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Review Article

The Potential of Strawberry (*Fragaria ananassa*) Fruit Extract in the Treatment of Hyperpigmentation: A Mini Review

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ABSTRACT

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Copyright: © 2025 Purnomo *et al.* This is an openaccess article distributed under the terms of the <u>Creative Commons</u> Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. Hyperpigmentation is a skin condition that significantly affects aesthetics. It is caused by an increase in melanogenesis or uneven distribution of melanin, resulting in the darkening of skin colour. The gold standard for treating hyperpigmentation is the use of hydroquinone, but this substance has many adverse effects on the body. Therefore, assessing the potential for the use of natural extracts, such as strawberries, for the treatment of hyperpigmentation is essential. The aim of this study was to identify the active compounds in strawberry extract, explain its mechanism of action in the treatment of hyperpigmentation, and evaluate its feasibility as a natural alternative in skincare formulations, providing a safe, effective, and sustainable solution for hyperpigmented skin. A literature search was conducted, and data were obtained from various databases such as PubMed, Google Scholar, NCBI, and ResearchGate. The results of the study indicated that ethanol extract of strawberry fruit can improve skin colour, skin hydration, and firmness, while also reducing the visibility of hyperpigmentation. The ethanol extract of strawberry fruit has the potential to act as a sunscreen and tyrosinase inhibitor, effectively inhibiting melanin formation, making it a promising treatment for hyperpigmentation.

Keywords: Strawberry, Fragaria ananassa, Fruit Extract, Hyperpigmentation.

Introduction

Hyperpigmentation is a common usually harmless skin condition that affect a lot of people around the world, especially in tropical countries.¹ The prevalence of hyperpigmentation in tropical countries is quite high due to the skin phototypes of people in these regions which is classified as Fitzpatrick skin phototypes IV and V. This skin phototypes rarely burn and tend to tan (darken) easily.¹ In addition, tropical climate conditions and intense sun exposure increase the incidence of hyperpigmentation. This condition results in various complaints that negatively impact both appearance and quality of life, especially when it affects exposed areas such as the face.² This can reduce a person's self-confidence when interacting with others, and if left untreated for a long time, it can cause stress and depression.² For this reason, prevention and treatment efforts are needed both before and after the appearance of hyperpigmentation on the skin. Melanin is a pigment molecule that is synthesized endogenously by melanocytes.³ Melanin is found in the skin and hair acting as a light and temperature protector, and as a coloring agent. Melanin is a protective pigment that can act as a free radical scavenger on the skin, but has the effect of producing a darker skin colour.

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The formation of melanin is a product of a complex biochemical event that begins with the amino acid tyrosine and its metabolite, 3,4dihydroxy phenylalanine (DOPA).³ The type and quantity of melanin produced by melanocytes are determined by genetics and can be affected by various external and internal factors, including hormonal fluctuations, inflammation, aging, and exposure to UV light.⁴ Exposure to ultraviolet (UV) rays is one of the main causes of hyperpigmentation.1 UV light triggers an increase in tyrosinase enzyme activity, which plays a role in stimulating melanin production by melanocytes. Melanin itself is a natural pigment found in the epidermis layer of the skin and has an important function as a natural protector of the skin from harmful UV radiation from the sun. However, excessive melanin production can lead to hyperpigmentation.⁵ This process occurs when the transfer of melanosomes, which contain melanin, from melanocytes to keratinocytes increases, resulting in an increased amount of melanin in the skin. As a result, excessive exposure to UV radiation can trigger excessive melanin formation and lead to abnormal accumulation of melanin, resulting in hyperpigmented patches on the skin.6

Hydroquinone, a hydroxy phenolic compound, is considered the gold standard for topical hyperpigmentation treatment. However, it can be toxic to melanocytes.¹ Hydroquinone has been linked to various side effects, such as exogenous ochronotic, contact dermatitis and skin irritation, especially in individuals with darker skin tones. Due to these adverse effects, it has been banned for use in cosmetic products in many countries, including those in the European Union.⁷ While hydroquinone has not been proven to increase cancer risk in humans, concerns about its safety have led to a growing demand for safer and effective alternative skin-lightening agents.⁸ Therefore, it is necessary to search for alternative treatments for hyperpigmentation that are safe for human health, one of such alternative agents could be plant-based natural lightening ingredients such as strawberries.

Strawberries contain vitamins, fiber, low calories, folate, potassium, and are rich in anthocyanin pigments as the flavonoid component.⁹ According to Cai *et al.*,¹⁰ strawberries have tyrosinase inhibitory activity which is attributed to their vitamin C and flavonoids content.¹⁰ Vitamin C inhibits the conversion of dihydroxyphenylalanine (DOPA)

to *O*-dopaquinone, and ultimately inhibit the formation of dopachrome and melanin.¹¹ Phenolic components (flavonoids) on the other hand act as alternative enzyme substrates due to their high affinity for the tyrosinase enzyme, so that the formation of dopachrome is inhibited.¹² Strawberries are potential source of bioactive ingredients that can prevent skin pigmentation through their tyrosinase enzyme inhibitory activity. However, research regarding the use of strawberries as treatment for hyperpigmentation is still limited. Therefore, this study was conducted to assess the potential of strawberry fruit extract (*Fragaria ananassa*) in treating hyperpigmentation through a review of literature.

Based on previous research, the molecular mechanism underlying the pink coloration of strawberry fruit skin was revealed through combined analysis of the transcriptome and metabolome. This study successfully identified key genes and metabolic pathways involved in the biosynthesis of pigments such as anthocyanins and flavonoids, which are responsible for the distinctive coloration.¹³

The novelty of this review lies in the specific exploration of bioactive components in strawberries, such as ellagic acid and vitamin C, which have unique potential in inhibiting the tyrosinase enzyme and reduce melanin production, a key mechanism in the treatment of hyperpigmentation. This study contributes to existing literature by integrating current scientific evidence related to the use of natural ingredients in dermatology, specifically to treat hyperpigmentation that is often a concern in cosmetics and skin health. The aim of this study was to identify the active compounds in strawberry fruit extract, elucidate its mechanism of action in treating hyperpigmentation, and evaluate its feasibility as a natural alternative in skincare product formulations that are safe, effective, available, and affordable by the community.

Materials and Methods

The study utilized a scoping review approach to analyze literature relevant to the potential of strawberry (Fragaria ananassa) fruit extract in treating hyperpigmentation. The literature search was conducted using databases such as PubMed, Google Scholar, NCBI, and ResearchGate, with keywords including "Effect," "Strawberry," "Fragaria ananassa," "Fruit Extract," and "Treating Hyperpigmentation." Articles were screened based on inclusion criteria: publications within 2014-2024, relevance to the topic, availability of full-text, and exclusion of reports or editorials. From an initial 2595 articles, only 10 met the criteria for inclusion. The methodology followed Arskey and O'Malley's framework, including defining research questions, identifying studies, selecting articles, data extraction, and presentation of findingsThe research review approach used in this study is a scoping review by analyzing various collections of literature that are adjusted to the subject matter of this study. The subject of this study is a collection of literature containing previous research related to the title of this study. Literature sources were obtained through searches using databases consisting of Pubmed, Google Scholar, NCBI, and Researchgate. The keywords used in this study to search for related articles are "Effect", "Strawberry", "Fragaria ananassa", "Fruit Extract", "Treating Hyperpigmentation". The search was carried out by considering the title, abstract, theory and methods used. The articles used in compiling this scoping review are related to the potential of strawberry (Fragaria ananassa) fruit extract in treating hyperpigmentation. The inclusion criteria applied in the article search are: 1) the range of article publications. , starting from 2014-2024 (the last 10 years); 2) is an international journal;.14

During data analysis, the information from 10 selected articles was systematically extracted into a table to organize details such as the author, publication year, participant demographics, sample size, methodologies employed, and key findings. This structured table aims to facilitate a clear presentation and comprehensive understanding of the review's findings. To ensure data quality and validity, a rigorous identification process was carried out. The procedure involved several steps: 1) examining the article titles for relevance to the study's topic, 2) verifying the authorship of each article, 3) assessing the journal's name, volume, issue, and publication year for credibility, and 4) analyzing the abstracts, as they provide concise yet informative summaries of the studies. The abstract evaluation was particularly critical in ensuring the selected articles offered complete and systematic data, improving the accuracy and reliability of the review process.

Results and Discussion

Study selection

The search process identified a total of 2595 articles from four databases: PubMed (185 articles), Google Scholar (2240 articles), NCBI (50 articles), and ResearchGate (120 articles). After removing 1205 duplicate entries, 1390 articles were left, out of which 640 articles were excluded based on the inclusion criteria for publication year, and 432 were excluded due to the irrelevance of their titles. An additional 275 articles were excluded because they lacked complete text. This screening process narrowed the selection to 43 articles, out of which 15 met the inclusion criteria. Finally, a critical appraisal of these 15 articles was conducted, resulting in 10 articles being deemed suitable for inclusion in the review.

Study characteristics

There were 10 articles reviewed in this study related to the potential of strawberry fruit extract (Fragaria ananassa) in the treatment of hyperpigmentation. The ages of the subjects of the study varied widely (45-70 years),¹⁵ and there was a study that used pigs of about 3-4 months old as research subjects,¹⁶ while the other studies did not mention the age of the subjects used,¹⁶ and 7 studies did not use human or animal samples.^{2,8,17-21} There were various methods for evaluating the potential of strawberry fruit extract (Fragaria ananassa) in treating hyperpigmentation, these included a randomized post-test only control group design experimental study using One Way ANOVA and Tamhane Post Hoc test.¹⁵ Another study used an experimental study using Statistica 12.0 (StatSoft Poland, Krakow), and the measurement of melanin level and erythema was performed using Mexameter.¹⁵ Furthermore, another study used the experimental study method using SPSS and the measurement of melanin levels using a light microscope.16 While some other studies used the systematic review method.^{2,17,20} Furthermore, other studies used the comparative study method,^{19,21} the experimental study method using STATISTICA software (Statsoft Inc., Tulsa, OK, USA),8 and the anti-tyrosinase activity test using the spectrophotometric method.18

The potential of strawberries (Fragaria ananassa) in treating hyperpigmentation

The skin plays a crucial role in facilitating interaction between the body and its surroundings. It safeguards the body from mechanical and chemical harm, helps regulate body temperature, supports both innate and adaptive immune functions, and serves as a sensory organ. Additionally, the skin is integral to personal identity, as it is deeply connected to physical appearance, self-esteem, and a sense of personal continuity.18 The fundamental self-concepts that influence the use of cosmetics, personal care products, and other aesthetic items are often related to hyperpigmentation on the skin, particularly on the face. This condition can disrupt one's appearance and diminish self-confidence.18 Research has shown that the use of depigmenting cream is able to exfoliate the skin and increase cell turnover, helping to remove cell pigment.²² However, most commonly used cosmetic products are chemical-based and are associated with side effects which are often inevitable.8 Cosmetic products contain a wide range of chemicals that can provide skincare benefits, but long-term use or inappropriate skin type can cause side effects. Some chemicals in cosmetic products, such as parabens, sulfates, and synthetic dyes, have the potential to cause irritation, allergies, or other skin reactions.²³ Using products that contain harsh ingredients or ingredients that are not compatible with the skin can worsen skin conditions, causing acne, redness, or even premature aging. It is therefore important to select products that suit the skin type and avoid harmful chemicals that can have a negative impact on skin health.²⁴ Hence, there is the need to investigate natural products derived from plants for their role in the prevention and treatment of hyperpigmentation. This literature review generally focused on the potential of strawberry fruit extract (Fragaria ananassa) in treating hyperpigmentation, and the results are presented in Table 1.

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Table 1: Summary of the literature review on related available research articles on the potential of strawberry fruit extract (Fragaria ananassa) in treating hyperpigmentation

S/N	Author, year	Age	Participant	Method	Research Result
1	Theresa <i>et al.</i> , 2024. ¹⁵	3-4 months	30 male local strains of guinea pigs, weighing 300- 350 grams	A randomized post-test-only control group design experimental study using One Way ANOVA and Tamhane Post Hoc Test	Tyrosinase inhibitory activity, and reduction of melanin levels was achieved by a dose of 12.5% strawberry ethanol extract cream
2	Markiewicz <i>et al.</i> , 2019 ¹⁴	45-70 years	17 women who experienced wrinkles, reduced skin firmness and elasticity, dryness, and uneven skin tone	An experimental study was conducted using Statistica 12.0 (StatSoft Poland, Krakow), with melanin levels and erythema measured using a Mexameter.	Microneedling combined with vitamin C enhanced firmness, skin tone and hydration, while reducing the appearance of hyperpigmentation.
3	Harahap <i>et al.</i> , 2022	Not mentioned	24 guinea pigs	An experimental study was conducted using SPSS, with melanin levels measured using a light microscope.	Melanin in the guinea pig skin tissue was significantly reduced by the application of strawberry extract.
4	Clark & Sivamani, 2016 2	Not mentioned	Not mentioned	Systematic review	Ellagic acid (EA) found in strawberries, effectively reduced skin pigmentation caused by UV exposure. It does so by inhibiting melanogenesis through the suppression of tyrosinase activity, which is achieved by chelating copper ions in the tyrosinase molecules. This highlights the potential of EA as a natural agent for controlling skin pigmentation.
5	Sarkar <i>et al.</i> , 2020 ¹⁷	Not mentioned	Not mentioned	Systematic review	Strawberries inhibited melanogenesis and possessed notable anti- inflammatory, antioxidant, and anticancer properties. Additionally, they reduced tyrosinase activity and prevented the proliferation of melanocytes.
6	Gasparrini <i>et al.</i> , 2017 ⁸	Not mentioned	Not mentioned	An experimental study was conducted using Statistica software.	Combined topical application of strawberry and Coenzyme Q10 demonstrated a significant photoprotective effect, as evidenced by a reduction in cell death and reactive oxygen species (ROS), an increase in antioxidant defense, a decrease in inflammatory markers, and enhanced mitochondrial function.
7	Lukitaningsih <i>et al.</i> , 2020 ¹⁸	Not mentioned	Not mentioned	Anti-tyrosinase activity was assessed using the spectrophotometric method.	The study demonstrated that both ethanol (SE) and ethyl acetate (SEA) strawberry extracts exhibited significant antioxidant activity, as evidenced by their EC ₅₀ and IC ₅₀ values in the FRAP and BCB assays. Additionally, the extracts showed potential for inhibiting tyrosinase, elastase, and collagenase enzymes. Strawberry extracts, particularly SE, may possess valuable bioactive properties with potential applications in skincare or provide antioxidant-related health benefits.

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8	Salas-Arias <i>et al.</i> , 2023 ¹⁹	Not mentioned	Not mentioned	This study analyzed and compared the polyphenolic profiles of leaves and fruits of the tropical highland strawberry (<i>Fragaria</i> x <i>ananassa</i> cv. Festival) using ultra-high-performance liquid chromatography and mass spectrometry	Strawberry leaf extracts demonstrated significantly higher total polyphenol content (122 times greater) and antioxidant activity (13 times higher ORAC) compared to strawberry fruit extracts. Additionally, the leaf extracts exhibited potential photoprotective effects against UV-induced damage in both human melanoma cells (SK-MEL-28) and murine embryo fibroblasts (NIH/3T3). Strawberry leaves may offer valuable bioactive properties for skin protection and cancer prevention.
9	Fierascu <i>et al.</i> , 2020 ²⁰	Not mentioned	Not mentioned	Systematic review	The extracts from ripe fruits, unripe fruits, and crowns demonstrated potential for skin-lightening, as evidenced by their ability to inhibit melanogenesis. This effect was strongly correlated with their tyrosinase-inhibitory activities, suggesting that these strawberry extracts could be promising candidates for skin-lightening applications.
10	Zhu <i>et al.</i> , 2015 ²¹	Not mentioned	Not mentioned	The <i>in vitro</i> antioxidant, anti-obesity, anti-allergy, and skin-lightening effects of extracts from ripe and unripe strawberry fruits, along with nine other plant parts of <i>Amaou</i> strawberry (<i>Fragaria</i> \times <i>ananassa</i> var. <i>Amaou</i>), were compared using various assays.	Ripe strawberry fruits demonstrated potential anti-obesity and skin- lightening effects. Even stronger bioactivity was observed in the extract of unripe fruits, as well as in other parts of the plant. This study provided evidence that extracts from both ripe and unripe strawberries, along with other parts of the plant, possess promising bioactive properties that could support their use in anti-obesity and skin-lightening applications.

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In this study, strawberries were chosen because they have high antioxidant capacity and phenolic content.²⁵ Ethanol extract of strawberry fruit contains secondary metabolites such as flavonoids, phenolic compounds, and saponins. The *Fragaria* x *ananassa* strawberry genotype has been found to contain phenolic compounds and anthocyanins.¹⁵ Research conducted by Theresa *et al.*¹⁶ stated that strawberry fruit water extract contains phenolic compounds, vitamin C, ellagic acid and anthocyanins. Anthocyanins are flavonoid compounds that act as antioxidants and have therapeutic potentials in the treatment of ROS-related diseases.¹⁶

Based on the results of the literature review, compounds that have been

successfully isolated and characterized from strawberry plants have potential as hyperpigmentation treatment agents. A summary of these compounds is presented in Table 2.

Flavonoids for example, can be used to prevent the adverse effects of UV radiation due to their UV-absorbing properties, antioxidant properties, and modulating effect on several signaling pathways in the skin.²⁰ Active compounds that are able to absorb, spread or reflect the energy of sunlight that reaches the human skin are often called sunscreen. Sunscreen provides protection against UV radiation.

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Sunscreen is essential in protecting the skin from the negative effects of sun exposure, especially from ultraviolet (UV) rays. UV rays, which consist of UVA and UVB, can damage the skin and cause various problems, such as premature aging, wrinkles, and even skin cancer. UVB exposure, for example, can cause skin burns, while UVA can penetrate deeper and damage the skin structure, accelerate the aging process, and increase the risk of skin cancer. Using sunscreen with the right SPF can reduce these risks by forming a protective layer that absorbs or reflects UV rays.26,27

In addition, sunscreen also helps keep the skin moisturized and prevents dehydration caused by direct sun exposure. Skin that is well protected from UV rays tends to be healthier, smoother and less irritated.²⁸ Regular use of sunscreen, especially during outdoor activities or in sunny weather, is an effective preventive measure in maintaining long-term skin health. With proper use, sunscreen can prevent skin damage caused by the sun, thus maintaining a youthful and healthy

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appearance.²⁹ Lack of understanding of the importance of sunscreen use can increase the risk of skin cancer, especially for individuals who are frequently exposed to the sun without protection. Without sufficient protection, ultraviolet (UV) rays from the sun can damage the DNA in skin cells, which over time can lead to mutations and the development of skin cancer. Many people may not realize that constant exposure to UV rays, while not causing direct sunburn, can cause cumulative damage to the skin.³⁰ Without sunscreen protection, UV rays cause an increase in the amount of melanin in the skin, which causes the skin to darken.²¹

Melanin pigmentation plays a crucial role in protecting the skin from the harmful effects of UV radiation by absorbing approximately 50-75% of UV radiation.¹¹ Although melanin functions as a protective agent for the skin, excessive production can lead to hyperpigmentation disorders, such as melasma, freckles, and age spots, particularly on the face.¹⁸ Skin pigmentation is primarily regulated by the synthesis of melanin in melanocytes, the transfer of melanosomes to keratinocytes, and the degradation of melanosomes. Tyrosinase, the key enzyme in melanin synthesis, catalyzes several steps, including the conversion of L-tyrosine to L-DOPA (L-3,4-dihydroxyphenylalanine) and the subsequent conversion of L-DOPA to dopaquinone. Through additional biochemical reactions, these processes lead to the production of two types of melanin: brown-black eumelanin and yellow-red pheomelanin. Various factors that could elicit skin pigmentation are DNA damage, autophagy disorders, oxidative stress and hormonal changes, all of which are also linked to skin aging and changes in skin characteristics.¹⁸ In the melanogenesis process, the components that play a role include tyrosinase (TYR), tyrosinase-related protein-1 (TYR-1) and tyrosinaserelated protein-2 (TYR-2).

Melanin synthesis begins with the catalytic process of hydroxylation of L-tyrosine to L-DOPA and oxidation of L-DOPA to dopaquinone by TYR. These compounds serve as the primary substrates for the synthesis of eumelanin and pheomelanin.⁷ When cysteine is present, it reacts with dopaquinone to produce 3-or-5-cysteinyl DOPA, which subsequently leads to the formation of pheomelanin. On the other hand, dopaquinone can also form dopachrome, which, through spontaneous decarboxylation, produces 5,6-dihydroxyindole (DHI). Upon oxidation and polymerization, DHI forms a dark brown/black polymer known as DHI-melanin.¹⁶ In the presence of TYRP-2, dopachrome undergoes tautomerization without losing its carboxylic acid group, resulting in the formation of DHI-2 carboxylic acid (DHICA). DHICA is then oxidized and polymerized to produce DHICA-melanin, which is a light brown form of melanin.¹⁵ Therefore, inhibition of melanocyte metabolic enzymes such as tyrosinase could be an important strategy to inhibit the process of melanogenesis in the skin.

Research by Markiewicz *et al.*¹⁵ explored the effects of microneedle mesotherapy with vitamin C on skin aging concerns in women, including wrinkles, reduced firmness and elasticity, dryness, and uneven skin tone. In their study, participants were subjected to four treatments with vitamin C serum (20% L-ascorbic acid solution at pH 3.5) every 10 days, with the solution freshly prepared before each application. The results demonstrated significant improvements in skin hydration, elasticity, and firmness, as well as enhanced skin colour. *In vivo* studies further confirmed the serum's effectiveness in enhancing hydration, firmness, and skin tone, suggesting that microneedling with vitamin C may reduce hyperpigmentation and improve skin colour, hydration, and firmness.¹⁵

In the studies by Theresa *et al.*¹⁶ and Harahap *et al.*²⁵ using guinea pig subjects, it was found that applying a cream formulation containing strawberry flesh ethanol extract before and after UVB exposure effectively reduced tyrosinase enzyme levels and melanin production in the skin compared to using a basic cream alone.^{16,25} In the study of Theresa *et al.*, it was also found that applying a 12.5% strawberry ethanol extract cream to the skin of male guinea pigs (*Cavia porcellus*) either before or after UVB exposure showed similar effectiveness in reducing melanin levels. However, the timing of application affected the cream's effectiveness in reducing tyrosinase enzyme levels.¹⁶ While in the study of Harahap *et al.*²⁵ it was found that melanin levels in skin

tissue decreased following treatment with the extract, indicating a significant effect on melanin pigment reduction in guinea pig skin tissue exposed to sunlight.²⁵

Several other studies conducted using experimental methods found that strawberry pulp extract possessed antioxidant activity and inhibited the tyrosinase, elastase, and collagenase enzymes. Inhibition of the tyrosinase enzyme has been shown to inhibit skin hyperpigmentation.^{8,18,19,21}

Furthermore, strawberry fruit extract has been shown to inhibit skin pigmentation induced by UV irradiation. Ellagic acid (EA) in the extract was found to suppresses melanogenesis by inhibiting tyrosinase activity. This inhibition occured through the chelation of copper atoms present in the tyrosinase molecules.^{2,17,20}

Conclusion

Strawberries contain vitamins and fibre, are low in calories, folate, potassium, and are rich in anthocyanin pigments, which are classified as flavonoid compounds. Strawberries have tyrosinase inhibitory activity which is attributed to their vitamin C and flavonoids content. Vitamin C has been shown to inhibit the conversion of dihydroxyphenylalanine (DOPA) to O-dopaquinone, and ultimately inhibit the formation of dopachrome and melanin, while the flavonoids component act as alternative enzyme substrates due to their high affinity for the tyrosinase enzyme, thereby inhibiting the formation of dopachrome. Strawberries are potential source of bioactive ingredients that can prevent skin pigmentation through their tyrosinase enzyme inhibitory activity. Therefore, strawberries have the potential for use in cosmetic formulations and skincare products for the treatment and prevention of hyperpigmentation. Further research is needed to optimize the stability and effectiveness of its bioactive components. Furthermore, the development of efficient extraction technique, and the application of nanotechnology can open up new opportunities to produce products with higher concentrations of active components and improved efficacy. In addition, long-term clinical studies are needed to confirm its safety and effectiveness in various skin types, so that strawberry could become a leading ingredient in a sustainable skincare industry.

Conflict of Interest

Authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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