Melasma in brown skin: part 2

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The first part of this series has touched on the relevance of melasma in the brown skin populace, from the definition, epidemiology, clinical patterns, etiopathogenesis to diagnosis and clinical assessment. This second part aims to optimize medical management of melasma, with emphasis on the topical and oral options available for people of brown skin.

MELASMA OR NOT?

It is vital to know pertinent skin conditions that must be differentiated from melasma. Success in management lies on the correct diagnosis, first and foremost. Below is a summarized list of common differentials, as seen in the brown skin populace (Table 1).

DIAGNOSIS	AGE/SEX	HISTORY	DISTRIBUTION	COLOR/LESION
Post-inflammatory Hyperpigmentation (PIH)	Any age/any gender	History of trauma, inflammation	Site of previous trauma, inflammation	Epidermal PIH- tan to dark brown; Dermal PIH- gray blue to gray brown
Exogenous Ochronosis	uncommon; no known age or sex predilection	Prolonged use of hydroquinone, worsened by keratolytic agents and sun exposure	Photodistributed along sites of contact with causative agent; symmetrical distribution on the face, neck, upper back, or dorsum of extremities	Brown gray or blue black
Acquired bilateral nevus of Ota-like macules (ABNOM)/ Hori's nevus	Predominantly females; mean age about 45yrs for both sexes	Becomes bluer with age among females	Zygomatic area (most common with females), forehead (most common with males), temporal area, nasal radix, upper eyelid	Brown, blue, slate gray
Solar Lentigenes	Children and adults	History of sun exposure	Sun-exposed parts	Well defined Macules; color varies from different shades of brown
Drug-induced hyperpigmentation	No age nor sex predilection; 10%-20% of acquired hyperpigmentation	History of drug intake and sun exposure	Sun-exposed areas	Bluish gray
Actinic Lichen Planus	Mostly younger than 30 years, mean 14 years; no sex predilection	Mainly in tropical areas in photosensitive individuals	Face, dorsal aspect of hands, outer aspect of forearms	Atrophic- (+) hyperpigmentation Dyschromic- white angular papules and plaques on the neck and dorsum of hands Classic plaque like – violaceous papules Pigmented- resembles melasma in the face and neck

Erythema dyschromicum perstans (EDP)	More common in children and young adults; equal prevalence in both genders	Slowly progressive, (+/-) pruritus	Symmetric, seen on the trunk, arms, neck	Macules and patches, ashen gray to brown-blue
Reihl's hypermelanosis	More common in middle aged dark skinned women, Mexicans and Asians	Develops rapidly on sites previously in contact with sensitizers; associated with (+) patch tests to cosmetics' components	Face (pronounced on the forehead and temples), neck	Reticular brownish gray to black hyperpigmentation
Ephelids	Develops in early childhood, may regress with age	Genetics/ ancestry	Face, dorsal aspects of the arms, upper trunk	Small light to dark brown macules

IT IS MELASMA. HOW TO DEAL WITH IT?

Melasma, as elusive as it is, has yet to find an agent that will resolve its complexity. How to decrease the pigmentation may not be an enigma, but to get the result every dermatologist wishes to achieve and every melasma patient wishes to attain are the enigma. Hitting the principles of management (i.e. impeding activity of melanocytes, hindering synthesis of melanin, interrupting to eliminating melanin granules, and shielding from ultraviolet rays) known to us, may not be enough. Not only the patient's condition has to be taken in its wholeness, but the patient's personality, as well. Apart from taking into account the kind of melasma, the skin color and phototype the patient has, one must also consider prior treatments, expectations and adherence to therapy.

Success in melasma management cannot be totally claimed if the initial decrease or elimination of hyperpigmentation is not maintained. An updated practical 7-point strategy is offered by the authors (2) for melasma management (Table 2)

Table 2. 7-Point Strategy for INITIAL Melasma Management

Proper Patient evaluation
- Proper history-taking
- Medications used and being used for melasma
- Medications being taken, being used for conditions other than melasma
- Proper physical examination of the melasma, clinically and diagnostically

Honing Patient expectation
- Patient orientation on how melasma will be managed
- Consideration of patient preferences as it affects life style and adherence
- Agreement as to step-by-step melasma management between the patient and the physician to ensure cooperation from the former

Sun protection
- Broad-spectrum sunscreens with SPF ≥30 + UVA filters serve as the gold standard for ultraviolet light (UVL) protection
- photoprotection not only from UVB but from UVA and visible light as well is in place [3,4]
- Usage should be consistent with daily sunscreen application both indoors and outdoors.
- Though some systemic drugs have photoprotective qualities (Figure 1), the practice of taking oral medications for sun protection has not taken over the application of topical sunscreens.
- Sun avoidance practices must be encouraged [5]

Melanocyte activity Reduction
- Know and avoid the factors that triggers or aggravate melasma

Melanin synthesis Inhibition
- Use of hypopigmenting agents that act on melanin synthesis on different stages (Figure 2)
- These agents may either interfere with tyrosinase transcription or glycosylation, inhibit tyrosinase by different modalities or reduce by-products and post-transcriptional control [6]

Melanin removal
- Certain procedural techniques aim at removing melanin, such as chemical exfoliation and microdermabrasion can be used as adjunct to melasma treatment
- Variable levels of success

Melanin granules disruption
- Lasers, light therapy and fractional resurfacing, of late, are being used and tried, in conjunction with topical depigmenting agents, to decrease in melasma pigmentation
- Variable levels of success

Figure 1. Systemic Drugs with photoprotective qualities (2)

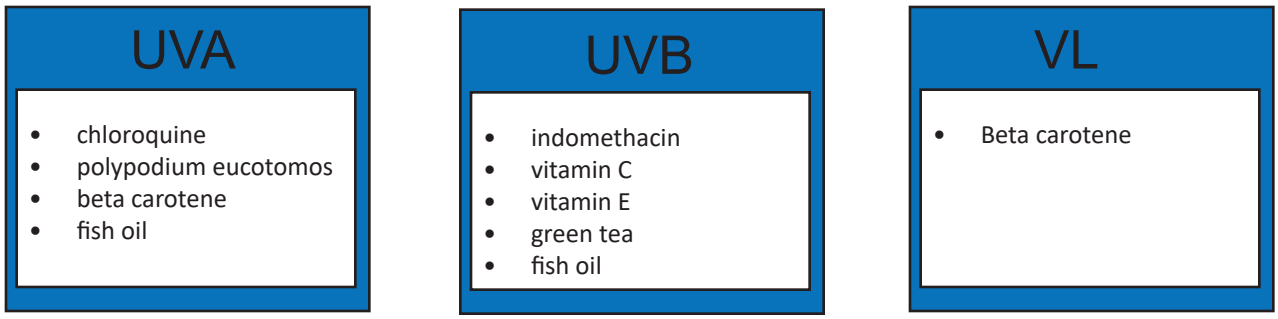
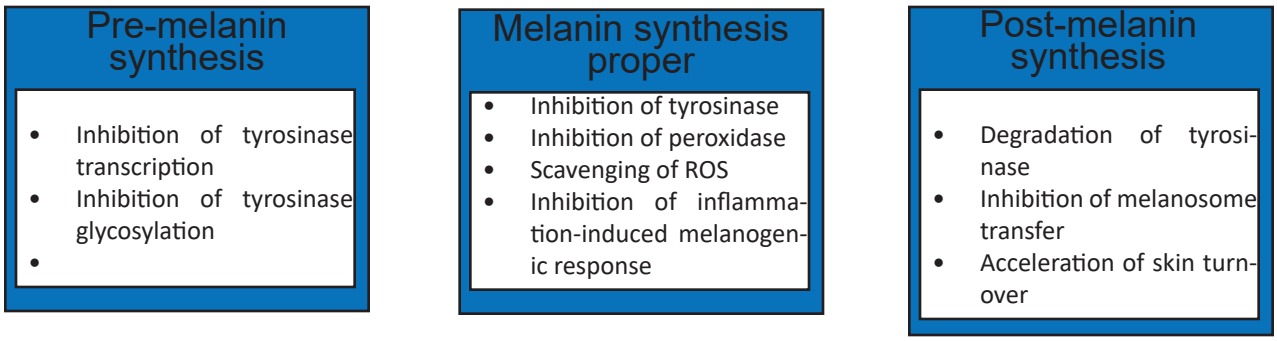


Figure 2. Different Levels of Melanin Synthesis Inhibition



TOPICAL MEDICATIONS – ALWAYS THE FIRST CHOICE

As it stands today, topical therapies are still the standard of treatment. Proofs to this are the multiple studies carried out and are being carried out to find agents that will decrease the degree of hyperpigmentation of melasma and that can maintain this improvement for a long period of time with the least of adverse reactions. Various topical agents either aim at obstructing melanin synthesis prior to, during or after the process and they are most effective for melasma affecting the epidermal layer (Table 3)

Table 3. Hypopigmenting Agents Acting at Different Levels of Melanin Synthesis [6,7]

PRE-MELANIN SYNTHESIS	
Tyrosinase Transcription Inhibitors	Tretinoin
Tyrosinase Glycosylation Inhibitors	Calcium-D-pantetheine-S-sulfonate (PaSSO3Ca), N-acetyl glucosamine (NAG)
MELANIN SYNTHESIS PROPER	
Tyrosinase Inhibitors	Hydroquinone (HQ), Azelaic Acid (AA), Kojic Acid (KA) 4-OH-anisole (Mequinol), 4-n-butylresorcinol, Licorice Extract, Rucinol, 4-S-cystaminylphenol (4-S-CAP), Acerola (Malphigia emarginata), Aloesin, Arbutin, Bearberry, Cinnamic Acid, Ellagic Acid, Macelignan, Methyl Gentisate (MG), Paper Mulberry extract, Resveratrol, Oxyresveratrol, Sophora extract
Peroxidase Inhibitors	Topical indomethacin, Green Tea, Methimazole
ROS Scavengers/ Reduction Agents	Ascorbic Acid and palmitate Mg-L-ascorbyl-2-PO4 (VC-PMG), Thioctic Acid, Alpha-tocopherol and ferulate, Pycnogenol, Hydrocoumarins, Tetrahydrocurcumin, Glutathione
Inflammation-Induced Melanogenic Response Inhibitors	Topical corticosteroids, Tranexamic Acid (TA), M. chamomilla, Glabridin
POST-MELANIN SYNTHESIS	
Tyrosinase Degradation	Linoleic Acid, Alpha-Linolenic Acid
Melanosome Transfer Inhibitors	Niacinamide, Octadecene Dioic Acid (ODA), Soybean extract, Serine Protease Inhibitors, Lectins and Neoglycoproteins
Skin Turnover Accelerators	Retinoic Acid (Tretinoin), Lactic Acid (LA), Liquiritin, Linoleic Acid, Glycolic Acid, Mandelic Acid, Lactobionic Acid

Several of these agents (i.e. hydroquinone, azelaic acid, kojic acid, retinoids) have been established as having veritable results in improving the state of one's melasma, whether alone, or in combination with other agents. (Table 4)

Table 4. Known Topical Agents used for Melasma

Hypopigmenting Agent	Mechanism of Action
HYDROQUINONE (HQ) 2%-4%	competitively ▼ tyrosinase
Comments *deemed as the gold standard anti-melasma agent *reported to be significantly superior to 5% ascorbic acid [8] *4% HQ resulted in higher efficacy than kojic acid 0.75% [9] and 4% niacinamide [10] but the difference was not statistically significant [11] *triple combination preparations showed superior efficacy than 4% HQ used alone [12-14] *its lightening effect in epidermal melasma seen within 8-12 weeks of usage [15,16]; maximum recommended duration of use is 16 weeks [11] *Adverse events reporting was lower than expected; incidence of exogenous ochronosis was not reported with 4% HQ even if used more than 3 months [11] *withdrawn in some countries [17], considering the risks brought about by prolonged incorrect usage * 4% HQ still being used in Asia, and still recommended for use in melasma among dark-skinned populace [11]	
AZELAIC ACID (AA) 20%	reversibly ▼ tyrosinase
Comments *combined with glycolic acid peel, MASI score decreased significantly [18] *superior to HQ 2% [19]; variable efficacy when compared to HQ 4% [19, 20] *combination with Nd:YAG laser yielded better results than laser alone in Indian patients with melasma [21] *recommended as monotherapy in melasma and as an adjuvant to Nd:YAG laser therapy in melasma [11]	
KOJIC ACID (KA) 1%-4%	deters catecholate action of tyrosinase, scavenges ROS
Comments *more stable than HQ but its ability to lighten is lesser compared to HQ [22] *Combination with 2% HQ was noted to most effective compared to 1% KA alone, KA with 0.1% betamethasone and combination products [23] *2% KA recommended in melasma; may be used with 2% HQ for better results [11]	
RETINOIDS (i.e. tretinoin 0.05%-0.1%, isotretinoin 0.05% and adapalene 0.1%)	▲epidermopoiesis downregulation of tyrosinase
Comments *act at the stage of melanosome transfer, reducing this transport hence interfering with tyrosinase transcription [24]. *Effect on melasma, however, varies from mild to moderate. [11, 25-27]	

Among the vitamins, C, E and niacinamide have been utilized in the treatment of melasma. Many topical depigmenting products in the market contain these vitamins, for the reason of its mode of actions adding to the effectivity of the products. (Table 5)

Table 5. Topical Vitamins used in Melasma Treatment

Hypopigmenting Agent	Mechanism of Action
VITAMIN C	chelates copper; antioxidant
Comments *5% L-ascorbic acid is inferior to 4% HQ [8] *magnesium 5% L-ascorbyl-2-phosphate found effective in reducing pigmentation of melasma [28] *iontophoresis boosts its permeation into the skin [29,30] *significant decrease in pigmentation when used with TCA 20% peel [31]	
VITAMIN E	Scavenges ROS; UVB absorption
Comments *(α-tocopherol, α-tocopheryl) together with vitamin C, synergistic action is produced in safeguarding against ultraviolet induced erythema [32,33].	
NIACINAMIDE	▼transfer of melanosome
Comments *good to excellent reduction in pigmentation in 44% of nicotinamide-treated areas compared to 55% with HQ4% [10]	

Other depigmenting agents have also been used for the topical treatment of melasma, with promising results. (Table 6)

Table 6. Other Topical Hypopigmenting Agents

Hypopigmenting Agent	Mechanism of Action
GLYCOLIC ACID (GA) 5%-10%	stratum corneum thinning
Comments *using 10% glycolic acid cream in addition to 4%HQ was inferior to HQ% monotherapy [34] *very few studies on the topical formulation, most were on the peel formulations [11]	
TOPICAL INDOMETHACIN 8%	Inhibits peroxidase
Comments: *shown to be effective for epidermal melasma especially on the upper lip [35] *applied twice daily for 12 weeks showed significant difference on mexameter readings between the treatment and placebo groups among Filipino women with epidermal and mixed melasma [36]	
DIOIC ACID 1%	Inhibits melanosome transfer
Comments Compared to 2% HQ, similar in efficacy in improvement of pigmentation of melasma [37]	
TRANEXAMIC ACID (TA)	inhibits UV-induced plasmin activity in keratinocytes
Comments 5% TA in liposomal form had lightening effects comparable to HQ [38] 3% TA in solution compared to dexamethasone 0.01%/HQ3% showed comparable effects [39]	
LIGNIN PEROXIDASE	melanin oxidation
Comments Purified active enzyme derived from fermented fungus Phanerochaete chrysosporium; Molecular structure similar to melanin [40] *compared with 2% HQ, twice daily application of lignin peroxidase cream on melasma of Asian patients revealed a more rapid and observable skin-lightening effect as early as day 7 [41] * report of equal efficacy to HQ4% in pigment lightening but superior to HQ4% in skin texture and roughness improvement [42]	
FLUTAMIDE 1%	Anti-androgenic; modify alpha MSH or cAMP elevating agents
Comments *shown to be as effective as 4% HQ based on mexameter assessment but more efficient than 4%HQ based on MASI improvement and patient satisfaction [43]	
OLIGOPEPTIDES	▼ tyrosinase
Comments Shown to be effective for cases of recalcitrant melasma [44]	

TRIPLE COMBINATION (TC)

Triple combination creams contain a hydroquinone, a steroid and a tretinoin in various formulations. These agents when combined produce a synergism that exceeds the the efficacy of a single substance. While providing its own lightening effect, tretinoin enhances the penetration of hydroquinone. The steroid decreases the irritation caused by hydroquinone and the retinoid, in addition to inhibiting melanin synthesis. Tretinoin further ameliorates the risk of skin atrophy associated with steroid use [45].

The earliest and most popular triple combination agent is Kligman's cream, consisting of hydroquinone 5%, tretinoin 0.1%, and dexamethasone 0.1%. While proven effective, this combination was found to have a high irritancy. Over a decade now, a TC containing fluocinolone acetonide 0.01%, HQ4% and tretinoin 0.05% has been used for melasma with proven superiority over HQ monotherapy and other combination formulations (Table 7)

Table 7. Triple Combination Cream

FLUOCINOLONE ACETONIDE (FA) 0.01% / HYDROQUINONE (HQ) 4% / TRETINOIN (RA) 0.05%	
STUDIES	**COMMENTS**
*strongly inhibits the production of melanin without destroying melanocytes [46,47] *Despite the inclusion of a topical steroid in this combination, only one patient in a trial group of 641 had skin atrophy as an adverse effect [46]	*better tolerated with significant efficacy in improving melasma [50,51] *Currently considered the best agents to address melasma [24, 46, 47, 52]

*sequential use with intense pulse light showed higher efficacy in decreasing pigmentation of moderate to severe melasma [48] *superior to 4% HQ monotherapy [12,19] and dual combinations (RA+HQ, RA+FA, and HQ+FA) [19, 49] *equal efficacy to a combination therapy of sequentially increasing glycolic acid (GA) peel from 20%-70% together with azelaic acid 20% cream [19] *GA peel can be added to TC to increase the efficacy [11]	*preferred over other steroid-containing combination fixed dose therapies (mometasone 0.1%+2%HQ+0.025%RA and 5%HQ + 0.1%dexamethasone+0.1% retinoic acid) [11] *duration of usage varies from 8-12 weeks [11] *long-term use as maintenance not recommended among the Indian population, but if used up to 6 months, 2x weekly application under supervision [11] *preferable to all other monotherapy and combination topical therapy when potency of the therapy is the priority [11]

As the search for an ideal depigmenting agent goes on, safety has always been an issue, aside from efficacy. This has led to discoveries of many "other" substances of botanical nature that share the known effective mechanism of actions of the known chemical depigmenting agents. Studies may not abound. However, there is always this promising result of producing a decrease in melasma's pigmentary disturbance. Botanicals are meant to be used for epidermal type of melasma and can be integrated into standard regimens [53]. Hence, botanicals for melasma exist, and serve as an option for patients and clinicians. (Table 8)

Table 8 Botanicals for Melasma Treatment

Botanicals	Derivation/Origin
ALOESIN - ▼ tyrosinase	Aloe vera (succulent perennial herb)
Comments: comparing its action alone and in combination with arbutin, there was a dose dependent suppression in the pigmentation with aloesin alone and a synergism was shown between arbutin and aloesin applications [54]	
ARBUTIN 3%-7% - ▼ tyrosinase	Bearberry (evergreen shrub), California buckeye
Comments *glycosylated form of HQ, considered safer alternative for long term and regular use due to its comparable efficacy and lesser adverse reactions [55, 56] *in conjunction with Q-switched Nd:YAG laser, favorable results were obtained [57]	
ELLAGIC ACID 1%	Green tea, strawberry, grapes, cherries, walnuts
Comments * compared with arbutin 1%, both showed efficacy in lightening melasma [58]	
LICORICE (Glycyrrhiza glabra) ▼ tyrosinase and scavenger of ROS (glabridin); Dispersion of melanin (liquiritin)	Camellia sinensis
in controlled clinical trials, both extracts were either used as is or in compounds where it is one of the ingredients comparing 4% liquiritin, 2% liquiritin and HQ, the former was shown to be significantly more effective [59] Glabridin was shown to be more efficacious than HQ [60]	
MULBERRY 75% extract ▼ tyrosinase; antioxidant	Perennial herb
Comments *compared to placebo, it showed significant improvement in MASI score [61]	
ORCHIDS ROS scavenger	Morus alba, perennial shrub/tree
Comments Orchid extract cream compared with Vita C 3% cream showed equivalent capacity to lighten melasma among Japanese women [62]	
RUMEX OCCIDENTALIS ▼ tyrosinase	Perennial herbs
Comments 3% extract in cream formulation showed depigmenting capacity equal to 4% HQ [63]	
SILYMARIN	Perennial herb
Comments significant pigment improvement and lesion size reduction of melasma [64]	
TETRAHYDROCURCUMIN 0.25% Scavenger of ROS	Milk Thistle Silybum mariamun
Comments: Compared to HQ 4%, capacity to decrease pigmentation shown to be comparable among Filipino women with epidermal melasma [65]	

ORAL MEDICATIONS – DO THEY HAVE A NICHE IN THE ARMAMENTARIUM FOR MELASMA?

To give or not to give: this is the dilemma of the clinician when confronted with a melasma case.
To take or not to take: this is the question of the patient to the clinician.

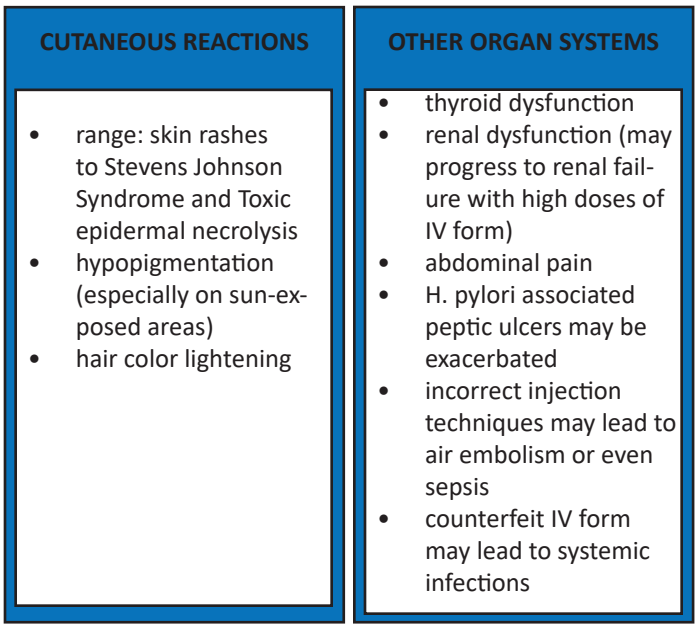
The systemic agents that may be relevant in the management of melasma among the brown skin populace is listed in the table below. (Table 9)

Table 8 Oral Depigmenting Agents

Depigmenting Agents	Mechanism of Action	Adverse Reaction
TRANEXAMIC ACID (TA)	>Synthetic derivative of lysine with antiplasmin activity >competitively ⇓tyrosinase >⇓ alpha-MSH >decreased epidermal pigmentation and melasma-associated dermal changes (i.e. number of vessels and mast cells) [66]	Few and generally mild , reversible (nausea, diarrhea, abdominal pain, rashes, alopecia, drowsiness, menstrual irregularities) [67] significant adverse event reported was a case of deep vein thrombosis in a patient who had existing protein S deficiency [68]
Comments: >taken daily at 500-750mg for 8-12 weeks, in conjunction with topical hypopigmenting cream or laser treatment, involving melasma patients showed a significant greater improvement of mMASI or MASI scores in the combination treatment group [69-71] revealing a pertinent role in decreasing hyperpigmentation of melasma >improvement noticed as early as 4 weeks [66, 72-74] >Sustained lightening of melasma pigmentation when oral TXA was added to topical HQ [71] >TXA added to either triple combination cream , IPL or laser significantly enhanced efficacy of melasma management [69, 70, 75] >Standard dose of TA – 500mg/day single or divided doses, taken for 2-6 months [67] >Maximum safe duration of treatment and minimum effective dosage are yet unknown [11] >Relapse rates varied from 9-27% [68, 72, 76, 77] > Screen for thromboembolism risk prior to initiation of treatment [68]; not for patients with coagulation disorders, pregnant or lactating [72] >the most useful systemic anti-melasma agent with the most number of studies proving its safety and efficacy [67]		
POLYPODIUM LEUCOTOMOS EXTRACT (PLE) - Fern from Polypodiaceae family	>Potent antioxidant, photo-immunoprotective against UVA and UVB [78] >inhibits metalloproteinase [79, 80]	No significant AE reported to date even with a maximum of 1200 mg/day for 90 days [79-81]
*Adjuvant for photo-aggravated conditions [82, 83,79] *Administered at daily doses from 120-1080mg [84] *240mg 2x a day for 60 days claimed to be safe and effective for reducing damaging effects of UVR [80] *Clinically efficient as an adjunct to sunscreen for the treatment of melasma in 54 female subjects who received PLE daily for 12 weeks. [79, 85] *At 480mg 2x daily, Effective adjuvant in combination with 4%HQ and sunscreen SPF 50 among Asian patients with melasma, with a a statistically significant reduction of mMASI and MelasQoL scores in the PLE group compared to those of the placebo group and significant improvement in mMASI scores from the first month of treatment [86]		
PYCNOGENOL- Pinus pinaster bark extract **PROCYANIDIN- Main active component** **Catechins, epicatechins, ferrulic acid- minor components [87]**	Antioxidant Anti-inflammatory ROS scavenger Reduces UV-induced erythema	Metallic taste No serious adverse reactions reported [67]
*procyanidin's antioxidant effect several times stronger than Vitamins C and E; it has the capacity to recycle vitamin C and regenerate vitamin E [88] *Procyanidin with vitamins A, C and E, administered at 48mg daily for 8 weeks to 56 Filipino female melasma patients, MASI scores taken on the malar regions showed a significant reduction in pigmentation [89] *80% of Chinese patients taking pycnogenol at 25mg 3x a day for 1 month, there was a significant reduction in pigment intensity of the melasma [88]		

GLUTATHIONE – thiol peptide	Direct inhibition of tyrosinase by binding with copper containing active sites Indirect inhibition of tyrosinase through its antioxidant effect and eventual scavenging of ROS [90]	Seen more with intravenous glutathione [67] (Figure 3)
*With oxidative stress playing a role in melasma, its antioxidative effect helps decrease pigmentation [91, 92] *20-40mg/kg/day in two divided doses *12 weeks duration is recommended to see results by most studies *500mg daily intake for 4 weeks showed significant reduction in melanin index among 60 Thai patients [93]; similar results with 500mg daily lozenge, melted in the mouth, for 8 weeks, among 30 Filipino patients [94]; both forms were well tolerated *Intravenous route not recommended because of safety concerns [67]		
CAROTENOID- naturally occurring pigments synthesized by plants (i.e. tomatoes), algae, and photosynthetic bacteria [81]	ROS scavenger [95]	Skin color change, especially if taken at high doses for long periods of time; reversible when discontinued [81]
*Forty four melasma patients, in a randomized controlled study, given 800MG DAILY for 84 days showed a greater reduction in the the erythema index and mMASI score [96]		
MELATONIN-pineal gland hormone	Antioxidant ROS Scavenger Inhibit alpha melanocyte-stimulating hormone MSH and reverse alpha MSH induced darkening [81]	Mild, transient drowsiness [97]
*MASI scores showed significant reduction in the treatment group of 36 melasma patients using melatonin 3mg daily for 90 days together with topical melatonin [97]		

Figure 3. Reported adverse effects of systemic glutathione, seen more with intravenous than oral formulations [90]



To give or not to give: consider the following:

- the benefits the systemic agents will give to the melasma patient
- the efficacy and safety of the drug must have evidence-based studies
- no contraindication on the patient's health condition or maintenance medications
- the patient is inquiring about systemic medications / amenable to taking the drug

CONCLUSION:

INITIAL SUCCESS IN TREATING MELASMA, HOW TO MAINTAIN?

This is the challenging phase each clinician has to face. Knowing the nature of melasma, initial success in lightening the pigmentation is not the end, but only the beginning. Going back to the 7-point strategy at the start of this article, we have modified another 7-point strategy on maintenance phase of melasma management.

Table 8 7-Point Strategy for Melasma - Maintenance Phase

Patient Follow up • Photographs at baseline and on follow-ups will aid tremendously in the assessment of improvement • Importance of Follow-up consultations must be emphasized and must not be missed • Review of adverse reactions must be recorded, if any	Melanin synthesis Inhibition • Not all agents that targeted melanin synthesis, used successfully in the initial part of therapy, may be continued for a very long time • Though tapering is advisable, there is no ideal tapering regimen; this will largely depend on the clinician's experience and expertise • Arellano et al [98] proposed several tapering regimens when using TC cream: twice a week application prevented severe melasma recurrence for a longer period of time; tapering monthly at 3x a week first then 2x a week then 1x a week for a total of 4 months was better for moderate melasma
Patient expectation • Expectations must be revisited and assessed if reached	Melanin removal and Melanin granules disruption • chemical exfoliation and microdermabrasion, as an adjunct in the management of melasma, with variable levels of success, are not advisable to be done in the maintenance phase
Sun protection • Avoidance of sun exposure must always be reiterated • Use of broad-spectrum sunscreen must be constant even if lightening or elimination of melasma has been achieved • Seek the shade, cover up with clothing, up the umbrella and other shading devices, less use of overhead lights and preference for indirect or shaded lamps with double envelope compact fluorescent lamps (CFLs) and light-emitting diode (LED) bulbs, use wide-screen computer monitors, avoid heat-emanating appliances and surfaces [5]	Melanin granules disruption • Lasers, light therapy and fractional resurfacing, also with variable levels of success, are not advisable in the maintenance phase
Melanocyte activity Reduction • Constant avoidance of the trigger/aggravating factors of melasma must be reiterated	

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