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Md Shahid Raza
Assistant Professor, Department of Dermatology & Cosmetology (Amraze Jild wa Tazeeniyat), F/O Al Farooque Unani Medical College & Hospital, Bye Pass Road, Village Arandiya, Indore, Madhya Pradesh, India

Nadeem Ahmad Shah
Assistant professor, Department of Dermatology & Cosmetology (Amraze Jild wa Tazeeniyat), F/O Kashmir Tibbia College Hospital & Research Centre, Jammu & Kashmir, India

Salim Akhtar
Professor, Department of Pharmacy (Ilmul Saidla) F/O Al Farooque Unani Medical College & Hospital, Bye Pass Road, Village Arandiya, Indore, Madhya Pradesh, India

Corresponding Author:
Md Shahid Raza
Assistant Professor, Department of Dermatology & Cosmetology (Amraze Jild wa Tazeeniyat), F/O Al Farooque Unani Medical College & Hospital, Bye Pass Road, Village Arandiya, Indore, Madhya Pradesh, India

Tyrosinase inhibitors: Unraveling the potential of Unani botanicals for enhancing facial complexion

Md Shahid Raza, Nadeem Ahmad Shah and Salim Akhtar

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Abstract

Introduction: The desire for a fair complexion is increasingly prevalent in contemporary society, with a growing preference for natural products over synthetic alternatives. The field of skin-lightening agents is continuously evolving, with ongoing updates to our understanding. In Unani medicine, terms like *Tahseen Lawn bashra* and *Tajjaliye bashra* specifically denote skin lightening, aligning with the modern concept of tyrosinase inhibition-the most frequently documented method for achieving lighter skin.

Objective: This research aims to systematically review and analyze 20 specific botanicals used in Unani medicine to ascertain their efficacy in tyrosinase inhibition and their potential for enhancing facial complexion. Through in-depth exploration and analysis, this study seeks to bridge the traditional knowledge of Unani medicine with modern scientific understanding, providing insights into natural remedies for achieving skin lightening and improved facial complexion

Materials and Methods: A systematic selection process identified 20 botanicals extensively utilized in Unani medicine for their purported effects on facial complexion enhancement. A comprehensive literature review spanning databases such as PubMed, Scopus, and Google Scholar focused on studies elucidating the tyrosinase inhibitory potential of these botanicals and their impact on skin lightening. Data extraction encompassed key botanical information, active compounds, mechanisms of tyrosinase inhibition, and reported outcomes on facial complexion. Comparative analysis and quality assessment were conducted to synthesize findings, providing insights into the efficacy of Unani botanicals in tyrosinase inhibition and their potential for enhancing facial complexion.

Result and Conclusion: The study revealed 20 distinct botanicals from Unani medicine exhibiting varying degrees of tyrosinase inhibition, attributed to specific active compounds within these botanicals. Correlating these inhibitory effects with reported outcomes on facial complexion highlighted their potential in ameliorating hyperpigmentation and promoting even skin tone. This study underscores the significant relationship between Unani botanicals, tyrosinase inhibition, and facial complexion enhancement, emphasizing their promising role in natural skin-lightening remedies. The findings advocate for further research to harness these botanicals therapeutic benefits and validate their application in dermatological contexts aimed at improving facial complexion.

Keywords: Skin lightening, *Tahseen lawn*, Tyrosinase inhibitors, Unani medicine, *Mohsine lawn*, Unani botanicals

Introduction

The pursuit of wellness in today's world encompasses beauty, health, fitness, and anti-aging endeavors, where the quest for fairer skin holds significant socio-medical importance [1, 2]. This drive has led to the emergence of various skin-lightening methodologies like dermabrasion, ultrasound, and laser therapy [2, 3]. Unhealthy skin not only poses social challenges but also impacts one's sense of cheerfulness and confidence, underscoring the pivotal role of maintaining healthy skin integrity [4].

Amidst this landscape, Unani herbal remedies stand out as compelling avenues for innovative skincare solutions. Drawing from the rich reservoir of Unani Medicine, these remedies offer promising alternatives to contemporary practices. Unani Medicine takes a holistic approach, perceiving skincare as more than altering skin color-it's a comprehensive enhancement of texture, tone, and radiance [5].

The burgeoning Indian cosmetic market, boasting an impressive annual growth rate of 15-20% that surpasses even the leading US and EU markets, mirrors the escalating demand for skincare products [6]. Rooted in the essence of Unani Medicine lies the development of Unani cosmetics and cosmeceuticals, designed not just to lighten skin tone but also to infuse a

smooth, appealing texture while enhancing complexion, radiance, and luminescence-a concept encapsulated by the term *Tahseen Lawn Bashra*.[7] This holistic philosophy embodies the pursuit of luminous, radiant skin that represents not just external beauty but also reflects profound skin health and vitality.

Contemporary depigmenting agents predominantly rely on various mechanisms, notably tyrosinase inhibition, to address hyperpigmentation [8]. Despite their widespread use, these agents often come with limitations, such as dermal sensitization and cytotoxic potential, as observed in the cases of Kojic acid and arbutin. Which are known tyrosinase inhibitors commonly used in cosmetic products for skin whitening and remove hyperpigmentation [9]. Notably, approximately 15% of the global population uses skin whitening products, with India, Japan, and China being significant hubs for their consumption. In India particularly, a substantial percentage of men (almost 80%) use fairness creams [10].

This realization of limitations in commonly used agents prompts the exploration of alternative solutions, leading to an investigation into the potential of Unani botanicals as enhancers of facial complexion and treatments for hyperpigmentation, with a specific focus on their antityrosinase activity, supported by empirical studies.

Unani Medicine's Perspective on Skin Color and Complexion

The Unani Medicine perspective on skin color revolves around the concept that the skin and body organs begin as white and undergo color changes based on the types of humors that reach them.[11] *Akbar Arzani's* writings in *'Mufarrah Al-Qulub'* affirm that the skin's original color is white and relies on "*Mulawwin madde*" or pigments for its coloring. In the absence of external coloring substances, the skin remains unchanged. This concept aligns with the idea of melanogenesis and melanin deposition, as indicated in *Arzani's* notes [11].

Moreover, the skin's color can be influenced by variations in heat and cold. Physicians attribute whitening of the skin to increased coldness and excessive phlegm, hindering pigment from reaching the external skin.[11,12] Conversely, warmer climates or individuals engaged in physical activities often exhibit relatively darker skin due to the amalgamation of pigmented substances with the external skin [12].

According to Unani Medicine, the most optimal and aesthetically pleasing skin occurs when the body's temperament is hot and moist.[12] This understanding emphasizes the significance of bodily balance in achieving the best skin condition, with the interplay of humors and environmental factors affecting skin complexion.

Modern concept of pigmentation

Human skin tones predominantly depend on the Melanin pigment's quantity, concentration, and arrangement, produced by melanocytes through melanogenesis in the basal epidermal layer [13].

Two primary Melanin types, Eumelanin and Pheomelanin, significantly influence skin tone variation. Individuals with darker skin tones typically possess higher Eumelanin levels compared to Pheomelanin, while the reverse is observed in lighter skin [14].

Melanin synthesis involves oxidative reactions from the amino acid tyrosine, mediated by the enzyme tyrosinase. Overactive tyrosinase can lead to hyperpigmentation issues such as melasma, age spots, lentigines, and linea nigra [15].

The pigmentation processes in the human body involve various physiological mechanisms, some of which are genetically regulated. These include the development and density of melanocytes, as well as the expression of enzymatic and structural components of melanosomes [16]. Additionally, other processes such as the synthesis and distribution of melanin in the skin, along with the transport of melanosomes to dendrites and keratinocytes, serve as targets for manipulation through skin-lightening agents [17].

Skin-lightening agents function by intervening in the melanogenesis pathway, melanin transfer, or skin shedding processes, aiming to reduce surface pigmentation. They typically operate through methods such as inhibiting tyrosinase, controlling MITF activity, regulating MC1R function, disrupting melanosome development and transport, or encouraging melanocyte removal, thereby reducing skin pigmentation [18].

Apart from Tyrosinase inhibitors, antioxidants, and various vitamins such as A, B, C, and E play roles as skin-lightening components, either directly or indirectly. Among these, Tyrosinase inhibition stands as the most extensively documented screening method in skin-lightening ingredient research [19, 20]. Tyrosinase, also known as polyphenol oxidase (PPO) or monophenol monooxygenase, is an enzyme containing copper found in melanocytes. It facilitates crucial reactions in melanogenesis, including the hydroxylation of tyrosine and the oxidation of the o-diphenyl product, L-DOPA [21]. This process generates a highly reactive intermediate that further oxidizes to produce melanin through a free radical-coupling pathway [22] Some well-known tyrosinase inhibitors, like hydroquinone and kojic acid, act by interacting with the copper present in the enzyme's active site, thereby reducing its enzymatic activity [23].

Antioxidants play a crucial role in hindering the oxidation process of tyrosine to DOPA quinone, along with effectively neutralizing free radicals. These actions aid in reducing the synthesis of melanin, thereby contributing to skin depigmentation effects [24].

Vitamins are recognized for their ability to enhance skin tone and texture, with specific applications in addressing skin issues. Vitamin A, employed for decades in treating melasma, operates through compounds like tretinoin [25]. Tretinoin acts as a skin-lightening agent by stimulating exfoliation and expediting the shedding of epidermal melanin. It achieves this by enhancing the turnover rate and encouraging the proliferation of keratinocytes [26]. Another derivative of retinoic acid, retinyl palmitate, is also utilized in skin-lightening cosmetic products. Within the spectrum of Vitamin B, two subclasses display skin-lightening properties: (a) Vitamin B3 (Niacinamide): This well-known antioxidant disrupts the transfer of melanosomes from melanocytes to keratinocytes, contributing to skin lightening. (b) Vitamin B5 (Panthenoic acid): A derivative of Vitamin B5, calcium pantetheine sulfonate, has shown interference with tyrosinase glycosylation, leading to depigmentation effects [27, 28].

Vitamin C plays a dual role in skin lightening by neutralizing free radicals induced by UV exposure and functioning as a tyrosinase inhibitor. This multifaceted action contributes to skin brightening [29]. On the other hand,

Vitamin E serves as an antioxidant within the body, shielding against UV-triggered hyperpigmentation [30].

Materials and methods

The study encompassed a meticulous selection process to identify 20 distinct botanicals integral to Unani medicine, known for their purported efficacy in enhancing facial complexion. A comprehensive literature review was conducted across prominent databases, including PubMed, Scopus, and Google Scholar, employing keywords like "Unani medicine," "tyrosinase inhibition," "skin lightening," and "facial complexion enhancement." The inclusion criteria targeted studies elucidating the tyrosinase inhibitory potential of these botanicals and their impact on skin lightening and facial complexion. Data extraction encompassed detailed information on traditional uses, active compounds, mechanisms of tyrosinase inhibition, and reported outcomes concerning facial complexion from these selected studies. Rigorous comparative analysis and quality assessment were applied to synthesize findings, focusing on correlations between tyrosinase inhibition, botanicals' active compounds, and their effects on facial complexion. Limitations within the selected studies were recognized, and conclusions were drawn to emphasize key insights and suggest directions for further research validation of Unani botanicals' therapeutic benefits in dermatological contexts.

Findings

Za'faran *(Crocus sativus L.)*

Za'faran, holds a prominent place in Unani Medicine as a complexion enhancer [31]. Its historical usage spans centuries, renowned for bestowing radiance, lightening skin tone, and remedying various skin issues such as dark pigmentation, under-eye circles, acne, and pimples [32]. Research underscores saffron's ability to absorb solar radiation, effectively acting as a natural sunscreen [33]. Studies by Vyas *et al*. demonstrated a significant skin-brightening effect using a 3% dry saffron extract in cream, lotion, and face powder formulations among individuals aged 18-28 during patch testing. These effects are attributed to crocin and crocetin, compounds present in saffron [34].

The skin-brightening and depigmentation effects of saffron are often linked to the antioxidant properties of crocin and crocetin [35]. Saffron contains over 150 carotenoid compounds, including safranal, zeaxanthin, lycopene, and various α- and β-carotenes, along with a rich source of riboflavin [35]. Methanolic extracts from *Crocus sativus* flowers have displayed increased tyrosinase inhibitory activity, notably from 10.78 at a concentration of 50 µg/ml to 28.22 at 1000 µg/mL. This enhanced activity, attributed to the presence of cyanidins, correlates with antioxidant properties [36, 37].

Kubo's research highlighted kaempferol, extracted from *Crocus sativus* petals, as a potent inhibitor of L-DOPA oxidation catalyzed by mushroom tyrosinase, indicating its potential in skin whitening with an IC50 value of 67 µg/mL [38]. Crocetin, a saffron-derived compound, exhibits efficacy in reducing melanin production within B16 melanoma cells by suppressing tyrosinase activity and levels of melanin synthesis-associated proteins (tyrosinase and MITF). Its antioxidant properties regulate cellular Reactive Oxygen Species (ROS) without causing harm [39].

In a specific study, 35 compounds were isolated and identified from saffron petals, among which crocusatin-K demonstrated robust tyrosinase inhibition in a competitive manner [40].

Sibr *(Aloe barbadenis Mill.)*

The historical use of the Aloe genus can be traced back to the 1st century C.E., as noted by the Unani physician Dioscorides [13]. He emphasized its versatile applications for treating mouth infections, sores, wounds, and as a purgative. Aloe's skin whitening effect is attributed to its *'jali'* (detergent) and *'Musakhkhin'* (Calorific) properties. Among its various dermatological effects, its water solution is effective for combating diffuse hair loss, promoting curly and dark hair [41]. Its vinegar solution is recommended for treating conditions like dandruff, alopecia areata, herpes, pruritus, scabies, urticaria, chronic ulcers. Additionally, its liniment is used for pediculosis and fungal infections [41].

Aloe finds prevalent use in cosmetic industries, particularly as skin whitening agents. Aloe's multifaceted utility extends to both ornamental and medicinal purposes [42]. Its composition, encompassing nearly 20 amino acids, essential minerals (calcium, magnesium, sodium), enzymes, vitamins, polysaccharides, nitrogen, and other constituents, positions it as a highly esteemed beauty herb [42].

The gel composition of *Aloe*, containing anthraquinone derivatives and C-glucosylanthrone derivatives like aloin A and B, emodin, desoxyaloin, aloinoside B and C, and elgonica dimer A, contributes significantly to its efficacy [13]. Beyond its chemical makeup, various Aloe species exhibit potent anti-tyrosinase activity. Compounds like aloesin are identified as reversible-competitive inhibitors of this enzyme, offering protective attributes against radiation [13, 43].

Extracts from Aloe vera gel, especially lyophilized and methanolic variants, exhibit remarkable inhibition of tyrosinase activity. This inhibition displays variability based on extraction methods and germplasms [44]. Aloesin, a potential regulator of melanogenesis, competitively inhibits tyrosinase, effectively limiting melanin production *in vitro* [45]. Additionally, aloesin and 2-o-ferulonyaloesin, isolated from aloe arborescens mill, show mushroom tyrosinase inhibition activity. They demonstrate synergistic action with arbutin for inhibiting melanin production, with aloesin identified as a non-competitive inhibitor of mushroom tyrosinase [46, 47].

Azad Darakht-E-Hindi (*Azadirachta indica*)

Neem, a renowned staple in India, holds immense value for its perceived beauty benefits and traditional use in treating skin ailments while detoxifying the blood [48]. In Unani Medicine, it is recommended for diseases stemming from all four humors. Though not commonly acknowledged as a skin whitening agent, purified neem oil and powdered leaves play substantial roles in numerous Unani cosmetics and cosmeceuticals, particularly in facial creams [31, 41].

Recent studies, however, have indicated its potential as a skin whitening agent, notably through the methanolic extract of neem bark, which exhibited substantial tyrosinase inhibition activity, reaching up to 43.59%. Similarly, neem leaf extracts showed a 10.10% activity in inhibiting tyrosinase [49]. The heartwood extract of neem has also been reported to possess significant antioxidant properties, attributed to its high phenolic content [50].

Further investigations into neem tree extracts unveiled potent anti-tyrosinase properties, identifying 20 limonoids

and 2 flavonoids as effective and safer melanogenesis inhibitors compared to the reference compound, arbutin. Notably, nimbin, a compound within neem, hindered melanogenesis by reducing the expression of tyrosinase and associated key proteins [51].

Moreover, promising results emerged from the topical application of neem leaf extract on UVB-exposed hairless mice, mitigating various signs of skin aging. This application demonstrated efficacy in reducing wrinkles, thickening, water loss, and erythema [52].

Zard Chob (*Curcuma longa*)

In Unani medicine, *Curcuma longa*, particularly its rhizomes, holds a revered status due to its multifaceted skin-friendly attributes. Renowned for its photoprotection, anti-wrinkle, anti-aging, antioxidant, astringent, anti-irritant, and moisturizing effects, this herb is extensively utilized [41, 53]. Specifically, the rhizome powder and extracts of Curcuma longa are pivotal constituents in various Unani formulations aimed at enhancing skin color, addressing melasma, and alleviating other hyperpigmented lesions [54-56].

Curcumin, a primary phytochemical in *Curcuma longa*, has gained traction in cosmetic applications due to its effective topical delivery to affected tissues. Research has demonstrated curcumin's ability to downregulate melanogenesis-related proteins, notably tyrosinase, leading to the suppression of melanogenesis in stimulated melanoma cells [57]. Studies have reported a noteworthy 88.56% inhibition of tyrosinase activity in turmeric rhizomes, supporting Zard Chob's efficacy as a skin whitening agent [58].

Recent studies highlighted the synthesis of curcumin-β-di-glucoside 3 (yield 71%) and tetrahydrocurcumin-β-di-glucoside 6 (yield 64%), showcasing enhanced antioxidant, antimicrobial, and cytotoxic properties in these glucosyl curcuminoids [59]. Investigations revealed that ethanol extracts of Curcuma longa possess superior antioxidant properties, while n-hexane extracts display the highest anti-tyrosinase potential. Researchers concluded that Zingiberaceae plants could serve as novel sources for antioxidants and anti-tyrosinase agents for further developments in cosmetics, food, or nutraceuticals [60].

Sandal Safed (*Santalum album*)

Sandal Safed, deeply revered in Unani Medicine, symbolizes vitality and embodies a rich legacy in cosmetics and skincare practices, catering to various skin types [41]. The abundance of sesquiterpenoid alcohols in sandalwood oil, constituting a significant portion (80-90%) of its composition, renders it a sought-after component in various cosmetic formulations within Unani practices, particularly those designed to enhance skin fairness [61]. Additionally, studies highlighting its low acute oral and dermal toxicity in laboratory animals further underscore its suitability and safety in cosmetic applications within the Unani system [62].

Recent research has shed light on α-santalol, a major component of sandalwood oil, exhibiting potent tyrosinase inhibition with an IC50 of 171 µg/mL, surpassing the inhibitory effectiveness of kojic acid and arbutin (with an IC50 of 149 µg/mL). This characteristic positions α-santalol as a promising candidate for skincare applications [61].

The core findings of these studies emphasize the dose-dependent inhibition of tyrosinase by santalol, as evidenced through detailed enzyme kinetics and activity assays [63]. These results signify the potential of α-santalol in preventing melanin formation and browning, offering promising prospects in various industries-ranging from agriculture to food and cosmetics-as an effective solution for skin-related concerns.

Nakhood *(Cicer arietinum)*

Commonly known as chickpea, this legume holds a significant place in Indian culinary traditions. Within Unani medicine, it stands out for its usage in the form of a dough known as "*Arad Nakhood'* [54]. This preparation is renowned for its remarkable ability to enhance facial complexion and tackle pigmentation issues when applied topically. Moreover, in numerous Unani skincare preparations aimed at promoting skin glow, *'Ghaza'* (preparation for skin radiance) frequently incorporates *nakhood* as a key ingredient [41, 56]. Unani physician Zakariya Razi also advocated its oral consumption for contributing to a glowing skin appearance [64].

Although research exploring the antityrosinase inhibitory effects of chickpea has been limited, a recent study revealed compelling results. This study demonstrated an impressive 100% inhibition of mushroom tyrosinase activity, suggesting the promising potential of chickpea-derived compounds in regulating melanin production [65].

Asl-us-soos (*Glycyrrhiza glabra*)

Asl-us-soos (Liquorice root) presents a rich array of properties beneficial for skin health, offering depigmenting, lightening, emollient, anti-acne, photoprotective, anti-aging, wound-healing, antimicrobial, and antioxidant effects [31, 41, 58]. Unani medicine recommends orally ingesting liquorice powder with sugar and fennel to enhance complexion [64]. The skin-related effects of G. glabra are primarily attributed to the antioxidant activity of its phytochemical components, particularly triterpenes, saponins (such as Glycyrrhizin), and flavonoids [53].

Glycyrrhizetic acid, a component of liquorice, regulates melanin secretion, effectively reducing dark pigmentation and promoting a fairer complexion. Recent research indicates that the methanolic extract of liquorice root serves as a potent tyrosinase inhibitor, displaying over 75% inhibition in human skin. Its efficacy, measured by the IC50 value, aligns with that of well-known skin whitening agents like Kojic acid [49].

In a clinical trial involving 100 female participants treated with a 2.5% *G. glabra* cream for four weeks, significant improvements in melasma symptoms were observed compared to a placebo group, without any reported side effects [66]. Glabridin, a major liquorice component, displayed remarkable inhibition of tyrosinase activity in melanoma cells at a concentration of 1.0 µg/ml, without affecting DNA synthesis. Studies also showcased its ability to inhibit UVB-induced pigmentation and inflammation in guinea pig skins at a 0.5% w/v concentration. Researchers found that the presence of hydroxyl groups at the 2 and 4 positions of glabridin is crucial for its tyrosinase inhibitory activity [67].

Moreover, isoliquiritigenin and glabrene from *G. glabra* competitively inhibited both mono and diphenolase activity of mushroom tyrosinase [68]. Recent investigations highlighted liquiritin, extracted from G. glabra leaves, as a potent tyrosinase inhibitor. Its depigmentation effects were clinically examined, demonstrating therapeutic usefulness in

treating melasma when applied as a 20% liquiritin-containing cream over four weeks [69].

Gule Surkh *(Rosa damascene)*

In the realm of Unani Medicine, Gule Surkh stands as a *muraqqab-ul-quwa* drug, esteemed for its multifaceted health benefits.[70] Within this traditional system, it holds a significant role as a potent visceral tonic, revered particularly for its prowess as a blood purifier, often recommended for ailments associated with the blood.[31] While the precise mechanisms behind its efficacy aren't explicitly defined, there are references indicating its potential for managing hyperpigmented lesions [41, 64].

Rosa damascene boasts compounds like carboxylic acids, linalool (C10H180O), eugenol, citronellol (C10H20), farnesol, nerol (C10H18), terpenes, myrcene, quercetin, kaempferol, and vitamin C. Its oil extract comprises 16-35% citronellol, 8-30% geraniol, 4-10% nerol, 4-16% nonadecane, 3-8% heneicosane, and 1-3% linalool [58].

Studies conducted by Hadipour *et al*. showcased the antimelanogenic potential of *R. damascena's* essential oil, MeOH, and various fractions. These extracts demonstrated promising antimelanogenic effects by suppressing mushroom tyrosinase activity and the production of Reactive Oxygen Species (ROS) [71].

Furthermore, another study highlighted *R. damascena's* significant inhibition of tyrosinase activity. This study reported a remarkable 91.8% inhibition of mushroom tyrosinase and complete inhibition (100%) of murine melanoma tyrosinase [65].

Ushbā *(Hemidesmus indicus)*

In Unani Medicine it is mainly employed as a blood purifier and for various chronic skin conditions. This herb is renowned for its ability to enhance overall health, vitality, and combat disorders attributed to imbalanced blood [31, 41].

Studies focusing on the methanolic extract of *H. indicus* root bark have highlighted its substantial antioxidant activity across several *in vitro* and ex vivo models. Specifically, when assessed for tyrosinase inhibition using l-DOPA as the substrate, the root extract exhibited an average inhibitory activity of 14.80% [49, 72].

Further exploration into the root extracts of *H. indicus* revealed the presence of 2-hydroxy-4-methoxybenzaldehyde, a prominent fragrant phenolic compound. This compound showcased inhibitory potential against both diphenolase and monophenolase activities of the tyrosinase enzyme. Interestingly, its efficacy was found to surpass that of vanillin, indicating significant potential in skin whitening applications [73].

Turb *(Raphanus sativus L.)*

Turb, holds a significant position in Unani Medicine owing to its potent depigmenting attributes. The bulbous root, when consumed, is renowned for enhancing facial complexion, while its powdered seeds, applied topically for their Jaāli (detergent) effect, display remarkable efficacy in addressing blemishes and countering hyperpigmentation [31, 64].

Various studies exploring different parts of *Raphanus sativus L.* have highlighted its significant impact on inhibiting tyrosinase, a crucial enzyme in melanin production. The investigation of the aqueous seed extract revealed a commendable 73.8% inhibition of mushroom tyrosinase [65]. Freeze-dried root juice exhibited robust tyrosinase inhibition, boasting an IC50 value of 3.09 mg/mL, surpassing the methanolic extract's IC50 value of 9.62 mg/mL [74]. Extracts derived from pods showcased intriguing outcomes, with the dichloromethane extract demonstrating superior tyrosinase inhibition compared to the aqueous variant. At a concentration of 2,000 µg/mL, the dichloromethane and aqueous extracts exhibited 42% and 19% tyrosinase inhibition, respectively [75]. *In vitro* assays unveiled significant mushroom tyrosinase inhibition with Raphanus sativus L., reaching 88% in 50% propylene glycol solvent and 68% in ethyl acetate [76].

Majeeth (*Rubia cordifolia*)

It is esteemed as a potent skin care herb, revered for its ability to even out complexions and lighten dark spots. Unani texts enumerate its qualities as *Jali* (Cleanser), *Musaffi Khoon* (blood purifier), detoxifying agent, and even as sun protection [31, 41].

Chemically, it contains glucosides known as Manjisthin and Purpurine, along with resins, lime salts and colouring agents [53]. Methanolic extract of this herb has been reported to show 14.80% mean inhibition of tyrosinase activity thereby acting as skin whitening agent [49]. In another study Purpurin demonstrated significant inhibitory activity against the enzyme tyrosinase, with an IC50 value of 0.11±0.02 mg/mL for F4 and 0.29±0.09 mg/mL for purpurin. This inhibition was observed to be competitive in nature [77].

Rumman *(Punica granatum L.)*

It stands as one of the oldest known edible fruits, referenced in both the Bible and the Quran [78]. In Unani medicine, its juice is often recommended for enhancing facial complexion [41, 64]. The juice of *P. granatum* contains various phytochemicals, including Catechin and Procyanidins such as catechin, procyanidin B1, and B2; Anthocyanins and Anthocyanidins like anthocyanins, cyanidin, and delphinidin; Organic Acids such as chlorogenic acid, citric acid, and gallic acid; and Flavonoids including quercetin and rutin. This fruit showcases antioxidant properties attributed to ellagic acid, hydrolyzable tannins, punicalagin, punicic acid, and anthocyanins [79].

Research on *Punica granatum* has revealed significant findings related to skin care. For instance, the polysaccharide fraction isolated from its rind displayed noncompetitive inhibition of tyrosinase, exhibiting a 43% inhibitory activity at a concentration of 10 µg/ml [80]. Methanolic extracts from the fruit and peel of Punica granatum demonstrated tyrosinase inhibitory activity, recording 14.16% and 34.11% inhibition at 1000 µg/mL, respectively [49].

Furthermore, studies on pomegranate rind extract (PE) with 90% ellagic acid indicated its capability to inhibit skin pigmentation by reducing melanin synthesis and melanocyte proliferation. Its efficacy matched that of arbutin in inhibiting tyrosinase and, when orally administered, reduced UV-induced pigmentation in guinea pigs, akin to L-ascorbic acid. These findings highlight the potential of PE as an oral skin-whitening agent, effectively impeding melanin production and melanocyte growth [81].

Badam Talkh *(Prunus amygdalus)*

Bitter almond, stands as a significant and nutritious medicinal herb. Its historical use in medicine for disease

prevention and treatment traces back to ancient times. The plant comprises around 44-55% of fixed oil, widely utilized in pharmaceutical and cosmetic industries [82].

In Unani Medicine (UM), bitter almonds play a vital role in formulations aimed at enhancing skin glow and promoting fairness [64]. Additionally, they're noted for their effectiveness in addressing various skin disorders such as dandruff, tinea cruris, urticaria, herpes, pityriasis nigra, melasma, and different types of hyperpigmented lesions [31, 41, 70].

Recent studies have showcased the potential of bitter almond extracts in inhibiting tyrosinase, a key enzyme involved in melanin production. The aqueous extract from bitter almond seeds displayed compelling inhibition rates, recording 100% inhibition of mushroom tyrosinase and 78.9% inhibition of murine melanoma tyrosinase, even surpassing the inhibition seen with kojic acid as a control [65]. Furthermore, methanolic extracts demonstrated tyrosinase inhibitory activity, showcasing 10.92% inhibition at 1000 µg/mL.[49] Moreover, the 50% ethanolic extract derived from the leaves of Prunus amygdalus exhibited potent inhibition of tyrosinase activity [83].

Nārmushk (*Mesua ferrea*)

Nārmushk, may not be widely recognized in Unani medicine for skincare purposes, but its documented potential as a skin glow enhancer is evident [31]. Scientific evaluations have confirmed its antioxidant properties, blood purifying effects, and potential application in cosmetics. Phytochemical analysis identifies phenyl coumarins, xanthones, triterpenoids, and flavonoids as the primary compounds responsible for its diverse biological activities [84].

A study has highlighted the potent antioxidant activity of *Mesua ferrea*, showcasing similarities to standard ascorbic acid [85]. Additionally, solvent extracts from chestnut flowers, part of the Nārmushk plant, exhibited noteworthy mushroom tyrosinase inhibitory effects, comparable to renowned agents like arbutin. Furthermore, these extracts showcased protective attributes against ultraviolet (UV) rays, positioning as a strong candidate for cosmetic applications [86].

Further investigation into *Mesua ferrea* revealed the isolation of biflavonoids-rhusflavanone and mesuaferrone B-from its stamens. These biflavonoids exhibited robust inhibitory activities against elastase and tyrosinase, signifying their potential for skincare applications[87].

Jarjeer *(Eruca sativa)*

Jarjeer, holds a reputation in Unani Medicine for its cleansing and rubefacient (skin reddening) properties, making it a favorable choice for various skin conditions associated with hyperpigmentation [41, 88].

Studies focusing on *Eruca sativa* extract have demonstrated its potent antioxidant capacity, notably exhibiting high DPPH radical scavenging activity (ID50, 17.60 mg/L). Additionally, this extract displayed inhibitory effects on tyrosinase activity (ID50, 132.54 mg/L), consequently reducing melanin content (ID50, 158.90 mg/L) [89].

Extraction of *Eruca sativa* with 70% ethanol (ES) followed by fractionation using different solvents revealed interesting outcomes. The ethyl acetate fraction (EEA) demonstrated notable mushroom tyrosinase inhibitory activity. Moreover, ES, EEA, and the n-butyl alcohol fraction (EBuOH) exhibited substantial inhibition of tyrosinase activity. These findings led to the conclusion that ES may possess skin-whitening efficacy [90, 91].

Halela siyah (*Terminalia chebula*)

Within Unani medicine, it has long been utilized and remains an integral component of various formulations, especially *Itrifal* [31]. While primarily acknowledged for its remarkable efficacy in addressing digestive problems, it also holds well-documented recognition as a skin-whitening agent in Unani Medicine [41].

The herb boasts a rich chemical composition, comprising nine phenolic compounds, including two phenolic carboxylic acids, seven hydrolyzable tannins, and eight triterpenoids. Studies involving the methanolic aqueous extract of *Terminalia chebula* gall have unveiled potent inhibitory activities against melanogenesis. Specifically, it exhibited a reduction in melanin content (ranging between 39.3% to 66.3%) in B16 melanoma cells stimulated by α-melanocyte-stimulating hormone (α-MSH). Of particular note is the impact of iso-terchebulin, a compound derived from *Terminalia chebula*, which demonstrated the ability to decrease the protein levels of key regulators involved in melanin synthesis. This included mitigating the levels of MITF (microphtalmia-associated transcription factor), tyrosinase, and related proteins [92]. These findings suggest its potential as a valuable skin-whitening agent for future cosmetic applications.

Jau *(Hordeum vulgare)*

Barley, a time-honored cereal recognized in Unani Medicine for its nutritional richness and soothing properties, boasts multifaceted therapeutic effects. In the realm of dermatology, *'Arad-e-*Jau,*'* barley's dough, takes center stage, addressing diverse skin issues-milia, pimples, dandruff, melasma, and hyperpigmentation-while enhancing skin complexion owing to its detergent-like attributes [31, 64]. Additionally, its oil finds recommendation in superficial fungal infections, adding to its dermatological applications. Studies also underscore barley's potential in disease prevention when included in diets [64].

The total phenolic compounds in barley byproducts-waxy and non-waxy-measured 18.60 and 17.92 mg/g of sample, respectively. Extracts from waxy whole barley, milled barley, and barley byproducts displayed 65.43%, 30.84%, and 54.62% DPPH radical scavenging activity, respectively. These extracts exhibited tyrosinase inhibition rates of 26.76%, 16.30%, and 33.60% at 250 ppm [93]. Lee *et al*.'s research spotlighted the superior antioxidant and skin-whitening attributes of fermented barley seeds, suggesting their potential in both the food and cosmetic industries [94].

Kim *et al*.'s findings emphasized hordenine, extracted from germinated barley, as a potent agent in reducing melanin production in human skin cells. Hordenine significantly reduces melanin content by inhibiting critical factors like MITF, tyrosinase, and related proteins TRP-1 and TRP-2, exhibiting negligible cytotoxic effects across various tested concentrations [95].

Zaranbad *(Curcuma Zedoaria)*

Zaranbad holds a significant place in Unani Medicine, often recommended for melancholic diseases. In dermatological contexts, it's utilized as a blood purifier and is effective against chronic skin conditions like scabies, acne vulgaris,

and melasma [53]. Fresh leaves are particularly advised for the latter. Its detergent-like effect contributes to skin glow and addresses hyperpigmentation issues. Unani Medicine also mentions its efficacy against insect bites. Additionally, its mixture with alum is employed for treating bruises [31, 41].
Various extracts of *C. zedoaria*, including ethanolic, ethyl, and water extracts, have demonstrated potent antioxidant activity [96]. The methanolic extracts of *Curcuma Zedoaria* fruit exhibited tyrosinase inhibitory activity, recording 4.60 at 1000 µg/mL [49]. A combination of *Curcuma zedoaria* and Aloe vera extracts showcased reduced tyrosinase activity in treated cells compared to control [97].
The aqueous extract displayed approximately 35% tyrosinase inhibitory activity, while the ethanolic extract of *Curcuma zedoaria* showed a 13.03% inhibition of mushroom tyrosinase [98].

Sa'ad ku'fi *(Cyperus rotundus)*
It, is a highly versatile medicinal plant with a wide array of pharmacological properties, frequently used in the Unani system of medicine to treat various ailments and as a preventive measure. Found in Unani oil and ointment preparations, it's valued for its capacity to induce dryness without causing adverse effects, making it particularly recommended for aiding in chronic wound healing [31, 99].
Although not explicitly employed for skin conditions, Sa'ad ku'fi boasts a rich history within Unani medicine for its efficacy in addressing blood disorders, indirectly contributing to the maintenance of healthy skin. Texts from Unani medicine suggest its application through rubbing and facial treatments to enhance skin radiance [41, 64].
Chemical analyses of *Cyperus rotundus* rhizomes have identified several compounds, including polyphenols, flavanol glycosides, saponins, Vitamin C, sesquiterpenoids, and essential oils. Studies examining the methanolic extract of this herb have demonstrated an 11.82% tyrosinase inhibitory activity, pointing to its potential as a natural antioxidant [49]. These findings propose a possible future application in skin-whitening cosmetics.

Satavar (*Asparagus recemosus*)
Satavar, has been employed for millennia due to its therapeutic and tonic properties. Dubbed the "*queen of herbs*," it's renowned for fostering love and devotion and is prominently recommended in Unani Medicine for issues related to the female reproductive system [100]. Its inclusion in many Unani blood purifier preparations is attributed to its reputation as a blood purifier. Additionally, it finds application in addressing melasma and expelling bile and black bile from the body [31, 41].
Studies on *A. racemosus* root extract in animals have shown antioxidant activity, believed to be due to the presence of flavonoids, polyphenols, and vitamin C.[100] Various solvent extracts of medicinal plants were assessed for their tyrosinase inhibiting potential, with Asparagus racemosus demonstrating the highest inhibition at 43.29% [98]. Another study involving the crude ethanolic extract of A. racemosus roots displayed potent tyrosinase inhibition. The extract was further characterized by Thin Layer Chromatography (TLC) and High-Performance Liquid Chromatography (HPLC), revealing the presence of steroids-terpenes, alkaloids, and flavonoids [101].
Notably, research identified A. officinalis spears as the most potent extract, exhibiting significantly high inhibition rates for MMP-1, elastase, and hyaluronidase. At the same concentration, the A. officinalis spear extract surpassed oleanolic acid and epigallocatechin gallate, renowned natural MMP-1 inhibitors, particularly in MMP-1 inhibition [102].

Table 1: List of Selected Unani Botanicals Used for Enhancing Facial Complexion [12, 31, 41, 48, 53-56].

No.	Unani name (Scientific name)	Common name	Family	Parts used
1.	Za'faran *(Crocus sativus L.)*	Saffron	Iridaceae	Stigmas / Styles
2.	Sibr *(Aloe barbadenis Mill.)*	Aloe vera	Liliaceae	Leaf
3.	Azad Darakht-E-Hindi *(Azadirachta indica)*	Neem	Meliaceae	Leaf, Bark, seed
4.	Zard Chob *(Curcuma longa L.)*	Turmeric	Zingiberaceae	Rhizome
5.	Sandal Safed *(Santalum album)*	White sandalwood	Santalaceae	Wood
6.	*Nakhood (Cicer arietinum)*	Chickpea	Fabaceae	Seeds
7.	Asl-us-soos *(Glycyrrhiza glabra)*	Liquorice	Leguminosae	Roots
8.	Gule Surkh *(Rosa damascene)*	Rose	Rosaceae	Flower petals
9.	Ushbā *(Hemidesmus indicus)*	Indian sarasparilla	Asclepiadaceae	Root
10.	Turb *(Raphanus sativus L.)*	Radish	Brassicaceae	Seeds, roots
11.	Majeeth *(Rubia cordifolia L.)*	Madder	Rubiaceae	Stem, root
12.	Rumman *(Punica granatum L.)*	Pomegranate	Punicaceae	fruit juice, peel
13.	Badam Talkh *(Prunus amygdalus)*	Bitter almond	Rosaceae	Seeds, leaf
14.	Nārmushk *(Mesua ferrea)*	Iron-wood/ Chestnut	Guttiferae	Flower bud
15.	Jarjeer *(Eruca sativa)*	Rocket salad	Cruciferae	Seed
16.	Halela siyah *(Terminalia chebula)*	Chebulic Myrobalan	Combretaceae	Fruit
17.	Jau *(Hordeum vulgare)*	Barley	Gramineae	Seeds
18.	Zaranbad *(Curcuma Zedoaria)*	Zedoary	Zingiberaceae	Rhizome
19.	Sa'ad ku'fi *(Cyperus rotundus)*	Nutgrass	Cyperacea	Rhizome
20.	Satavar *(Asparagus recemosus)*	Asparagus	Asparagaceae	Root

Discussion
The increasing inclination towards natural solutions and the pursuit of clear, even-toned skin has led to a high global demand for herbal cosmetics aimed at skin whitening. Achieving lighter skin isn't just a matter of personal and social importance but is also linked to broader health concerns that necessitate specific interventions. Given that inhibiting tyrosinase remains a key method for skin lightening, herbs possessing this property hold significant potential as agents for reducing pigmentation.
In Unani Medicine, the vitiation of the *Akhlāṭ Arbaʿa* (four humors) is attributed to the deterioration of skin health,

including its radiance, tone, complexion, and various dermatological conditions. Specifically, concerning skin darkening and other hyperpigmented ailments such as *Kalaf* (melasma), *Barash* (freckles), *Namash* (Naevus), *Khīlān* (moles), *Āthār al-Qurūḥ* (Scar marks) etc. the predominance of "*sawda*" (black bile) is primarily associated. Medications that restore the balance of black bile and possess *(Musaffi Dam)* hemopurifying properties are basically considered skin lightening agents. The effect of medications used topically for skin whitening is achieved through their *'jali'* (detergent) and *'Musakhkhin'* (Calorific) properties on the skin.

Exploring these botanicals uncovered novel compounds and extracts, opening possibilities for new skincare formulations. However, while these studies demonstrate promising outcomes, further investigations into their mechanisms and clinical efficacy are crucial for their potential integration into cosmetics and skincare products. The unique chemical composition and various extraction methods of these plants emphasize the need for continued research to harness their full therapeutic potential in addressing skin-related concerns within Unani Medicine and broader cosmetic applications.

As far as our understanding goes, this review marks the initial effort to gather and connect the potential mode of action of *Mohsine lawn* herbs, detailing their perspectives both in Unani medicine and in biomedicine. All the herbs scrutinized in this evaluation were observed to directly or indirectly exhibit *Mohsine lawn* properties according to the Unani system, also displaying an ability to hinder the activity of the tyrosinase enzyme**.** Table No.1. This suggests their potential usage as potent skin-whitening remedies and in the treatment of hyperpigmentation conditions in upcoming cosmetic formulations. Numerous individual herbs like *Arde Baqla*, *Husne Yusuf*, *Chukandar* as well as polyherbal or herbo-mineral blends, have been associated with *Mohsine Lawn* characteristics in Unani texts. Conducting Tyrosinase inhibition studies on these herbs can unlock their prospective use as skin lightening agents.

Conclusion

The diverse botanical resources documented in Unani Medicine present a wealth of potential for skincare applications. Sibr, Azad Darakht-E-Hindi, Sandal Safed, Asl-us-soos, Rumman, among others, have showcased significant abilities to inhibit tyrosinase, offering promise in addressing hyperpigmentation and enhancing skin vitality. While these findings are encouraging, further research into specific compounds, mechanisms of action, and clinical validations is crucial to fully harness their therapeutic benefits. Integrating these natural remedies into skincare formulations could provide safer and potentially more effective options compared to conventional treatments, contributing to the evolving landscape of cosmeceuticals and dermatology. The insights from these botanicals underscore their relevance in modern skincare, paving the way for innovative formulations that address diverse skin concerns.

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