Clinical, Cosmetic and Investigational Dermatology Dovepress

Open Access Full Text Article REVIEW

# Prevention of Melasma During Pregnancy: Risk Factors and Photoprotection-Focused Strategies

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**Abstract:** Melasma is a benign but emotionally distressing skin condition that reduces patients' quality of life, with prevalence rates during pregnancy ranging from 36.4% to 75%. Troublingly, up to 30% of cases are reported to persist after delivery, even ten years later. And recurrence and aggravation are common in subsequent pregnancies. This review examines the risk factors and mechanisms associated with melasma during pregnancy and summarized corresponding preventive strategies. We emphasize the critical role of photoprotection, including the use of sunscreens from the first trimester, in reducing the incidence of melasma.

**Keywords:** melasma, pregnancy, risk factors, prevention, photoprotection

## Introduction

Melasma is a chronic acquired skin condition, characterized by symmetric, light-to-dark brown hyperpigmentation in areas exposed to sunlight. During pregnancy, melasma, also known as "mask of pregnancy" or "chloasma gravidarum".[1] It primarily affects women with darker skin types (Fitzpatrick phototypes III-VI).[2] The prevalence of melasma during pregnancy varies widely depending on population and geographical regions, ranging from 36.4% to 75%.[3,4]

Pregnancy is a period that accompanied by numerous profound physiologic changes that affect all systems of the body. Endocrinological, immunological, metabolic, and vascular changes may influence the skin in various ways.[5,6] In most literature, melasma during pregnancy is classified as a physiological skin change. Compared to other conditions that might occur during pregnancy, melasma is generally considered a mild clinical disorder, however, is worrisome to patients. Though benign, melasma negatively influences expectant mothers' emotional health, recreation, leisure and social life, which in turn reduces the quality of their life.[3] As reported, they were filled with feelings such as ashamed, low self-esteem, dissatisfaction, anhedonia, and lack of motivation.[7]

The precise mechanism of melasma during pregnancy remains elusive. As far as the current literature is concerned, it is triggered by a combination of hormonal factors, sun exposure, and genetic background.[8] Table 1 presents the risk factors of melasma during pregnancy, some of which are specific to this condition, while others are common to melasma.

A study carried out in Turkey revealed that, among the risk factors of melasma during pregnancy, there were statistically significant in parity, chronic disease, history of melasma in previous pregnancy and family history ($p < 0.05$).[3] The probability of developing melasma during pregnancy in multiparae was higher than that in primiparae. While other variables existed, pregnant women with a history of melasma during previous pregnancies were about 44 times more likely to develop the condition than women without that history. As for family history of melasma during pregnancy, 37.6% of the pregnant women had it in their mothers and 25.9% in their sisters.[3] A complex segregation analysis (CSA) conducted in Brazil suggests that melasma may adhere to an autosomal dominant inheritance pattern.[14] Existing studies, through transcriptomic analysis comparing melasma-affected skin with adjacent healthy skin, have identified numerous differentially expressed genes. These genes are involved in processes such as melanogenesis, melanosomes transfer, repair, angiogenesis, lipid metabolism, energy metabolism, and oxidative stress.[15,16]

Received: 25 July 2024
Accepted: 7 October 2024
Published: 15 October 2024

**Table 1** Risk Factors of Melasma During Pregnancy

| Specific to Melasma During Pregnancy | Nonspecific |
|---|---|
| History of melasma in previous pregnancy | Fitzpatrick phototypes III–VI |
| Family history of melasma during pregnancy | Sun exposure |
| Multiparae | Thyroid autoimmunity and thyroid hormone abnormalities |
| Delaying first pregnancy | Nutrition |
| Multiple pregnancy | Anxiety and stress |
| | Sleep deprivation |
| | Drugs use (anticonvulsants, antidepressant, anxiolytic, etc) |
| | Air pollution |
| | Others |

**Note**: Data from these studies[3,9–13].

Another survey demonstrated that mothers who performed more activities outdoors or delayed their first pregnancy were more probable to develop melasma during pregnancy. The risk increased by about 8% for each year of age at first pregnancy. Women with multiple pregnancies had an increased risk of occurring melasma during pregnancy, even in their first pregnancy.[17]

Melasma during pregnancy may be transient, typically regresses within a year after delivery.[3] Nevertheless, it is reported that up to 30% of cases had persistence even after 10 years.[18] And recurrence and aggravation are common in subsequent pregnancies.[9] In addition to gestational rebound and postpartum self-improvement, melasma during pregnancy also has the characteristic of treatment-resistant.[19] Physiological and hormonal changes during pregnancy increase the risk of post-inflammatory hyperpigmentation and poor wound healing.[20] Therefore, following the principle of "cause no harm", in most cases, the treatment of melasma is not recommended during pregnancy.

Since melasma typically appears during the second trimester of pregnancy,[21] it is crucial for high-risk individuals to take preventative measures in the initial stages of pregnancy. Implementing prevention strategies during the initial stages of pregnancy can greatly reduce the occurrence of melasma.

## Photoprotection

Though exact impact of different wavelengths of sunlight and their combination on melasma are so far not fully understood, sun exposure plays a vital role in the pathogenesis of melasma. So that some scholars regard melasma as a photoaging disorder.[22] The effect of ultraviolet radiation (UVR) has been paid attention for decades. Generally, UVR affects melasma in a very complex and diverse way. It involves melanocytes, fibroblasts, keratinocytes, mast cells and sebocytes, as well as related factors and enzymes. And chronic UVR exposure induces melanin increase, basement membrane (BM) disruption, solar elastosis, oxidative stress, neovascularization and inflammation.[23–25] UVB (290–320 nm) and UVA (320–400 nm) are the clinically relevant UVR wavelengths. UVB affects fundamentally on the epidermis and BM, while UVA enters the upper dermis. Some scholars proposed a hypothesis suggesting that the sex steroid hormones also amplify the effects of UVR on melanogenesis, which further contributes to the hyperpigmentation observed in melasma.[26] Besides, recent literatures highlight the role of visible light (VL). VL penetrates deep into the dermis and skin appendages, but only shorter wavelengths (420–470 nm, blue and violet) participate in melasma lesions.[27] Unfortunately, UVA1 and VL have chronical and synergistic effect on melasma.[27]

Genetic background and hormonal changes caused by pregnancy are inevitable, therefore, photoprotection is the most important and effective measure to prevent melasma in the early stages of pregnancy. A study clearly proved that using a well-tolerated broad-spectrum sunscreen since first trimester could decrease the incidence of melasma during pregnancy in more than 90%.[28] In general, photoprotection includes avoiding sun exposure, seeking shade, using sunscreens, hats, sunglasses and sunshades.[29] Table 2 shows tips for various photoprotection methods.

Since UVA and visible light can penetrate through clouds and window panes, in addition to reducing outdoor activities, avoidance of sun exposure should include staying away from windows, especially during peak radiation

**Table 2** Tips for Photoprotection

| Measures | Tips |
|---|---|
| Avoiding sun exposure | Reduce outdoor activities and stay away from windows during peak radiation times. |
| Seeking shade | Shade can protect the skin from direct exposure to UVR, which is most effective during midday, but UVR can also reach the skin from other angles. |
| Using sunglasses | Sunglasses' protection effectiveness is strongly influenced by geometry, wearing position, head positions, and exposure conditions. Goggles provide the best protection from the sun. |
| Using hats | Choose a wide-brimmed hat. |
| Using sunshades | Choose a sunshade with low UV transmission. |
| Apply sunscreens | Choose a broad-spectrum physical sunscreen with a high SPF or a tinted sunscreen. Apply 20 min before sun exposure, and repeat every second hour or after contacting with water. |

**Note**: Data from these studies[32–37].

times. Fortunately, short-term exposure to low-dose of UVA, UVB as well as blue light, when conducting daily indoor activities (away from windows), has been shown to be irrelevant for melasma.[30,31]

Seeking shade is a convenient method to protect oneself from direct sunlight exposure, but it does not provide adequate protection.[38] Sunglasses, hats and sunshades reduce UVR and visible light exposure in corresponding areas.[29] Hats with wide-brimmed are recommended because they optimally cover the head and neck.[29] People also need to apply sunscreen when engaging in outdoor activities or staying close to windows for long periods of time.

Although there is no evidence that sunscreens pose any health risks, physical(inorganic) sunscreens are considered a safer option for pregnant women, owing to the systemic absorption of chemical (organic) sunscreens (many ingredients can be found in urine and breast milk).[32,39] The components of a physical sunscreen typically include zinc oxide (ZnO), titanium oxide ($TnO_2$), iron oxide, calamine, kaoline, icthamol, red veterinary petrolatum, etc.[19] ZnO and $TnO_2$ are the only two inorganic filters approved by the US Food and Drug Administration (FDA). Utilizing both of them could ensure a broad-spectrum protection for UVR in general, however, lack protection against VL.[40] Luckily, this deficiency can be remedied by tinted sunscreens. The ingredients of tinted sunscreens include iron oxide and titanium dioxide pigments, which provide effective photoprotection against both UVR and VL. By combining different amounts of iron oxides and pigmentary titanium dioxide, diverse shades of tinted sunscreen products have been developed for all Fitzpatrick skin phototypes, which exactly meets the aesthetic needs of women.[33] The characteristics of various sunscreens are shown in Figure 1.

The World Health Organization (WHO) recommends that sunscreen should be applied 20 min before sun exposure, and repeated every second hour or after contacting with water.[34] People typically apply sunscreen much less than the standard amount of sunscreen (2 mg/cm$^2$). Early reapplication and use of a higher sun protection factor (SPF) sunscreen are helpful to make up for the insufficiency.[41] As for concerns about using sunscreen that may lead to vitamin D deficiency, oral intake of vitamin D through supplementation and many foods is an easy way to get enough vitamin D.[38]

As researchers delve deeper into the study of sunscreen, they have made numerous discoveries and developed various hypotheses. Several herbal substances, including green tea extract, Eclipta prostrata, and cinnamaldehyde, have shown the prospect as adsorbents and antioxidants of UVR and with few side effects.[42,43] Adding antioxidants and free radical scavengers to sunscreen may help prevent some harmful effects of VL and also potentially protect against the damaging effects of infrared radiation.[44] Because the defects in the skin barrier can lead to pigmentation, some scholars have proposed adding moisturizers to sunscreen as it can help repair the skin barrier.[45] The authors hope that more commercial sunscreens will be available that are safe, comprehensive, and tailored to the needs of different people in the future.

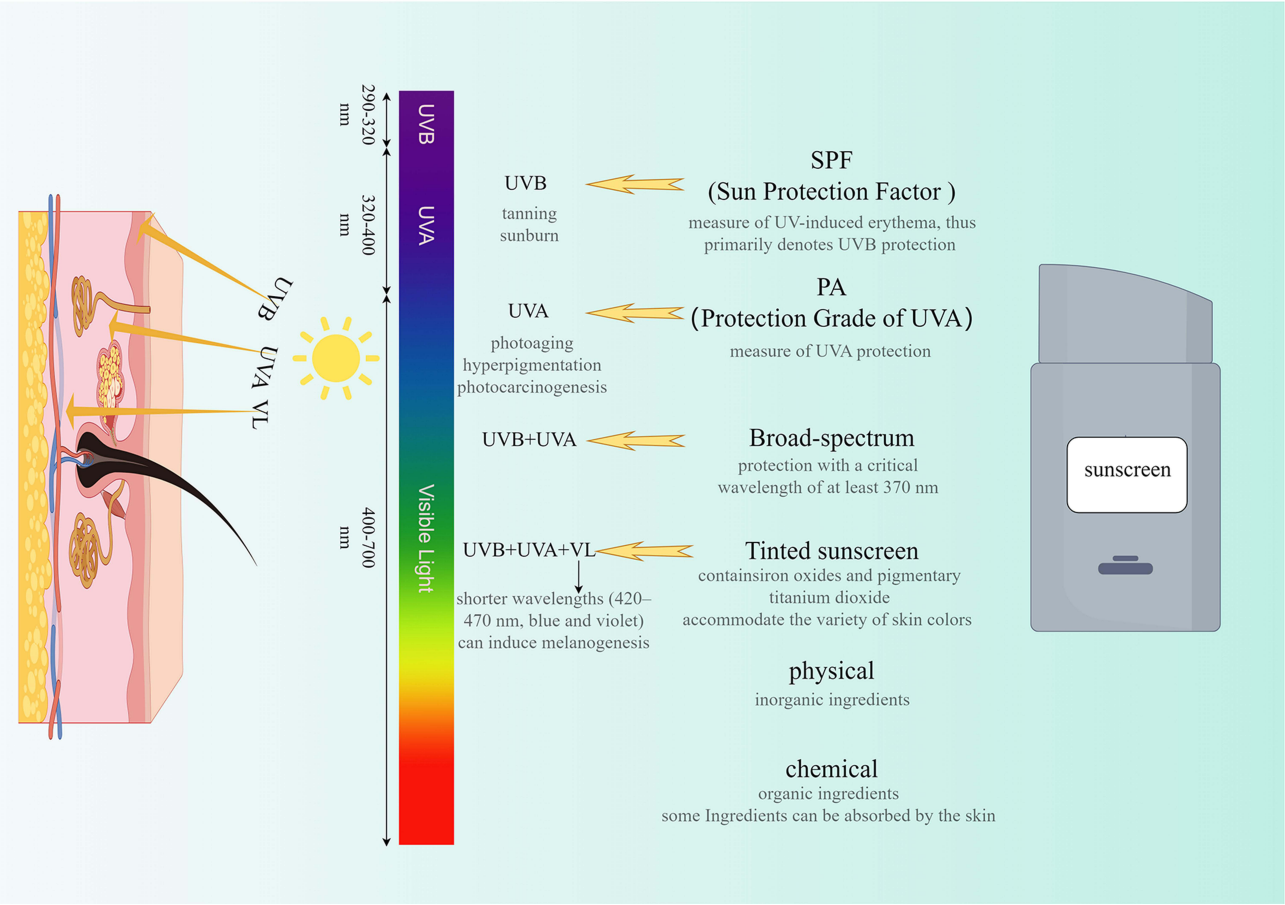


**Figure 1** The spectrum of light influencing melasma and the labeling of sunscreens (By Figdraw).

## Chronic Diseases

In order to meet the metabolic needs of the fetus and mother, the maternal thyroid hormone changes physiologically during pregnancy. But thyroid autoimmunity and thyroid hormone abnormalities are considered to be associated with melasma. Studies examining the association between melasma and thyroid diseases have produced inconsistent and contradictory conclusions. After conducting a case-control study, Yadav et al found that patients with melasma had lower thyroid function, but the difference was not statistically significant compared to the control group.[46] A cross-sectional study in Iran also showed no association between melasma and thyroid disease.[47] Rahman et al compared thyroid hormone levels in subjects with varying severities of melasma and found no significant differences.[48] In contrast, other studies have clearly indicated that thyroid disease is a risk factor for melasma. A case-control trial in India found that 73.33% of subjects with melasma had anti-TPO or anti-TG antibodies, compared to only 10% in the control group, with a higher prevalence of thyroid autoimmunity among patients with melasma.[49] Another cross-sectional study in India also showed a 65% positivity rate for anti-TPO.[50] Both Khan et al and Mehmood et al reported a higher proportion of hypothyroidism.[51,52] Finally, two meta-analyses collectively concluded that patients with melasma had higher levels of TSH and anti-TPO antibodies.[10,53] Based on the grading criteria for evidence-based medicine, the authors are inclined to agree that there is an association between melasma and thyroid disease.

Therefore, thyroid evaluation should be conducted during pregnancy, and if abnormalities are found, treatment should be carried out under the guidance of an endocrinologist.

By the way, melasma is also called “liver spot”. People tend to relate liver disease to melasma,[54] but in fact, there is not enough clinical evidence to confirm this. A case-control study showed a higher serum LDL level in melasma patients

compared to healthy women, however, there were no differences in the incidence and grade of fatty liver disease between the two groups.[55]

## Nutrition

Diet plays a crucial role in maintaining and improving overall human health. There is increasing evidence suggests that skin condition is related to the potential role of dietary compounds and gastrointestinal microbiota in the gut skin axis.[56] Suruchi et al found that patients with melasma mostly (91.66%) suffered from severe protein deficiency, despite their wealth.[57] They proposed a hypothesis that skin and hair tissue consciously and selectively self-destruct in the presence of high carbohydrate and low protein. This helps explain the relationship between protein deficiency and melasma. They also believed that an inadequate supply of amino acids would limit the skin's ability to repair light damage. However, this study is cross-sectional and lacks a control group; the measurement of protein levels was estimated through the subjects' daily food intake, which lacks objective indicators. Nevertheless, it provides an intriguing perspective that warrants further validation through more rigorous clinical trials with objective measures. Additionally, their hypothesis necessitates verification through animal studies to substantiate its credibility.

Zinc is an essential trace element that is indispensable for normal growth and development at all stages of life. It has various biological functions such as antioxidant, maintaining the completeness of the tissue barriers, and participating in immune regulation.[58] A study conducted in Iran confirmed a significant relationship between low zinc levels and melasma.[59] Among a total of 118 patients with melasma, 45.8% had serum zinc deficiency, compared with 23.7% of healthy control patients. Accordingly, the researchers speculated that zinc deficiency might be involved in the pathogenesis of melasma. Another recent study reported zinc deficiency in 43.3% of patients with melasma and suggested that zinc supplementation could be recommended as part of the routine treatment for melasma.[60] Some other researchers, recognizing the antioxidant capabilities of zinc, have directly investigated the use of oral or topical zinc in the treatment of melasma. However, further clinical trials are necessary to establish whether there is a correlation between melasma and zinc deficiency.

Vitamins, lycopene, flavonoids, carotenoids, astaxanthin and other nutrients have been reported to have antioxidant properties.[61] However, more of these dietary antioxidants is not always better, because they can become pro oxidants at high doses.[56] Actually, for each specific physiological or pathological condition, there is a need to understand the balance between reactive oxygen species (ROS) and antioxidants. Supplements are not advocated.[62]

Intake of adequate protein and dietary antioxidants from fresh foods such as lean meat, fish, fruits and vegetables aligns perfectly with the dietary guidelines for pregnant women in various countries. Zinc is not valued as much by pregnant women as other trace elements such as iron, calcium and magnesium. But for individuals at high risk of melasma, zinc screening and oral zinc supplementation may be beneficial in preventing the occurrence of melasma.[2]

## Mental Health and Sleep

Numerous studies have reported that patients with melasma exhibit a higher prevalence of anxiety and depression.[63,64] However, there is a bidirectional causal relationship between them, which can easily lead to a vicious cycle. Research by Handel et al and Kunninpuram et al has confirmed that anxiety traits and stress are risk factors for melasma.[65,66] What's worse, pregnant women are inherently more likely to experience anxiety and depression, carrying a psychological burden.[67]

Some scholars also categorize melasma under the realm of psychodermatology, where anxiety and depression are involved in the pathophysiology of melasma.[68,69] The neuroendocrine and immune systems play significant roles in this process.[70] The pathways of stress and anxiety involve the disruptions in the function of hypothalamus-pituitary-adrenal (HPA) axis. The activation of HPA axis is relevant to pigmentary disorders as well.[71] There is also an evidence to suggest that stress leads to damage to the skin barrier, oxidative stress and deterioration of recovery.[70,72] To make matters worse, antidepressant/anxiolytic use is also a risk factor for melasma.[65]

In modern industrialized societies, sleep deprivation and sleep quality are global health concerns. Psychosocial factors can affect sleep, and insufficient sleep may trigger or further intensify feelings of anxiety.[73] Lyu et al have confirmed through observational studies that psychological stress can damage the skin barrier through sleep deprivation and severe

anxiety.[74] Jang et al's two studies both concluded that long-term sleep deficiency leads to a decrease in skin elasticity and reduced hydration.[75,76] Furthermore, a clinical trial revealed that facial skin yellowing can be exacerbated by insufficient sleep, and even after sleep deprivation ceases, the higher degree of yellowing can persist.[77] Sleep deprivation also plays a role in skin aging and the skin microbiome.[78]

An increasing amount of molecular imaging evidence suggests that specific neurotransmitter mechanisms involved in sleep-wake regulation are related to anxiety.[73] Hyperactivation of the HPA axis, increased levels of circulating stress hormones, impaired skin barrier function, and oxidative stress damage can all be induced by sleep deprivation, potentially leading to the development of melasma.[79,80]

Valuing mental health, improving anxiety symptoms and sleep are not only of great significance for improving quality of life, but also help prevent or treat melasma. There are many non-pharmacological interventions that can improve mental health and sleep, such as lifestyle interventions, sleep manipulation and psychological counseling.[73]

## Environment

Melasma and photoaging are both associated with rising air pollution levels.[11] A cross-sectional study from China observed that women from more heavily polluted cities faced compromised barrier function and had a relatively darker complexion.[81] It was found that exposure to air pollution associated with traffic, such as diesel exhaust particles (DEPs), nitrogen dioxide ($NO_2$) and fine particulate matter (PM), could potentially lead to skin hyperpigmentation.[82,83] The DEPs-induced oxidative stress response appears to stimulate increased melanin synthesis.[84] $PM_{2.5}$ has been discovered to activate the aryl hydrocarbon receptor (AhR), induce skin inflammation, and generate reactive oxygen species, which may lead to melanogenesis.[85] Pigmented spots have also been proven to be the consequence of an interplay between UVR and traffic-related air pollution.[86] Therefore, it is important to take measures to minimize exposure to traffic-related air pollution, and adopt antioxidant and sun protection measures that are safe for pregnant women to mitigate the risk of developing melasma caused by air pollution.[87,88]

Additionally, cigarette smoke is one of the environmental factors that contribute to skin aging and hyperpigmentation.[87] This is evidenced by the darker skin tone of Japanese women who smoke compared to non-smokers.[89] Even areas that are not directly exposed to smoke are affected. Smoking disrupts the homeostasis of barrier proteins and lipids, altering the activity of melanocytes.[90,91] Nicotine may also accumulate in human tissues containing melanin, which could potentially increase melanin synthesis.[92] At present, there is no direct evidence to prove the relationship between smoking and melasma. However, for the health of the mother and fetus, the authors still recommend avoiding smoking and environments contaminated by cigarettes.

## Miscellaneous

The use of cosmetics is also one of the exogenous factors of melasma.[18] This may be related to the presence of heavy metals and photosensitive substances in certain cosmetics. Cosmetics can also cause contact dermatitis, which triggers skin inflammation that can lead to melasma.[12,93] Thus, cosmetics must be chosen carefully. Antimalarial drugs, anticonvulsants, amiodarone, and other drugs can cause skin pigmentation by stimulating melanogenesis or depositing in the surface layers.[18] This requires communication with the relevant doctor to avoid the aforementioned drugs, if feasible. Moreover, it was found that the severity of melasma increased with the duration of exposure to cooking or occupational heat.[21] Reducing cooking or occupational heat exposure may be helpful.

## Limitations and Recommendations

Perhaps due to variations in prevalence rates, research on melasma has been predominantly focused on regions such as Asia, the Middle East, and Brazil. Despite its impact on the quality of life for those affected, studies on melasma during pregnancy are limited. We endeavor to provide a comprehensive summary of the risk factors for melasma during pregnancy, with the aim of better preventing its occurrence. However, some factors, such as protein deficiency, zinc deficiency, and sleep deprivation, lack robust evidence and have unclear mechanisms of action. Therefore, we recommend conducting more prospective studies on the risk factors and mechanisms of melasma during pregnancy across different regions.

## Conclusion

During pregnancy, the female body undergoes significant physiological changes that may lead to the development of melasma. It is important for physicians to provide adequate reassurance to their patients and avoid unnecessary stress. To mitigate the incidence of melasma, pregnant women should receive accessible and accurate education about identifying and avoiding risk factors, as well as taking preventive measures.

## Abbreviations

UVR, ultraviolet radiation; BM, basement membrane; VL, visible light; ZnO, zinc oxide; $TnO_2$, titanium oxide; FDA, Food and Drug Administration; WHO, World Health Organization; SPF, sun protection factor; PLE, polypodium leucotomos; CSA, complex segregation analysis; ROS, reactive oxygen species; HPA, hypothalamus-pituitary-adrenal; DEPs, diesel exhaust particles; $NO_2$, nitrogen dioxide; PM, particulate matter; AhR, aryl hydrocarbon receptor.

## Consent for Publication

The manuscript is published with the consent of all authors.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This review was supported by grants from Clinical efficacy evaluation of Picosure 755 honeycomb picosecond laser combined with Qichu whitening cream in the treatment of melasma and experimental study on melanocyte metabolism and tyrosinase expression in a mouse model, under No. 2023YFS0331; Development and Application of Qichu whitening formula in treating melasma, under No. 2024zd022; A clinical study and mechanism explanation of Sanhuang Zengmian Tang's regulation of fibroblast aging and treatment of qi and yin deficiency type melasma based on SCF/c-kit/MAPK signaling pathwayl, under No.2024YFFK0165.

## Disclosure

The authors declare that they have no competing interest in this work.

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