bilateral epidermal melasma. The treatment was given for 12 weeks and compared with the vehicle in a split-face trial.^[34] 78.2% of patients showed a decrease in the melanin index. However, results were not significant as compared with vehicle. Another finding seen in this study was the erythema induced by topical TA.

In a study conducted by Lee *et al.* in 100 Korean women with melasma, TA was used intradermally (4 mg/ml) every week

for 12 weeks.^[35] The treatment caused a significant decrease in MASI score (13.22 vs. 9.02 at week 8 and vs. 7.57 at week 12, $P < 0.05$ for both) with minimal side effects.

The advantage with TA is its good safety profile. Furthermore, it is temperature stable, UV insensitive and does not get oxidized easily, hence it can be used in SLCs. More studies are needed to evaluate its anti-melasma potential.

4-n-Butylresorcinol

It is a derivative of resorcinol that inhibits tyrosinase and tyrosinase related protein, enzymes in the melanin biosynthetic pathway.^[36] Studies have shown good efficacy and safety with 4-n-butylresorcinol in patients with melasma.^[37]

Huh *et al.* conducted a randomized controlled split-face trial in 23 patients with melasma to evaluate the efficacy and safety of liposome-encapsulated 4-n-butylresorcinol 0.1% cream. They found a statistically significant reduction ($P < 0.043$) in the melanin index on the treatment side.^[38]

Oligopeptides

Oligopeptides have emerged as a new class of tyrosinase inhibitors with a good efficacy and cytotoxicity profile. In a study carried out by Ubeid *et al.*, the inhibitory activity of octapeptides and HQ was assessed using mushroom and human tyrosinase and melanin content through human primary melanocytes.^[39] It was seen that octapeptides P16-18 outperformed HQ in all categories tested. They showed minimal toxicity toward major human skin cell types.

Hantash and Jimenez carried out a split-face, double-blind, randomized and placebo controlled pilot study to evaluate the efficacy of an emulsion containing 0.01% decapeptide-12 (Lumixyl cream) in five patients with Fitzpatrick phototype IV and moderate, recalcitrant melasma.^[40] The preparation was used twice daily for 16 weeks. Ten- and five-point grading scales were used to assess the improvement in melasma and volunteer satisfaction. All patients showed statistically significant improvement with minimal side effects. The same authors evaluated the efficacy of the Lumixyl Topical Brightening system (0.01% oligopeptide cream, an antioxidant cleanser, 20% glycolic acid [GA] lotion and physical sunscreen) in patients with mild to moderate melasma and found improvement in all patients with no side effects.^[41]

Silymarin

Silymarin, is derived from the of milk thistle plant silybum marianum. It is a polypeptide flavonoid whose main component is silybin (silibinin) that has been found to have antioxidant properties. It reduces the harmful effects of UV radiation and also inhibits melanin production in a dose-dependent manner.

In a study performed by Altaei, 96 adults with melasma were divided into three groups receiving: (1) silymarin cream 0.1%, (2) silymarin cream 0.2%, and (3) placebo.^[42] The treatment was applied twice daily for 4 weeks. Response was assessed using lesion size, MASI score, physician global assessment and subjective assessment. All patients treated with silymarin cream showed excellent improvement and lesion size reduction from the first week. No adverse effects were seen.

Orchid extracts

Orchid extracts contain various flavonoids that act as antioxidant. Tadokoro *et al.* performed a study to assess the efficacy of a cosmetic formulation containing plant extracts including orchid extracts, compared to topical 3% vitamin C derivative in Japanese female patients with melasma.^[43] The efficacy was evaluated by colorimetric measurements and subjectively using a questionnaire. They found that after eight weeks of treatment, the plant extract preparation was significantly effective in improving the pigmentation and lesion size and was similar in efficacy to vitamin C derivative.

Table 3 highlights the botanical/plant extracts that are being used for the treatment of melasma.^[44]

NEWER CHEMICAL PEELS

A number of new peeling agents are being developed for the treatment of melasma out of which the following deserve mention.

Tretinoin peel

Tretinoin is widely used for the treatment of melasma as an over-the-counter lightening agent. Considering its efficacy, peeling with tretinoin may improve pigmentation in melasma. Faghihi *et al.* performed a randomized, double-blinded clinical trial to compare the efficacy of 1% tretinoin peel versus 70% GA peel in 63 female patients with bilateral melasma.^[45] One side of the face was treated with 70% GA and the opposite side with 1% tretinoin peel for four sessions at two week intervals. It was found that the efficacy of 1% tretinoin peel was similar to 70% GA. Postprocedure discomfort as expressed by the patients was significantly lower with 1% tretinoin.

Tretinoin can also be used as a peeling mask. Ghersetich *et al.* evaluated the efficacy of 10% tretinoin peeling mask using standardized digital photos, mexameter measurement and MASI evaluation in 20 female patients with Fitzpatrick skin type II-VI.^[46] They found moderate or marked improvement in all patients using these three parameters without any adverse events. At 10 weeks, the difference in the average MASI calculated at baseline and after 10 weeks was 2.9.

Obagi blue peel

It is composed of a fixed concentration of trichloroacetic acid (TCA) with a blue peel base. The latter contains glycerine,

saponins and blue color base that is non-ionic. It ensures a slow and uniform penetration of TCA by reducing the surface tension of TCA, water and glycerine.

In a split-face comparative study, 18 Korean women with moderate-to-severe melasma were treated with a single session of 1550-nm fractional photothermolysis (FP) on one cheek, and with a 15% TCA peel on the other cheek. MASI score and subjective patient-rated overall improvement were used to assess treatment efficacy at 4 and 12 weeks. Both treatment groups showed significant improvement of melasma after 4 weeks of therapy, but recurrence was observed at 12 weeks in the TCA peel group.^[47]

Another new peeling agent being used is the amino fruit acid peel. It is a potent antioxidant and also acts against photopigmentation. Ilknur *et al.* performed a single blind randomized right-left comparison study in patients with

Table 3: Botanical extracts being used for the treatment of melasma

Plant extract	Active component	Mechanism of action
Grape seed extract	Proanthocyanidin	Antioxidant
Orchid extract	Contain flavonoids	Antioxidant
<i>Aloe vera</i> extract	Aloin	Melanin aggregating effects
Pycnogenol	Procyanidins, polyphenolic monomers, cinnamic acid	Antioxidant
Marine algae extract		Inhibition of tyrosinase
Cinnamic acid		Inhibition of tyrosinase
Flavonoids		Antioxidant
Green tea extracts	Epigallocatechin-3-gallate	Antioxidant? inhibition of tyrosinase
Coffee berry	Chlorogenic acid	Antioxidant
	Proanthocyanidins	
Mulberry extract	Contain methanolic extracts	Inhibition of dopa oxidase activity of tyrosinase Superoxide scavenging activity
Soy	Phospholipids Essential fatty oils STI BBI	Inhibition of melanosome transfer by inhibiting PAR-2 activation
Licorice extract	Glabridin	Inhibits UVB induced pigmentation
Umbelliferone	7-hydroxycoumarin	Absorbs UV light, antioxidant
Boswellia	Boswellic acid	Anti-inflammatory, pro-apoptotic, mechanism not clear

BBI: Bowman-Birk protease inhibitor, STI: Soybean trypsin inhibitor, UV: Ultraviolet, UVB: Ultraviolet B

melasma using GA and amino fruit acid peels. Modified MASI score was performed at baseline and at 3 and 6 months. It decreased significantly in both groups; adverse effects were less with amino fruit acid peels.^[48]

Lasers for melasma

Various lasers that have been used for melasma include the following:^[49]

1. Green light: Flashlamp-pumped PDL (510 nm), frequency doubled Q switched neodymium: Yttrium aluminium garnet-532 nm (QS Nd: YAG)
2. Red light: Q switched ruby (694 nm), Q switched alexandrite (755 nm)
3. Near-infrared: QS Nd: YAG (1064 nm).

The concept of FP has been applied for the treatment of melasma as well. Fractional lasers have been used for the treatment of pigmented lesions, including melasma.

The overview of lasers being currently used for melasma is given in Table 4.

QS Nd:YAG is the most widely used laser for the treatment of melasma. The fluence used is less than 5 J/cm², spot size 6 mm, and frequency of 10 Hz. The number of treatment sessions varies from 5 to 10 at 1-week intervals.

Nowadays, technique called "laser toning" or "laser facial" has become increasingly popular for the treatment of melasma. This involves the use of a large spot size (6-8 mm), low fluence (1.6-3.5 J/cm²), multiple passed QS 1064 nm Nd: YAG laser performed every 1-2 weeks for several weeks.^[50] Although good efficacy has been seen with this technique, side effects have also been reported. These include hypopigmentation, depigmentation, rebound hyperpigmentation, physical urticaria, acneiform eruption, petechiae, and herpes simplex reactivation.

Combination of ablative and pigment selective lasers has also been tried in melasma. Ablative lasers remove the epidermis containing excess melanin; this is followed by the use of Q switched pigment selective laser that can target the dermal melanophages.

Angsuwarangsee and Polnikorn studied the efficacy of combined ultrapulse CO₂ laser and Q switched alexandrite laser (QSAL) alone in six patients with melasma. The site that received combination treatment showed significant response compared with the site that was treated with QSAL alone.^[51] However, side effects in the form of contact dermatitis and hyperpigmentation were observed in few patients, especially in those with dark skin. Hence, the use of combination of lasers should only be used for refractory melasma.

Table 4: Overview of lasers being currently used in the treatment of melasma

Lasers	Frequency Settings (nm)	Comments
QS Nd: YAG	1064 Fluence: <5 J/cm ² Spot size: 6 mm Frequency: 10 Hz	Minimal damage to epidermis Deeper penetration Targets dermal melanin Most widely used for melasma
QS ruby laser	694 Fluence: 2-7 J/cm ²	More selective for melanin Conflicting results in studies More studies needed
Er: YAG laser	2940 5-8 J/cm ²	Limited studies Higher incidence of PIH
PDL	585 7-10 J/cm ²	Targets vascular component of melasma Good results in combination with TCC Decreases relapses
Fractional laser	1550 2000-2500 MTZ/cm ² 10-15 mj/mb	Does not create open wound Complications less Recovery rate faster Greater depths of penetration Dermal melasma can be targeted Safe and comparable in efficacy and recurrence rate with TCC Should be used when TCC ineffective
IPL	500 filter initially Later higher	Effective for epidermal melasma Dermal/mixed melasma: Higher fluencies needed, risk of PIH in dark skin

PIH: Postinflammatory hyperpigmentation, TCC: Triple combination cream, IPL: Intense pulse light, PDL: Pulsed dye laser, QS Nd:YAG: Q switched neodymium: Yttrium aluminum garnet, Er: YAG: Erbium: Yttrium aluminum garnet

CONCLUSION

Melasma is a complex disorder and various factors are involved in its pathogenesis, identification of which will help us in developing better treatment options with more efficacy, less side effects and longer periods of remission. Newer compounds, especially botanical extracts and device-based treatments are being developed and add to the list of options available for treatment. However, more randomized controlled trials are needed to evaluate their efficacy compared to the well-known treatments available. There is also need to define the role of combination therapy and design protocols to provide optimum results and prevent relapses.

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