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Treatment of Melasma (Kalaf) Through Unani Medicine: A Mechanistic Approach

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Abstract

Melasma is a hyperpigmented skin disorder that predominantly affects women between 20 and 40 years of age. Beyond its physical manifestation, the condition exerts a significant psychological and social burden on patients. Treatment remains challenging, especially in individuals with darker skin types. Conventional therapies including chemical peels, topical depigmenting agents, ultraviolet (UV) protection, and light- or laser-based therapies generally provide short-term improvement but rarely achieve sustained remission. Recurrence is common, and many treatments are associated with side effects such as erythema, peeling, burning, or stinging sensations, particularly with long-term use. Traditional approaches such as sunscreen, bleaching agents, topical corticosteroids, and tretinoin are more effective in epidermal melasma but offer limited efficacy for other forms. Consequently, there is a growing need for safe, effective, and sustainable therapeutic options. Unani medicine has long been recognized for its efficacy in treating dermatological conditions without adverse effects. In classical Unani literature, eminent physicians including Abu al-Qasim al-Zahrawi, Zakariya al-Razi, Ibn Sina, and Muhammad ibn Tabari have documented numerous single and compound formulations for hyperpigmentation disorders. This review highlights the therapeutic potential of Unani medicines in the management of melasma (Kalaf).

Keywords: Melasma; Kalaf; Hyperpigmentation; Unani Medicine; Herbal Drugs

Introduction

Melasma is an acquired, chronic pigmentary disorder that predominantly affects women. Also referred to as chloasma or the "mask of pregnancy," the condition has a high prevalence among pregnant women [1]. Clinically, it is characterized by symmetrical light-brown to bluish-grey macules and patches with irregular, serrated, or well-defined borders. These lesions most commonly appear on sun-exposed areas, particularly the face (forehead, cheeks, temples, upper lip, chin, and nose), but may also affect the neck and, less frequently, the forearms. Seasonal exacerbation during summer is a hallmark feature of the disease.

Although melasma is benign, its psychosocial implications are profound. The conspicuous involvement of facial skin often leads to impaired self-image, reduced self-esteem, and emotional distress, significantly diminishing quality of life. Many patients report feelings of shame, loss of confidence, social withdrawal, and reduced work productivity as a result of the condition [2,3].

Epidemiological studies indicate a strong female predominance, with a male-to-female ratio of approximately 1:10. The majority of cases occur in the third and fourth decades of life, although lesions may also develop in later years 14% of patients present after the age of 40, and 6% after 50 years [4].

Unani Concept of Kalaf (Melasma)

In the Unani system of medicine, melasma is referred to as Kalaf. It is described as a hyperpigmentary condition resulting from the predominance of Ghalba-e-Sawda (black bile) in the blood or skin. According to classical Unani scholars, thick melancholic vapours (Ghaleez Sawdawi Bukharat) originating from the stomach or liver ascend to the face, where they become trapped beneath the skin, giving rise to dark patches.

Several internal and external factors may aggravate the production of black bile, including psychological disturbances (stress, anger, grief, anxiety) and dietary or lifestyle triggers such as excessive consumption of spicy foods, alcohol, and smoking [5].

Line of Treatment in Unani Medicine [6,7]

The management of Kalaf is based on two fundamental therapeutic principles:

1. Istifragh (Evacuation) of the morbid humor through Munzij-Mus'hil (concoctive and purgative) drugs.

2. Local application of agents possessing Jāli (detergent), Muhallil (resolvent), and Laze' (counter-irritant) properties.

Important Single Drugs in the Management of Kalaf

Maghz-e-Badam Talkh (Prunus amygdalus – bitter almond)

Rich in antioxidants, fatty acids, proteins, vitamins, and minerals, bitter almond exerts a nutritive (Mughazzi) effect. Its high protein and vitamin E content help lighten hyperpigmented lesions while nourishing and enhancing skin complexion [5,8].

Āb-e-Lemūn (Citrus lemon – lemon juice)

Containing polyphenols, citric acid, vitamin C, terpenes, and tannins, lemon juice assists in reducing pigmentation. Its citric acid acts as a Jāli (detergent), exfoliating the superficial skin layers and improving complexion [9–11].

Kāf-e-Dariya (Cuttlefish bone)

Composed largely of chitin, a natural polymer, cuttlefish bone exhibits Qāshir (exfoliative) properties. It is frequently used in cosmetic preparations for skin renewal and lightening [7].

Unani Formulation

One notable formulation is Tila-e-Kalaf, which contains ingredients such as lentil (Lens culinaris), bitter almond (Prunus amygdalus), and fig (Ficus carica). Clinical studies indicate that this formulation demonstrates significant efficacy in melasma management, with outcomes comparable to conventional therapies such as hydroquinone [12].

Epidemiology

The prevalence of melasma varies widely across populations, ranging from 1.5% to 33.3%. It affects approximately 50–70% of pregnant women, highlighting its strong association with hormonal changes. Although less common, men can also develop melasma. In an Indian study on the etiology and histology of male melasma, Sarkar et al. reported that men account for 20.5–25.83% of cases, with the malar pattern being more common than the mandibular or centrofacial patterns [13].

Melasma may begin as early as adolescence and is thought to be mediated by hormonal factors. It can affect individuals of all skin types, but it is significantly more prevalent in darker skin phototypes (Fitzpatrick IV–VI), especially among those with high ultraviolet (UV) exposure. [14] In Southeast Asia, melasma represents 0.25–4% of dermatology consultations and is the most frequent pigmentary disorder among Indians. The condition is most commonly observed in the 20–40 year age group, with a clear female predominance [15–17].

Etiopathogenesis

The precise cause of melasma remains uncertain, but multiple factors have been implicated, including genetic predisposition, UV radiation, pregnancy, estrogen and progesterone therapy, thyroid dysfunction, cosmetics, and certain medications (e.g., phototoxic and anti-seizure drugs).

Melanocyte Biology

UV radiation stimulates melanocytes by upregulating melanocortin-1 receptors (MC1-R), increasing the binding of melanocyte-stimulating hormone (MSH) and enhancing melanin production [18].

Proopiomelanocortin (POMC), cleaved into α-MSH and ACTH in response to UV exposure, [19] binds to MC1-R and activates protein kinase A (PKA). PKA phosphorylates the cAMP response element-binding protein (CREB), which upregulates microphthalmia-

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associated transcription factor (MITF)—a central regulator of melanogenesis. MITF promotes expression of tyrosinase, a key enzyme in melanin synthesis [20].

UV radiation also triggers the production of 1,2-diacylglycerols (DAGs) via phospholipase C and D (PLC/PLD) pathways. DAGs activate tyrosine-dependent pathways that further enhance melanogenesis [21].

Role of P53

The tumor suppressor protein p53 is another key regulator of UV-induced pigmentation. Following UVB-induced DNA damage in keratinocytes, p53 upregulates POMC expression, increasing α-MSH release and subsequent melanogenesis. Additionally, p53 stimulates hepatocyte nuclear factor-1α (HNF-1α), which enhances tyrosinase transcription, thereby promoting melanin synthesis even in the absence of keratinocyte signaling. [22,23]

Solar Elastosis And Photoaging

Solar elastosis refers to the accumulation of abnormal elastic tissue in the dermis, primarily resulting from chronic sun exposure and photoaging. In melasma, solar elastosis is frequently observed, with lesional skin demonstrating thicker, more curled, and fragmented elastic fibers compared to normal skin. [24] Ultraviolet B (UVB) radiation plays a pivotal role by stimulating keratinocytes to enhance melanin production through the release of growth factors, cytokines, and mediators such as inducible nitric oxide synthase (iNOS). Additionally, UVB exposure increases plasmin activity, which elevates arachidonic acid and α-melanocyte–stimulating hormone (α-MSH) levels, thereby amplifying melanogenesis and contributing to hyperpigmentation. Beyond UVB, visible light has also been implicated in melasma, particularly among individuals with darker skin phototypes (Fitzpatrick IV–VI). This occurs through activation of the opsin-3 photoreceptor, which may further drive the condition's pathogenesis [1,25,26].

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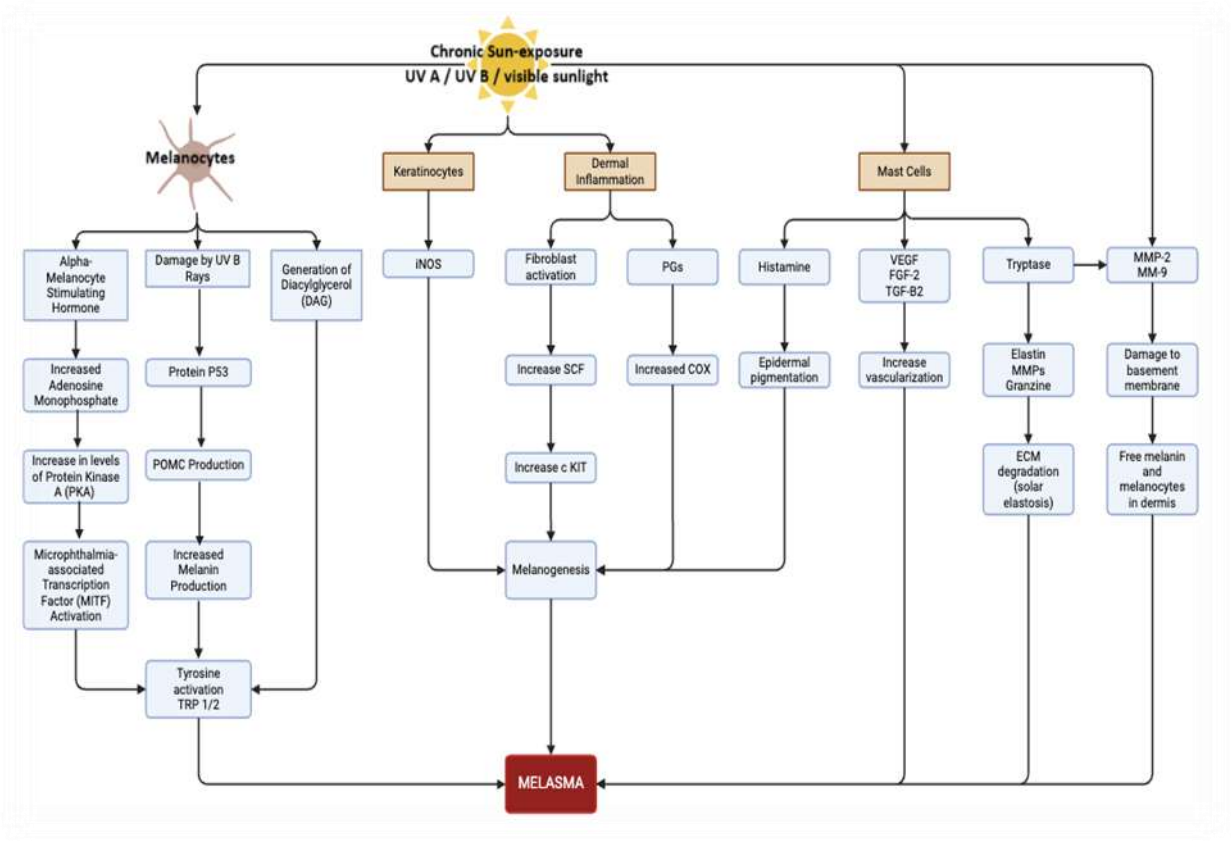
Figure 1: Etiopathogenesis of Melasma



Mast Cells and Neovascularization

Melasma-affected skin shows a significantly higher density of mast cells compared to unaffected skin. Upon UV exposure, these mast cells release histamine, [23,27] which binds to H2 receptors and activates the tyrosinase pathway, thereby promoting melanogenesis. This establishes a link between UV-induced inflammation and subsequent hyperpigmentation. In addition, UV radiation stimulates mast cell tryptase production, which activates matrix metalloproteinases (MMPs), leading to type IV collagen degradation and basement membrane disruption. Granzyme B released from mast cells further damages the extracellular matrix (ECM). Tryptase also contributes to solar elastosis by stimulating elastin production. Beyond pigmentary changes, mast cells facilitate hypervascularization in melasma lesions through the release of angiogenic factors such as vascular endothelial growth factor (VEGF), fibroblast growth factor-2 (FGF-2), and transforming growth factor-beta (TGF-β). These factors collectively increase vessel size, density, and dilation, underscoring mast cells as potential therapeutic targets in melasma management [24].

Basement Membrane Damage

Basement membrane abnormalities are pivotal in melasma pathophysiology. UV radiation activates MMP2 and MMP9, which degrade type IV and VI collagen, compromising the structural integrity of the basement membrane. Moreover, cadherin 11—found to be upregulated in melasma—promotes melanogenesis by enhancing fibroblast–melanocyte interactions and increasing MMP1 and MMP2 expression, furthering collagen degradation and elastosis. Damage to the basement membrane also facilitates the migration of melanocytes and melanin into the dermis, contributing to the chronicity and recurrence of melasma. Therapeutic strategies aimed at restoring basement membrane integrity may therefore reduce relapse rates [24,28].

Dermal Inflammation

Chronic UV exposure induces dermal inflammation, which activates fibroblasts to secrete stem cell factor

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(SCF). SCF binds to its receptor, c-kit, initiating the tyrosine kinase signaling cascade that enhances melanogenesis. Inflammatory mediators such as COX-2 and prostaglandins are also elevated in melasma lesions, further stimulating melanocyte activity and sustaining pigmentation [29–31].

Hormonal Influence

Hormonal factors, particularly estrogen, play a central role in melasma pathogenesis. This explains the condition's higher prevalence among women of reproductive age, oral contraceptive users, and pregnant women. Elevated expression of estrogen and progesterone receptors in melasma lesions activates tyrosinase and melanogenesis-related pathways. Estrogen also increases melanocyte sensitivity and promotes melanosome transfer, a process partly mediated by PDZK1. Furthermore, female hormones upregulate the transcription of melanogenesis-associated genes, making estrogen a critical therapeutic target for melasma intervention [32,33].

Unani Perspective on Etiopathogenesis

Classical Unani scholars described the causative factors of melasma (Kālo'n or Bhuur) with remarkable insight. They attributed its occurrence to prolonged exposure to excessive abnormal external heat, Dam-e-Muharraq (charred blood), Sawda-e-Muharraq (charred melancholic blood), Ghiza-e-Kaseef (indigestible/heavy food), persistent local pressure, pregnancy, and systemic disorders such as Ḍu'f al-Kabid (hepatic insufficiency) and Ṣighar al-Kabid (liver atrophy). These traditional perspectives closely parallel modern concepts of systemic, environmental, and hormonal contributors to melasma [5,34,35].

Classification

In modern pathology, melasma (chloasma) is classified into three main types:

Epidermal: Characterized by excess melanin in the basal and suprabasal epidermal layers, often more responsive to treatment.

Dermal: Defined by melanophages and melanin deposition within the dermis, typically more resistant to therapy.

Mixed: A combination of both epidermal and dermal patterns, frequently observed in clinical practice.

In Unani medicine, classification is based on causative factors, with the following types described:

Kalaf-e-Rehmi: Melasma associated with hormonal imbalance, particularly during pregnancy or due to oral contraceptive use.

Kalaf-e-Kabdi: Melasma linked to liver dysfunction, such as hepatic insufficiency or atrophy.

Kalaf-e-Zarabi: Melasma arising from facial skin trauma, injury, or abrasion.

Kalaf-e-Hurri: Melasma caused by excessive sun exposure or external heat.

Treatment

Conventional (Modern) Treatment

Modern therapeutic approaches include topical corticosteroids, tretinoin, azelaic acid, mercury-based compounds, hydroquinone, chemical peels, and laser therapy. While effective, these methods are often associated with adverse effects such as erythema, skin peeling, burning, and stinging sensations, which may limit long-term use.

Unani Treatment

In the Unani system of medicine, treatment of Kalaf (melasma) encompasses drug therapy, dietotherapy, and Ilāj bi'l-Tadbīr (regimental therapy). Medicinal plants used in Unani practice are selected for their diverse pharmacological properties, including:

Jālī (detergent/cleansing) – removes superficial impurities and pigmentation.

Qāshir (scaling/exfoliating) – helps shed pigmented layers.

Ghassāl (abluent/washing) – cleanses and refreshes the skin.

Munaffiṭ (vesicant) – draws out morbid matter.

Muḥammir (rubefacient) – improves local circulation.

Rad'-i-Mawād (divergent) – redirects accumulated morbid matter away from the skin.

Mughadhdhī (nutritive) – strengthens and nourishes skin tissue.

This holistic approach emphasizes not only topical application but also systemic correction of underlying imbalances, aiming to minimize recurrence and enhance overall skin health.

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In Table-1, some of the significant single Unani herbal medicines together with their documented mechanism of action are listed.

Table-1:Unani Single Drugs for the Treatment of Kalaf (Melasma)

S. No	Scientific Name	Unani Name	Chemical Constituents	Mechanism of Actions	References
1.	*Ficus Carica*	Anjeer	➢ Flavonoids (Quercetin & Luteonlin), carotenoids, and triterpenes flavonoids which are reported to be found in drugs are responsible for their antioxidant property. ➢ Ethanolic extract of of F. benghalensis enhances the production of collagen	Anti-oxidant, Anti-Ageing, Wound healing	[36–38]
2.	*Prunus amygdala*	Badam Talkh	➢ Mandelic acid- reported to be found in the drug is responsible for its anti-inflammatory as well as helps in hypermelanosis. Property. ➢ Phenolic acids and Flavonoids (Flavonoid - kaempferol, myricetin, naringenin are found in extract; Phenolic acids - caffeic acid, vanillic acid, hydroxycinnamic acid, rosmarinic acid, ferulic acid, are found in the extract of bitter almond), which exert antioxidant property.	Anti-inflammatory Inhibits Hypermelanosis	[39]
3.	*Lens clunaris*	Masoor	➢ Phytosterols, BBI, exhibits Anti-inflammatory ➢ Vitamin E, Vitamin C, and Polyphenolics reported for Antioxidant properties.	➢ Anti-inflammatory ➢ Antioxidant property	[40]
4.	*Emblica Officinalis*	Amla	Emblicanin α & β Punigluconin Pedunculagin	Antioxidant Tyrosinase inhibition	[41]
5.	*Curcuma longa*	Haldi	Curcumin, Demethoxycurcumin,	Anti-inflammatory, Antioxidant	[42]

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			Bisdemethoxycurcumin, Diacetyl curcumin		
6.	*Crocus sativus*	Zafran	α β carotenes & Cyanidins Kaempferol	Antioxidant Tyrosinase inhibitor	[43]
7.	*Santalum album*	Sandal	α santalo	Tyrosinase inhibition	[44]
8.	*Aloe barbadensis*	Elva	Aleosin	Tyrosinase inhibition, antioxidant	[45]
9.	*Rubia cordifoli*	Fawwah	Manjishthin, Purpurine & Phenylcoumarin	Tyrosinase inhibition	[46]
10.	*Saussurea lappa*	Qust	Methanolic extract	Tyrosinase inhibition	[47]
11.	*Azadirachta indica*	Neem	Methanolic extract	Tyrosinase inhibition Antifungal	[48]

Discussion

The Unani system of medicine, with its long and distinguished history, has played a significant role in disease management, health promotion, and preventive care. Its holistic approach emphasizes restoring the balance of humors through time-tested drugs, diet, and regimental therapies, many of which have been refined over centuries of clinical practice.

In the context of Kalaf (melasma), Unani medicine offers a promising alternative to conventional therapies, particularly through the use of medicinal herbs. Unlike modern treatments that primarily target pigmentation, the Unani approach addresses both the visible manifestations and the underlying etiological factors, thereby aiming for long-term correction and prevention of recurrence.

Several herbs traditionally prescribed in Unani medicine are recognized for their skin-lightening, anti-inflammatory, and detoxifying properties. Their therapeutic effects can often be attributed to bioactive compounds. For instance, Bitter almond (Prunus amygdalus) contains prunasin, which has demonstrated the ability to inhibit melanin synthesis. Fig (Ficus carica) is rich in antioxidants that counter oxidative stress, a key factor in melanogenesis. Similarly, lentils (Masoor) are described in Unani literature to aid in Tanqiya-i Mawād (expulsion of unhealthy substances), thereby contributing to internal detoxification and improved skin health.

While these traditional insights are valuable, integration with modern medicine is essential to optimize outcomes. Scientific validation through pharmacological studies and clinical trials is needed to confirm efficacy, ensure safety, and establish standardized formulations and dosages. Furthermore, potential herb–drug interactions must be carefully evaluated to avoid adverse effects in patients receiving concurrent allopathic therapy.

Despite these limitations, the Unani system provides a unique therapeutic framework that combines internal correction with external treatment. This dual approach holds the potential to complement conventional methods and may pave the way for integrative strategies in melasma management.

Conclusion

In summary, the Unani approach to melasma treatment—rooted in humoral balance and supported by medicinal herbs—offers a holistic and potentially effective alternative to conventional therapies. By targeting both systemic and local factors, Unani medicine not only alleviates pigmentation but also

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promotes overall skin and systemic health. However, the full therapeutic potential of these remedies can only be realized through scientific validation, standardization, and integration with modern medical practices. Future research focusing on large-scale clinical studies and molecular mechanisms will be crucial to bridging the gap between traditional wisdom and modern dermatological science.

Declarations

Conflict of Interest

The authors declared no conflicts of interest with respect to the authorship, and/or publication of this article.

References

1. T. Passeron, M. Picardo, Melasma, a photoaging disorder, Pigment Cell Melanoma Res 31 (2018) 461–465. https://doi.org/10.1111/pcmr.12684.
2. J. Jiang, O. Akinseye, A. Tovar-Garza, A.G. Pandya, The effect of melasma on self-esteem: A pilot study, Int J Womens Dermatol 4 (2018) 38–42. https://doi.org/10.1016/j.ijwd.2017.11.003.
3. B. Doolan, M. Gupta, Melasma, Australian Journal for General Practitioners 50 (2021) 880–885. https://www1.racgp.org.au/ajgp/2021/december/melasma.

A. Horti, N. Husain, S. Shaikh, S. Imran, S.N.A. Abbas, K.A.K. Khan, The Perspective of Unani Medicine in Understanding Melasma – A Review, Current Cosmetic Science 03 (2024). https://doi.org/10.2174/0126667797282730240117071740.

4. Z. Aquil, M. Khalid, Q. Uddin, W. Ahmad, Potential role of Unani medicinal plants in management of Kalaf (Chloasma): A review Unani System of Medicine View project Unani Medicine View project, 2019. https://www.researchgate.net/publication/335227969.
5. M. Kabiruddin, Sharah Asbab wa Alamat, Aijaz Publishing House, New Delhi, 1969.
6. Z. Razi, Kitab ul Mansoori - Urdu Translation, Central Council for Research in Unani Medicine, 1991.
7. N.G.K.R. Najmi, Khazain ul Adviya, 001 ed., Karkhana Paisa Akhbar, Lahore, Lahore, n.d. https://www.rekhta.org/ebooks/detail/khazain-ul-adviya-volume-007-mohammad-najmul-gani-khan-ebooks (accessed August 20, 2024).
8. R.M.P. Gutiérrez, R.L. Perez, Raphanus sativus (Radish): their chemistry and biology., The Scientific World Journal 4 (2004) 811–837. https://doi.org/10.1100/tsw.2004.131.
9. D.M. Thappa, Melasma (Chloasma) : A Review With Current Treatment Options, Indian J Dermatol 49 (2004).
10. D. Dubey, l. Chaudhari, A. Biharee, P. Kumar, An overview of important natural products and phytomedicines used for management of melasma,World Journal of Pharmaceutical Research (2021). Https://doi.org/10.20959/wjpr20214-20123.
11. Y. Shamsi, S. Nikhat, M. Manjhi, M. Wasi Akhtar, S. Ahmad, Clinical evaluation of a topical Unani pharmacopoeial formulation Tila-e-Kalf in the management of melasma (Kalf): A randomized controlled clinical trial, Original Research Article AJP 13 (2022) 255–264. https://doi.org/10.22038/AJP.2022.21346.
12. R. Sarkar, R. Jain, P. Puri, Melasma in Indian Males, Dermatol Surg 29 (2003) 204. https://doi.org/10.1097/00042728-200302000-00022.
13. M.K. Trivedi, F.C. Yang, B.K. Cho, A review of laser and light therapy in melasma, Int J Womens Dermatol 3 (2017) 11–20. https://doi.org/10.1016/j.ijwd.2017.01.004.

A. Handel, L. Miot, H. Miot, Melasma: A clinical and epidemiological review, An Bras Dermatol 89 (2014) 771–782. https://doi.org/10.1590/abd1806-4841.20143063.

14. O.A. Ogbechie-Godec, N. Elbuluk, Melasma: an Up-to-Date Comprehensive Review, Dermatol Ther (Heidelb) 7 (2017) 305–318. https://doi.org/10.1007/s13555-017-0194-1.
15. N. Sarma, Evidence-based review, grade of recommendation, and suggested treatment recommendations for melasma, Indian Dermatol Online J 8 (2017) 406–442.
16. J. Bolognia, M. Murray, J. Pawelek, UVB-Induced melanogenesis may be mediated through the MSH-receptor system, Journal of Investigative Dermatology 92 (1989) 651–656. https://doi.org/10.1016/0022-202X(89)90177-2.
17. S. Im, J. Kim, W.Y. On, W.H. Kang, Increased expression of α-melanocyte-stimulating hormone

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in the lesional skin of melasma [8], Br J Dermatol 146 (2002) 165–167. https://doi.org/10.1046/j.1365-2133.2002.4513_3.x.

18. L.D. Miot, H.A. Miot, J. Polettini, M.G. Silva, M.E. Marques, Morphologic Changes and the Expression of Alpha-Melanocyte Stimulating Hormone and Melanocortin-1 Receptor in Melasma Lesions: A Comparative Study, Am J Dermatopathol 32 (2010). https://journals.lww.com/amjdermatopathology/fulltext/2010/10000/morphologic_changes_and_the_expression_of.6.aspx.
19. C.J. Carsberg, J. Ohanian, P.S. Friedmann, Ultraviolet radiation stimulates a biphasic pattern of 1,2-diacylglycerol formation in cultured human melanocytes and keratinocytes by activation of phospholipases C and D, Biochemical Journal 305 (1995) 471–477. https://doi.org/10.1042/bj3050471.
20. R. Cui, H.R. Widlund, E. Feige, J.Y. Lin, D.L. Wilensky, V.E. Igras, J. D'Orazio, C.Y. Fung, C.F. Schanbacher, S.R. Granter, D.E. Fisher, Central Role of p53 in the Suntan Response and Pathologic Hyperpigmentation, Cell 128 (2007) 853–864. https://doi.org/10.1016/j.cell.2006.12.045.

I. Ferreira, S. Videira, D.F. Lima Moura, S. Magina, Mechanisms regulating melanogenesis * Mecanismos reguladores da melanogênese, 2013.

21. S.H. Kwon, Y.J. Hwang, S.K. Lee, K.C. Park, Heterogeneous pathology of Melasma and its clinical implications, Int J Mol Sci 17 (2016). https://doi.org/10.3390/ijms17060824.
22. G. Imokawa, Y. Yada, N. Morisaki, M. Kimura, Biological characterization of human fibroblast-derived mitogenic factors for human melanocytes, 1998.
23. M. Taraz, S. Niknam, A.H. Ehsani, Tranexamic acid in treatment of melasma: A comprehensive review of clinical studies, Dermatol Ther 30 (2017). https://doi.org/10.1111/dth.12465.
24. R. Malaviya, A.R. Morrison, A.P. Pentland, Histamine in human epidermal cells is induced by ultraviolet light injury, Journal of Investigative Dermatology 106 (1996) 785–789. https://doi.org/10.1111/1523-1747.ep12346356.
25. N.H. Kim, S.H. Choi, T.R. Lee, C.H. Lee, A.Y. Lee, Cadherin 11 involved in basement membrane damage and dermal changes in melasma, Acta Derm Venereol 96 (2016) 635–641. https://doi.org/10.2340/00015555-2315.
26. H.Y. Kang, J.S. Hwang, J.Y. Lee, J.H. Ahn, J.Y. Kim, E.S. Lee, W.H. Kang, The dermal stem cell factor and c-kit are overexpressed in melasma, British Journal of Dermatology 154 (2006) 1094–1099. https://doi.org/10.1111/j.1365-2133.2006.07179.x.
27. K. Gledhill, L.E. Rhodes, M. Brownrigg, A.K. Haylett, M. Masoodi, A.J. Thody, A. Nicolaou, D.J. Tobin, Prostaglandin-E2 is produced by adult human epidermal melanocytes in response to UVB in a melanogenesis-independent manner, Pigment Cell Melanoma Res 23 (2010) 394–403. https://doi.org/10.1111/j.1755-148X.2010.00696.x.
28. D.J. Lee, J. Lee, J. Ha, K.C. Park, J.P. Ortonne, H.Y. Kang, Defective barrier function in melasma skin, Journal of the European Academy of Dermatology and Venereology 26 (2012) 1533–1537. https://doi.org/10.1111/j.1468-3083.2011.04337.x.

A. Ogita, Y. Funasaka, S.I. Ansai, S. Kawana, H. Saeki, Melasma in a male patient due to estrogen therapy for prostate cancer, Ann Dermatol 27 (2015) 763–764. https://doi.org/10.5021/ad.2015.27.6.763.

29. S. Kippenberger, S. Loitsch, F. Solano, A. Bernd, R. Kaufmann, Quantification of Tyrosinase, TRP-1, and TRP-2 Transcripts in Human Melanocytes by Reverse Transcriptase-Competitive Multiplex PCR – Regulation by Steroid Hormones, Journal of Investigative Dermatology 110 (1998) 364–367. https://doi.org/10.1038/jid.1998.1.
30. Ahmad HW, Moalajat, Qaumi Council Baraye Farogh Urdu Zaban, New Delhi, 2006.

A. Sultana, T.A. Khan, Clinical Evaluation: Unani Concepts and Management, S. R. Scientific Publications, 2010.

31. Y. Shamsi, S. Ansari, S. Nikhat, A. Professor, FICUS CARICA L.: A PANACEA OF NUTRITIONAL AND MEDICINAL BENEFITS, (2020). https://doi.org/10.5667/tang.2020.0001.
32. J. Ahmad, I. khan, Evaluation of Antioxidant and Antimicrobial Activity of Ficus Carica Leaves: an In Vitro Approach, Plant Pathology & Microbiology 4 (2013). https://doi.org/10.4172/2157-7471.1000157.

Volume 8, Issue 4; July-August 2025; Page No 506-515

33. S. Murugesu, J. Selamat, V. Perumal, Phytochemistry, pharmacological properties, and recent applications of ficus benghalensis and ficus religiosa, Plants 10 (2021). https://doi.org/10.3390/plants10122749.
34. M. Siddiqui, W. Begum, Almond (Prunus amygdalus L.): A source of revitalizing health and its therapeutic application, Journal of Drug Delivery and Therapeutics 13 (2023) 176–182. https://doi.org/10.22270/jddt.v13i11.6296.
35. M.A.I.E. Faris, H.R. Takruri, A.Y. Issa, Role of lentils (Lens culinaris L.) in human health and nutrition: A review, Med J Nutrition Metab 6 (2013) 3–16. https://doi.org/10.1007/s12349-012-0109-8.
36. M. Sharma, G. Pandey, K. Verma, Antioxidant, immunomodulatory and anticancer activities of Emblica officinalis: An overview, International Research Journal of Pharmacy 2 (2011) 38–42.
A. Niranjan, D. Prof, Chemical constituents and biological activities of turmeric (Curcuma longa L.) -A review, J Food Sci Technol 45 (2008) 109–116. https://www.researchgate.net/publication/283863862_Chemical_constituents_and_biological_activities_of_turmeric_Curcuma_longa_L_-A_review#:~:text=-A%20review.%20Abhishek (accessed September 4, 2024).
A. El Midaoui, I. Ghzaiel, D. Vervandier-Fasseur, M. Ksila, A. Zarrouk, T. Nury, F. Khallouki, A. El Hessni, S.O. Ibrahimi, N. Latruffe, R. Couture, O. Kharoubi, F. Brahmi, S. Hammami, O.M. Kouki, M. Hammami, T. Ghrairi, A. Vejux, G. Lizard, Saffron (Crocus sativus L.): A Source of Nutrients for Health and for the Treatment of Neuropsychiatric and Age-Related Diseases, Nutrients 14 (2022). https://doi.org/10.3390/nu14030597.
A. Aftab, S. Sultana, A. Rashid, M. Akram, H. Anwar, Santulum album: Medicinal and Pharmacological Properties, (2023). https://doi.org/10.56557/JOMAHR/2023/v8i18127.
37. M. Añibarro-Ortega, J. Pinela, L. Barros, A. Ćirić, S.P. Silva, E. Coelho, A. Mocan, R.C. Calhelha, M. Soković, M.A. Coimbra, I.C.F.R. Ferreira, Compositional features and bioactive properties of aloe vera leaf (Fillet, mucilage, and rind) and flower, Antioxidants 8 (2019). https://doi.org/10.3390/antiox8100444.
38. R. Biswas, P.K. Mukherjee, M.K. Dalai, P.K. Mandal, M. Nag, Tyrosinase inhibitory potential of purpurin in Rubia cordifolia-A bioactivity guided approach, Ind Crops Prod 74 (2015) 319–326. https://doi.org/10.1016/j.indcrop.2015.04.066.
39. K. Zahara, S. Tabassum, S. Sabir, M. Arshad, R. Qureshi, M.S. Amjad, S.K. Chaudhari, A review of therapeutic potential of Saussurea lappa-An endangered plant from Himalaya, Asian Pac J Trop Med 7 (2014) S60–S69. https://doi.org/10.1016/S1995-7645(14)60204-2.
40. S. Uzzaman, Pharmacological activities of neem (Azadirachta indica): A review, International Journal of Pharmacognosy and Life Science 1 (2020) 38–41. https://doi.org/10.33545/27072827.2020.v1.i1a.8.

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