

Exploring the skin whitening properties of natural products: A comprehensive review

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ABSTRACT

Natural products have been gaining popularity in recent years as a safe skin-safe alternative solution to synthetic products on the market. In particular, natural ingredients have been found to have skin-whitening properties by inhibiting melanin production and reducing hyperpigmentation. This review provides the analysis of some mechanisms and effectiveness of natural products in achieving even skin tone and reducing the appearance of dark spots. Several natural ingredients, such as chemical compounds in licorice root, green tea extract, and vitamin C, have been tested for their ability to reduce tyrosinase activity and melanin synthesis, as well as for their anti-inflammatory and antioxidant properties. In addition, the selection of uses and further research into the safety and effectiveness of natural products. Overall, natural products represent a safe and effective solution to achieving brighter, more radiant skin.

Keywords: skin-whitening property, melanin production, nature products

1. INTRODUCTION

Beauty care is a topic of interest and promotion. Besides, there are many chemical beauty treatments to whiten the skin and there are also physical treatments such as laser therapy, but there are also many adverse effects on the skin. This review therefore introduces some natural skin-safe alternatives to synthetic products on the market. Such as licorice root, green tea extract, and vitamin C are natural products that have been tested for their ability to reduce tyrosinase activity and melanin synthesis, as well as for their anti-inflammatory and antioxidant properties [1 - 3]. This review to highlight some of the mechanisms of natural product sources, safe products to users.

1.1. Chemicals

There are many scientific studies and literature reviews available on the synthesis of chemicals for skin whitening. However, it is important that the use of certain chemicals for skin whitening has been linked to adverse effects and regarding their safety and efficacy [4].

One class of chemicals commonly used for skin whitening is hydroquinone. Hydroquinone

inhibits the production of melanin by inhibiting the activity of the enzyme tyrosinase, which is involved in melanin synthesis. However, it can lead to side effects such as skin irritation, ochronosis, and even carcinogenesis. As a result, some countries have banned the use of hydroquinone in skincare products or restricted its use to prescription-only formulations [4]. Other compounds used for skin whitening include arbutin, kojic acid, and azelaic acid. These chemicals work by inhibiting tyrosinase activity or melanin synthesis, but their efficacy and safety have also been questioned [4].

Synthetic skin whitening agents are often designed to target specific pathways involved in melanin synthesis, such as tyrosinase inhibition or melanosome transfer inhibition. On the other hand, natural products have been investigated for their potential as safe and effective skin whitening agents. Many natural compounds have been shown to inhibit tyrosinase activity and reduce melanin synthesis, such as arbutin, licorice extract, and mulberry extract. Implement mechanisms, such as inhibition of tyrosinase activity, reduction of oxidative stress and

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inhibition of melanosome transfer. In addition, natural compounds have been found to have fewer side effects compared to synthetic compounds [4].

While natural compounds may offer potential as safe and effective skin whitening agents, there are some limitations to their use. For example, natural compounds may have lower potency compared to synthetic compounds, which may require higher concentrations or longer treatment durations to achieve similar clinical outcome. In addition, natural compounds may have variability in their composition and quality, which may affect their efficacy and safety [4].

1.2. Physical therapy

There are several physical methods that have been investigated for their potential to whiten the skin. These methods include laser therapy, intense pulsed light (IPL) therapy, micro-dermabrasion, and chemical peels. Laser therapy: Laser therapy involves the use of high-intensity light to target and destroy melanin in the skin. Different types of lasers, such as Q-switched lasers, have been used for skin whitening and have been found to be effective in reducing hyperpigmentation. However, laser therapy can be expensive and may have potential side effects such as skin irritation, redness, and scarring [5].

Intense pulsed light (IPL) therapy: IPL therapy uses pulses of high-intensity light to target melanin in the skin. IPL therapy has been found to be effective in reducing hyperpigmentation and improving skin tone, but like laser therapy, it can be expensive and may have potential side effects such as skin irritation, redness, and scarring [6]. Micro-dermabrasion involves the use of a special device to exfoliate the skin and remove dead skin cells. This method can improve the appearance of hyperpigmentation and promote skin whitening, but it may require multiple treatments and can cause skin irritation [7]. Chemical peels involve applying a chemical solution to the skin, causing the outer layer of skin to peel off, revealing brighter, smoother skin underneath. Chemical peels are effective in reducing hyperpigmentation and improving skin tone, but biological peels must be followed to avoid skin irritation [8].

1.3. Others

In addition, other physical methods have been investigated for their potential to whiten the skin. These methods include cryotherapy, dermabrasion, and micro needling. Cryotherapy: Cryotherapy involves the use of extreme cold to freeze and destroy the melanin-producing cells in the skin. This method is effective in reducing hyperpigmentation and improving skin tone, but it may cause skin irritation and blistering [9].

Dermabrasion: Dermabrasion involves the use of a special device to mechanically abrade the skin and remove the outer layer of skin cells. This method can improve the appearance of hyperpigmentation and promote skin whitening, but it may require multiple treatments and can cause skin irritation and scarring [10].

Micro needling: Micro needling involves the use of a device with tiny needles to puncture the skin and create micro-injuries. This method stimulates the production of collagen and elastin in the skin and can improve the appearance of hyper-pigmentation and promote skin whitening. However, micro needling may cause skin irritation and redness, and it should only be performed by a licensed healthcare provider [11].

1.4. Advantages of natural products

Natural products have been well-known in recent years due to their perceived safety and efficacy in various skincare applications. There are several factors that make natural products appealing to consumers and potentially superior to synthetic products: Safety: Natural products are perceived to be safer than synthetic products because they are made from natural ingredients and are less likely to cause allergic reactions or other adverse effects [12].

Some natural products, such as *Aloe vera* and Chamomile, have been shown to have anti-inflammatory and soothing properties, which can be beneficial for sensitive or irritated skin [12]. Efficacy: Natural products have been found to be effective in a variety of skincare applications, such as reducing inflammation, improving skin texture and tone, and reducing the appearance of hyperpigmentation. Some natural products, such as licorice root and green tea extract, have been shown to have skin-whitening effects by

inhibiting melanin production [12].

However, it is important to note that not all natural products are safer or more effective than synthetic products, and some natural products can still cause adverse reactions in certain individuals. Furthermore, the efficacy of natural products can vary depending on the specific formulation, concentration, and purity of the ingredients [12]. The primary focus of this review is to examine the skin whitening properties of natural products as well as update the recent research in the field.

2. MECHANISM OF ACTION

Melanin is the pigment that gives our skin, hair and eyes the color. Melanin synthesis is a biochemical process that occurs in cells. This process is regulated by the activity of the enzyme tyrosinase, which catalyzes the conversion of the amino acid tyrosine to dopaquinone, an important precursor in melanin synthesis [13]. Therefore, tyrosinase produced by melanocytes. This leads to a reduction in hyperpigmentation, dark spots and an improvement in skin tone [13].

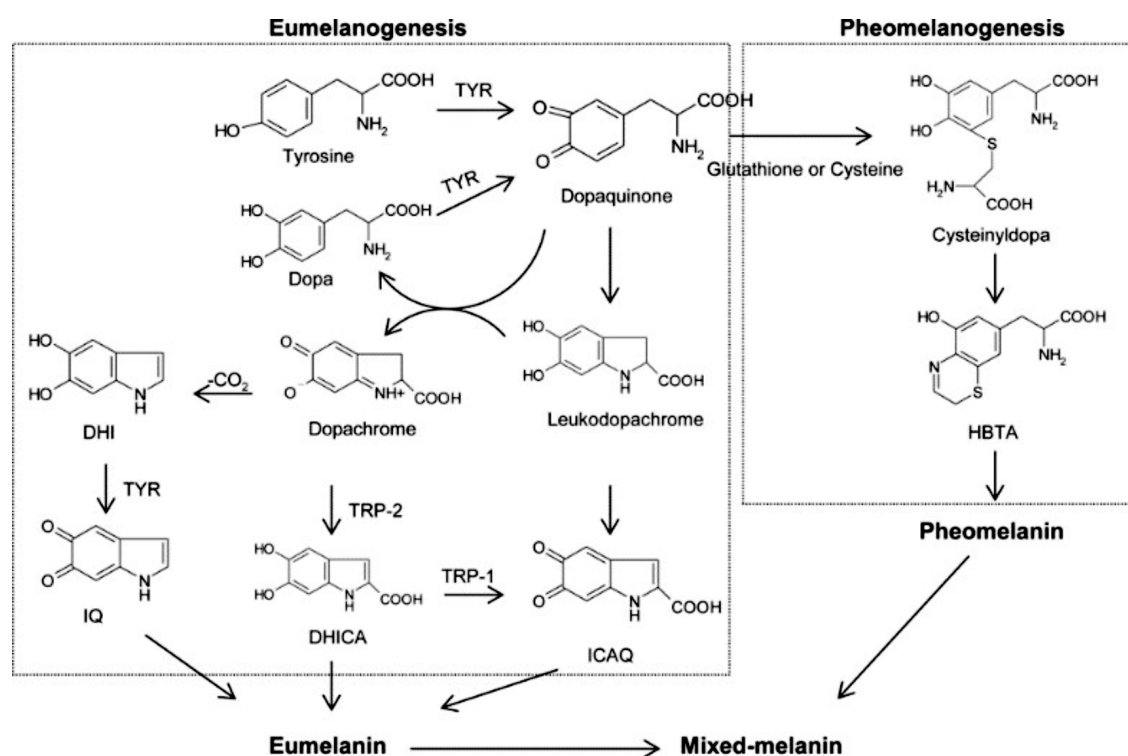


Figure 1. Conditioning mechanism [13]

Several natural products have been identified as potential tyrosinase inhibitors, including kojic acid, arbutin, licorice extract, and mulberry extract. Kojic acid is a fungal metabolite that inhibits tyrosinase activity by chelating copper ions in the active site of the enzyme [13]. Arbutin is a naturally occurring hydroquinone derivative found to inhibit tyrosinase activity through a noncompetitive mechanism [14]. Licorice extract contains a compound called glabridin, which has been found to inhibit tyrosinase activity and reduce skin pigmentation [13, 15]. Mulberry extract contains a compound called oxyresveratrol, which has been found to inhibit tyrosinase activity and reduce melanin synthesis [13, 15].

These compounds have also been shown to be effective in reducing hyperpigmentation and improving skin tone in cultured cell models as well as in clinical studies. Other natural ingredients with tyrosinase inhibitory activity include green tea extract and vitamin C. In addition to inhibiting tyrosinase activity, natural products may also have antioxidant and anti-inflammatory properties that can contribute to their skin whitening effects. For example, resveratrol, a natural compound found in grapes, has been shown to inhibit tyrosinase activity and reduce melanin synthesis, as well as reduce inflammation and oxidative stress in the skin [15]. Overall, the inhibition of tyrosinase activity is a promising mechanism for achieving

skin whitening effects, and natural products have shown potential in this area. Further research is needed to fully understand the efficacy and safety of natural products for skin whitening applications.

3. NATURAL PRODUCTS

3.1. Vitamin C

Vitamin C inhibits melanin production by reducing the activity of the enzyme tyrosinase, the enzyme involved in melanin production. It also acts as an antioxidant, protecting the skin from damage caused by UV radiation and environmental stressors. [4]. There is also some research showing the importance of vitamin C in dermatology and its many beneficial effects, including sun protection, collagen synthesis, and anti-inflammatory properties [1]. There are also various functions of vitamin C in the skin, such as its role in collagen production and antioxidant activity, and vitamin C can help improve skin health and aging [2]. In several studies, the inhibitory effect of vitamin C on melanin synthesis and expression of metalloproteinases (MMPs) in melanoma cells, suggests that vitamin C may have potential as a substance whiten skin [16]. These studies suggest that vitamin C may have skin whitening effects through various mechanisms. For example, vitamin C may work by inhibiting melanogenesis, reducing oxidative stress, and promoting collagen synthesis, which can lead to brighter, more even skin tone.

3.2. Licorice extract

Licorice extract contains a compound called glabridin, which inhibits the activity of tyrosinase

and reduces the production of melanin. It also has anti-inflammatory properties that can help to reduce skin pigmentation caused by inflammation [3]. Glabridin and glycyrrhizic acid were found to have anti-melanogenic effects on activated melanocytes [17]. Licorice extract was also found to promote skin whitening by inhibiting melanin synthesis through the phosphatidylinositol 3-kinase/protein kinase B/mitogen-activated protein kinase (PI3K/Akt/MAPK) pathway [18]. Furthermore, a study explored the use of glycyrrhetic acid modified hydroxypropyl chitosan for topical skin whitening [19].

These studies suggest that licorice extract may have skin whitening effects through various mechanisms, such as inhibiting tyrosinase activity, reducing oxidative stress, and suppressing melanin synthesis via the PI3K/Akt/MAPK signaling pathway. Additionally, some studies have examined the use of licorice extract in topical formulations for skin whitening purposes.

3.3. Arbutin

Arbutin inhibits the activity of tyrosinase, which is involved in the production of melanin, by binding to the active site of the enzyme and blocking its activity. It also reduces the levels of the protein TRP-1, which is involved in the synthesis of melanin [20]. Several studies have shown that arbutin acts as an inhibitor of the antioxidant tyrosinase catalytic activity, removing reactive oxygen species (ROS). It can activate the red blood cell factor 2 (Nrf2)-binding antioxidant response factors (ARE) pathway to enhance cellular antioxidant capacity [21].

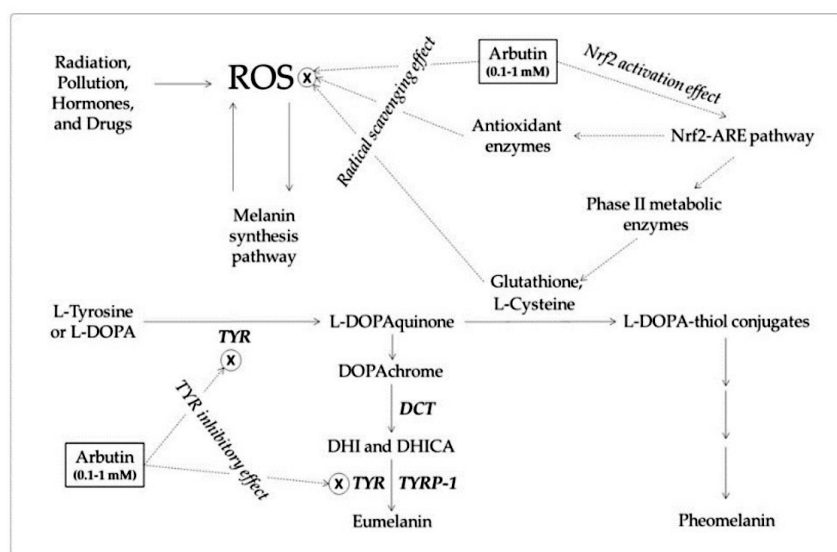


Figure 2. The skin whitening mechanism of Arbutin [14]

Arbutin may have skin whitening effects through various mechanisms, such as inhibiting tyrosinase activity, regulating oxidative stress, and modulating autophagy. Some studies have also investigated the use of arbutin in animal models and observed its potential to reverse skin darkening caused by various factors [14]. Overall, these findings suggest that arbutin may be a promising ingredient for skin whitening

and brightening purposes.

3.4. Kojic acid

Kojic acid inhibits the activity of tyrosinase by chelating copper ions that are required for the enzymatic activity of tyrosinase. It also acts as an antioxidant and can help to reduce the levels of reactive oxygen species (ROS) that can stimulate melanin production [22].

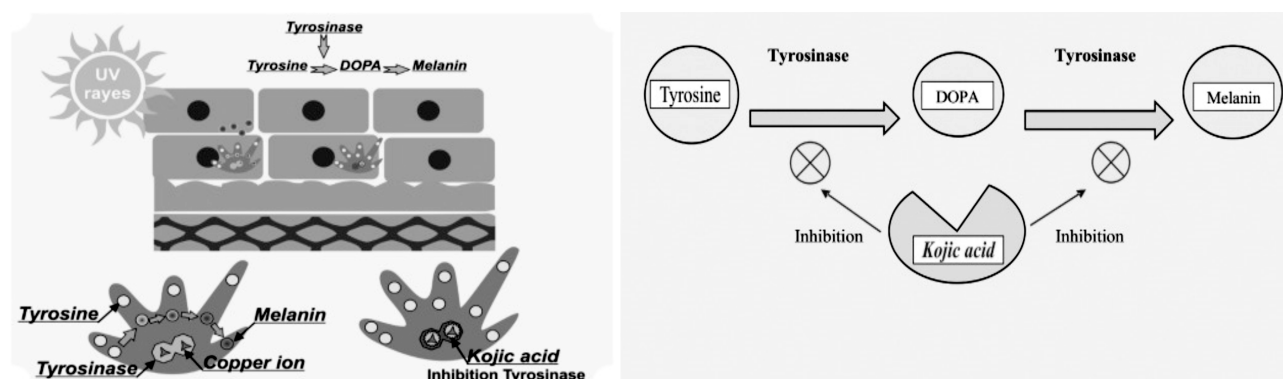


Figure 3. The skin whitening mechanism of Kojic acid [22]

Kojic acid is a natural compound with skin-whitening properties that inhibit the production of melanin, the pigment that gives skin its color, by blocking the enzyme tyrosinase involved in melanin synthesis. Several studies describe the mechanisms by which kojic acid inhibits melanogenesis in human epidermal melanocytes and melanocytes, highlighting its ability to inhibit tyrosinase activity, to modulate expression microphthalmia-associated transcription factor and inhibits the mitogen-activated protein kinase signaling pathway. In addition, kojic acids have potential in the treatment of various skin disorders, such as hyperpigmentation, melasma and skin aging, through their antioxidant and anti-inflammatory effects [23].

Additionally, recent studies have investigated the potential of kojic acid derivatives for skin whitening purposes. Overall, these findings suggest that kojic acid and its derivatives may be promising ingredients for skin brightening and whitening purposes.

3.5. Mulberry extract

Mulberry extract contains a compound called morin, which inhibits tyrosinase activity and reduces melanin production. It also has antioxidant properties that can help protect the skin from damage caused by UV radiation that can

lead to hyperpigmentation [24].

Several studies showed that mulberry extract induces mitochondrial biogenesis and protects human skin fibroblasts from oxidative stress-mediated apoptosis [25]. Mulberry leaf extract inhibits melanogenesis through regulation of the PI3K/Akt and MAPK/ERK signaling pathways [26]. Taken together, these studies suggest that mulberry extract could have potential applications in skin care and may offer protective effects against UV radiation and other stressors that can damage skin cells.

3.6. Niacinamide

Niacinamide inhibits the transfer of melanosomes, which are organelles that contain melanin, from melanocytes to keratinocytes, reducing the production of melanin. It also has anti-inflammatory properties that can help to reduce skin pigmentation caused by inflammation [27].

Several studies indicate that the use of niacinamide, a form of vitamin B3, to reduce hyperpigmentation and improve skin texture. These studies were randomized, double-blind, placebo-controlled clinical studies to evaluate the efficacy and safety of niacinamide in the topical treatment of skin discoloration [28]. The results suggest that niacinamide is an effective and safe treatment option for reducing hyperpigmentation

and improving skin texture. The studies also investigate the potential benefits of niacinamide for reducing cutaneous pigmentation and redness in Asian patients.

4. ADDITIONAL RESEARCHES

4.1. Asian-native herbs

These studies provide important insights of natural extracts and substances as alternatives to conventional skin-whitening agents. Another, these recent research provide further evidence for the potential use of Asian herbs in the treatment of hyperpigmentation and skin whitening.

4.2. Challenges and prospect

Natural products have gained attention for their potential in skin whitening due to their relatively safe profile compared to synthetic chemicals. However, there are still several challenges that need to be addressed in the development of natural whitening agents.

One of the challenges is the variability in the composition and quality of natural products due to factors such as growing conditions, harvesting methods, and storage conditions. This can lead to inconsistencies in the effectiveness of the natural product.

Another challenge is the difficulty in identifying the active components responsible for the whitening effect in natural products, as they often contain complex mixtures of compounds. This makes it challenging to standardize the composition of the natural product and optimize its efficacy. Furthermore, the stability of natural products in cosmetic formulations can be a

challenge. Natural products can degrade rapidly due to factors such as pH, temperature, and exposure to air and light, which can affect their potency and shelf-life.

Despite these challenges, natural products offer promising prospects for the development of safe and effective skin whitening agents. Further research is needed to identify the active components in natural products, optimize their stability in cosmetic formulations, and develop standardized methods for evaluating their efficacy. In addition, the use of nanotechnology has been proposed as a potential solution to overcome some of the challenges associated with natural products. Nanoparticles can protect the natural product from degradation, enhance its stability, and facilitate its absorption into the skin, thus improving its efficacy. Overall, the development of natural skin whitening agents requires a multidisciplinary approach involving collaboration between botanists, chemists, pharmacologists, and cosmetic scientists to address the challenges and optimize the potential of natural products.

5. CONCLUSION

The knowledge of herbal cosmetics is well known but people are not aware its medicinal and magical benefits compared to chemically inert material. In addition, researchs have demonstrated great effects such as skin lightening, anti-aging, anti-inflammatory ..., and relatively safe when using cosmetics from medicinal herbs. However, there are still several challenges that need to be addressed in the development of natural whitening agents for their purity, preservation, and effectiveness.

REFERENCES

- [1] Telang PS, "Vitamin C in dermatology", *Indian Dermatol Online J*,4(2),143-146, 2013.
- [2] Pullar JM, Carr AC, Vissers MCM, "The roles of vitamin C in skin health", *Nutrients*, 9(8),866, 2017.
- [3] Damle Joshi, Monica, "*Glycyrrhiza glabra* (Liquorice) - a potent medicinal herb", *International Journal of Herbal Medicine*, 132. 132-136, 2014.
- [4] Tchanque-Fossuo, C. N., & Taylor, H. O., "Current concepts in skin whitening agents", *Dermatologic clinics*, 37(2),147-153, 2019.
- [5] Polnikorn, N., "Treatment of refractory melasma with the MedLite C6 Q-switched Nd: YAG laser and alpha arbutin: a prospective study", *Journal of cosmetic and laser therapy*, 14(3), 115-120, 2012.
- [6] Cho, S. B., Lee, S. J., Kang, J. M., Kim, Y. K., & Chung, W. S., "Intense pulsed light therapy for the treatment of melasma in Asian patients", *Dermatologic surgery*, 40(11), 1196-1203, 2014.
- [7] Kwon, H. H., Lee, S. Y., Yoon, H. S., & Youn, J. I., "Comparative study of 1550 nm fractional photothermolysis and microdermabrasion for

facial melasma in Asian patients: a randomized prospective clinical trial", *Journal of cosmetic and laser therapy*, 15(6), 310-316, 2013.

[8] Khunger, N., "Standard guidelines of care for chemical peels", *Indian journal of dermatology*, 59(2), 95, 2014.

[9] Jin, S. P., Cho, S., Park, M. Y., Shin, J. U., & Lee, J. H., "Treatment of melasma with cryotherapy", *Dermatologic surgery*, 42(4), 496-502, 2016.

[10] Farid, K., & Zedan, W., "Dermabrasion in facial skin resurfacing: an overview. *Journal of cosmetic dermatology*", 15(2), 111-124, 2016.

[11] Alster, T. S., & Graham, P. M., "Microneedling: a review and practical guide", *Dermatologic surgery*, 44(3), 397-404, 2018.

[12] S, Laxmi., "Herbal Cosmetics and Cosmeceuticals: An Overview", *Joshi and Pawar Nat Prod Chem Res*, Volume 3, Issue 2, 1000169, 2015.

[13] Chang TS, "An updated review of tyrosinase inhibitors", *Int J Mol Sci*, 10(6), 2440-2475, 2009.

[14] Sugimoto K, Nishimura T, Nomura K, Sugimoto K, Kuriki T, Ishii Y, et al, "Inhibitory effects of α -arbutin on melanin synthesis in cultured human melanoma cells and a three-dimensional human skin model", *Biol Pharm Bull*, 27(4), 510-4, 2004.

[15] Kim YJ, Uyama H, "Tyrosinase inhibitors from natural and synthetic sources: structure, inhibition mechanism and perspective for the future", *Cell Mol Life Sci*, 62(15), 1707-23, 2005.

[16] Machado-Santelli GM, Carvalho FA, Lemos M, Farsky SHP, "The effect of ascorbic acid on melanoma cell proliferation and the expression of MMP-2 and MMP-9", *J Venom Anim Toxins incl Trop Dis*, 16(3), 448-456, 2010.

[17] Lee JM, Kim YJ, Jung E, Lee JS, Yoon DH, Kim YH, "Anti-melanogenic effects of glabridin and glycyrrhizic acid in activated melanocytes", *Biomol Ther (Seoul)*, 26(5), 422-429, 2018.

[18] Li S, Zhang C, Wang J, et al, "Licorice extract promotes skin whitening by inhibiting melanin synthesis via the phosphatidylinositol 3-kinase/protein kinase B/mitogen-activated protein kinase pathway", *Exp Dermatol*, 28(2), 198-204, 2019.

[19] Zhang M, Du GJ, Wang Y, et al, "Topical application of glycyrrhetic acid modified hydroxypropyl chitosan for skin-whitening: formulation optimization, characterization, and evaluation", *Int J Nanomedicine*, 14, 6771-6785, 2019.

[20] Wang Y, Zhang J, Liu Y, et al, "Arbutin inhibits melanin synthesis through the tyrosinase pathway", *Biol Pharm Bull*, 41(7), 1114-1119, 2018.

[21] Boo, Y.C, "Arbutin as a Skin Depigmenting Agent with Antimelanogenic and Antioxidant Properties", *Antioxidants*, 10, 1129, 2021.

[22] Saeedi M, Eslamifar M, Khezri K, et al, "Kojic Acid Applications in Cosmetic and Pharmaceutical Preparations", *Biomed Res Int*, 9646274, 2019.

[23] Kim J, Lee J, Kwon SH, et al, "Kojic acid inhibits melanogenesis in alpha-MSH-stimulated B16F10 melanoma cells by suppressing tyrosinase activity and modulating microphthalmia-associated transcription factor expression", *Biomol Ther (Seoul)*, 26(3), 268-273, 2018.

[24] Kim JE, Park HS, "Mulberry Extract Inhibits Melanin Synthesis by Regulating Tyrosinase Expression in Murine B16 Melanoma Cells", *Ann Dermatol*, 28(2), 147-155, 2016.

[25] Zhang, Y., Liu, Y., Liu, Y., Zhang, X., Wang, X., & Wang, S., "Mulberry extract-induced mitochondrial biogenesis attenuates oxidative stress-mediated apoptosis in human skin fibroblasts", *Journal of cellular biochemistry*, 120(5), 7596-7607, 2019.

[26] Hsu, S., Chen, J., Li, D., & Lee, C, "Mulberry leaf extract inhibits melanogenesis through regulating the PI3K/Akt and MAPK/ERK signaling pathways." *Journal of food and drug analysis*, 26(1), 275-282, 2018.

[27] Bissett DL, "Niacinamide: A B vitamin that improves aging facial skin appearance." *Dermatol Surg*, 31(7 Pt 2), 860-866, 2005.

[28] Kim, S. K., Kim, M. K., Lee, J. H., Kim, H. R., Lee, M. K., & Kim, Y. J., "A randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of a novel niacinamide-containing formulation for reduction of hyperpigmentation and improvement of skin texture in patients with moderate to severe facial hyperpigmentation". *Journal of cosmetic dermatology*, 17(2), 223-229, 2018.

Khám phá đặc tính làm trắng da của các sản phẩm tự nhiên: Đánh giá tổng quan

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TÓM TẮT

Các sản phẩm tự nhiên đã trở nên phổ biến trong những năm gần đây như một giải pháp thay thế an toàn cho da so với các sản phẩm tổng hợp trên thị trường. Đặc biệt, các thành phần tự nhiên được phát hiện có đặc tính làm trắng da bằng cách ức chế sản xuất melanin và sắc tố da. Đánh giá này cung cấp một số phân tích về cơ chế và hiệu quả của các sản phẩm tự nhiên trong việc làm đều màu da và giảm sự xuất hiện của các sắc tố. Một số thành phần tự nhiên như các chất có trong rễ cam thảo, chiết xuất trà xanh và vitamin C, được kiểm tra về khả năng làm giảm hoạt động tyrosinase và tổng hợp melanin, cũng như đặc tính chống viêm và chống oxy hóa của chúng. Ngoài ra, việc lựa chọn sử dụng và nhu cầu nghiên cứu sâu hơn về tính an toàn và hiệu quả của các sản phẩm tự nhiên. Nhìn chung, các sản phẩm tự nhiên như một giải pháp an toàn và hiệu quả để đạt được làn da sáng hơn, rạng rỡ hơn.

Từ khóa: đặc tính làm trắng da, sản xuất melanin, sản phẩm từ thiên nhiên

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