Traditional Chinese Herbal Medicine for Whitening

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Abstract
Melanin is the chief pigment responsible for the pigmentation of human skin. Increasing evidence indicates that traditional Chinese drugs with skin-whitening effects are attracting the attention of consumers and researchers because they are perceived to be milder, safer, and healthier than synthetic alternatives. This commentary summarizes the current research on Chinese herbal medicines that inhibit melanin and their biological activities. The findings presented in this study suggest that these traditional Chinese herbal medicines might be potential candidates for novel skin-whitening agents.

Keywords
traditional Chinese herbal medicine, melanogenesis mechanism, skin-whitening

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Melanin is the pigment responsible for the color of human skin and hair. Melanin serves as a double-edged sword that imposes both protective and spot-causing effects on the skin. Melanin plays a critical role in protecting the skin against ultraviolet (UV) damage, but high or uneven melanin production can cause freckles and age spots.¹ Melanogenesis is a critical pathway that regulates skin pigmentation and the development of skin-lightening/whitening drugs or cosmetics.² Traditional Chinese herbal medicine extracts are effective at inhibiting skin pigmentation in recent years and are highly efficient, low cost, and have few side effects, indicating they could have broad application prospects leading to large social and economic benefits.

Current Mechanisms for Inhibiting Melanin Production
There are several melanin production mechanisms, as shown in Figure 1. The alpha-melanocyte stimulating hormone (α-MSH) specifically binded to the G protein-coupled melanocortin type 1 receptor (MC1R), which resulted in a stimulation of adenylate cyclase enhancing the concentration of intracellular cyclic adenosine monophosphate (cAMP).³ Intracellular cAMP-activated protein kinase A (PKA) that phosphorylates Ser-133 residue of the cAMP responsive element-binding protein (CREB).⁴ Conversely, the expression of microphthalmia-associated transcription factor (MITF) which was a primary helix loop-helix protein essential for melanocyte development and differentiation was increased by phosphor (p)-CREB.⁵ At last, MITF bound to the M box of tyrosinase promoter for the activation of transcription, thus resulting in the promotion of melanin biosynthesis. Phosphorylation of glycogen synthase 3β (GSK-3β) was inhibited by the activation of the Wnt pathway, which resulted in the accumulation of β-catenin. The cumulate β-catenin was carried into the nucleus and shaped a complex with the lymphoid-enhancing factor/T-cell factor transcription factor, after which caused the upregulation of MITF expression.⁶ Binding of the stem cell factor to the extracellular domain of c-kit, a tyrosine kinase receptor, prompted dimerization of the receptor, and then a downstream of phosphatidylinositol 3′a-kinase and Ras-mitogen-activated protein kinase (Ras-MAPK) was activated via the Shc and Grb2 adaptors proteins.⁷ The c-kit...
The activation of the tyrosinase enzyme was at the endpoint of this cascade. The production and secretion of endothelin-1 (ET-1) were induced by exposure of the skin to UVB. Then the ET-1 stimulated melanocytes located in the vicinity of keratinocytes by binding to endothelin B receptor that activated intracellular signaling cascades chiefly composed of the protein kinase C pathways, which resulted in a synergistic increase of proliferation and melanin production by melanocytes.

Therefore, the key to inhibiting melanin is to prevent the formation and block the release of melanin.

**Inhibition of Melanin Synthesis Through Multiple Signaling Pathways**

**AMP-activated protein kinase/MAPK.** Kazinol U has been shown to have antimelanogenesis activity through inhibiting the expression of MITF; inactivating its downstream target genes, tyrosinase, tyrosinase-related protein (TRP)1 and TRP2; and AMP-activated protein kinase and MAPK proteins. The members of the MAPK family, extracellular signal-regulated protein kinase (ERK) and c-Jun N-terminal kinase (JNK), play important roles in regulating melanogenesis.

**Wnt/β-catenin.** β-catenin, which accumulates with the activation of Wnt/β-catenin signaling, is related to melanocyte differentiation and forms a complex with lymphocyte enhancer factor-1 to upregulate the expression of the MITF gene. Moreover, β-catenin directly interacts with the MITF protein itself and then activates MITF-specific target genes.

Cardamomin is a chalcone from *Alpinia katsumadai* Hayata that inhibits pigmentation in melanocytes by suppressing the Wnt/β-catenin signaling pathway. Recombinant Wnt5a adenoviruses infect melan-a cells and then make use of noncanonical Wnt/Ror2 pathway activation to inhibit the canonical Wnt pathway, leading to inhibition of melanin synthesis via downregulation of pigment cell-specific genes in melanocytes.

**Inhibition of Tyrosinase Activity**

The formation of dopaquinone is catalyzed by tyrosinase, which is a precursor of melanin. Therefore, the development of agents that can regulate the enzymatic activity of

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*Figure 1. The mechanism of melanin production. cAMP, cyclic adenosine monophosphate; CREB, cAMP responsive element-binding protein; ET-1, endothelin-1; ETB-R, endothelin B receptor; ERK, extracellular signal-regulated protein kinase; GSK-3β, glycogen synthase 3β; LEF, lymphoid-enhancing factor; α-MSH, alpha-melanocyte-stimulating hormone; MITF, microphthalmia-associated transcription factor; PKA, protein kinase A; PKC, protein kinase C; SCF, stem cell factor; TCF, T-cell factor; TRP, tyrosinase-related protein; TYR, tyrosinase.*
tyrosinase could have significant value in controlling the melanin content in the skin.\textsuperscript{35} Nature has a myriad of sources of tyrosinase inhibitors, such as flavonoids,\textsuperscript{36,38} β-arbutin,\textsuperscript{39} chalcones,\textsuperscript{40} resveratrol,\textsuperscript{41} and others, and natural sources usually attract more attention than chemically synthesized compounds for using cosmetic products.\textsuperscript{42}

\section*{Inhibition of Melanin Transport}

Keratinocyte-secreted substances activate melanocytes to promote melanin synthesis, which is catalyzed by tyrosinase, the rate-limiting enzyme, and TRP-1 and TRP-2 in melanosomes.\textsuperscript{43,44} Then, mature melanosomes including melanin are transported from the perinuclear area to the tips of melanocyte dendrites.\textsuperscript{45} Kinesin, a motor protein, delivers melanosomes on microtubules to the perinuclear region.\textsuperscript{46,47} Furthermore, the Rab27a and MyosinVa compound transport melanosomes associated with actin located at the tips of dendrites.\textsuperscript{46,48} Finally, melanosomes are combined with surrounding keratinocytes in globules and are scattered throughout the skin.\textsuperscript{49} In previous research, Manassantin B has been shown to be an inhibitor of the interaction between MyosinVa and melanophilin, which inhibits melanosome transport and decreases the melanin content when melanocytes are stimulated by α-MSH.\textsuperscript{50} Although it suppresses melanosome transfer, niacinamide does not affect tyrosinase activity, melanin synthesis, or the melanocyte number in a monolayer culture system.\textsuperscript{51} Ebselen is a nonprotein cell-permeable glutathione peroxidase mimic that seems to be a new depigmenting compound for skin whitening.

\section*{Active Autophagy}

Autophagy is an intracellular process by which autophagosomes are formed by sequestering cytosol and organelles in double-membrane-bound structures that later deliver their contents to lysosomes/vacuoles for degradation.\textsuperscript{56-59} Recent studies have shown that autophagy may also be related to the biogenesis of melanin and degradation of melanosomes, suggesting that its activation is involved in skin color by reducing the production of melanin pigments.\textsuperscript{50} 3-MA, an autophagy inhibitor, also increases tyrosinase protein levels.\textsuperscript{61} LED photo modulation at a 585 nm wavelength reduces the melanin content of inhuman epidermal melanocytes (HEMs), via dose-dependent inhibition of melanogenesis and induction of HEM autophagy.\textsuperscript{62} It has been shown that β-mangostin from seedcases of \textit{Garcinia mangostana} control α-MSH-mediated melanogenesis by inhibiting autophagy, which clearly recovers the premelanosome protein and tyrosinase degraded in B16F10 melanoma cells and a 3-dimensional human skin model.\textsuperscript{2} Tranexamic acid (TXA) has been frequently used to decrease melanin synthesis in patients with melasma and as a raw material for functional whitening cosmetics. TXA can decrease melanin synthesis in melanoma B16F1 cells via activating the ERK signaling pathway and the autophagy system.\textsuperscript{60} 3-O-glyceryl-2-O-hexyl ascorbate (VC-HG) suppresses melanogenesis by activating the autophagy system.\textsuperscript{61} In \textit{Rhizoma arisaema-tet} extract-treated B16F1 cells, autophagy is activated, which inhibits α-MSH-stimulated growth of melanogenesis and down-regulates the expression of TRP1 proteins in cells.\textsuperscript{62} Shufeng Huoxue Fumula regulates melanin metabolism and enhances tyrosinase activity and melanogenesis through the autophagy pathway to inhibit the proliferation of B16 cells in vitro.\textsuperscript{65} According to research that interrupting intracellular melanosome transport by knocking down MyosinVa degrades melanosomes through activating the autophagy system and then reduces the accumulation of melanosomes in cells, but these phenomena are only found in M-KD cells activated by theophylline.\textsuperscript{66} Resveratrol is a type of natural phenol, and its antimelanogenesis activity is suppressed by the inhibition of autophagy.\textsuperscript{67} 3′-Hydroxydaidzein (3′-ODI), as an autophagy inducer, significantly reduces α-MSH-mediated melanogenesis in melanoma cells and melanocytes. Additionally, the inhibition of autophagy notably decreases the antimelanogenic effects of 3′-ODI in α-MSH-stimulated melanoma cells.\textsuperscript{68} ARP101, which is a matrix metallopeptidase -2 inhibitor, strongly induces autophagy and autophagy-associated cell death in various cancer cells.\textsuperscript{69,70} ARP101 inhibits melanogenesis and suppresses the expression of tyrosinase and TRP1 by regulating autophagy.\textsuperscript{71}

\section*{Inhibition of Oxidative Stress}

Meyer has shown that the main components of polyphenolic compounds from \textit{Panax ginseng} C.A are antioxidants and inhibit melanogenesis.\textsuperscript{72} Metallothionein expressed in melanocytes acts as an inducible intracellular antioxidant,\textsuperscript{73,81} and its induction may be an effective method to suppress melanogenesis induced by nitric oxide and other melanogens.\textsuperscript{82}

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\section*{Ginseng}

\textit{Panax ginseng} C. A. Meyer is a very well-known medical herb in Asian countries. Like Kwangmi Kim, extracts, powders, or some constituents of ginseng inhibit melanogenesis in vivo or in vitro.\textsuperscript{83} We prefer to concentrate on the updated
The ethyl acetate extract of *Panax ginseng* (Gb-AuNPs), which produces gold nanoparticles with versatile properties for cosmetic applications, can effectively scavenge and gradually suppress cellular tyrosinase and melanin in α-MSH-stimulated B16 cells. Ginsenoside Rh23, Rh2, and Rh6; vina-ginsenoside R13; vina-ginsenoside R4; picrinose A; 20-O-β-D-glucopyranosyl-3β, 6α, 12β, and 20β; and 25-pentahydrammar-23-ene can be isolated from hydroponic *P. ginseng* leaves together and not only have inhibitory activities on melanin biosynthesis without cytotoxic effects in melana-a cells but also enhance depigmentation in zebrafish as an alternative animal model. Twelve ginsenosides have been isolated and used to test antimelanogenesis effects. Only aglycones of Rh4 notably decrease the melanin content and tyrosinase activity via downregulation of cAMP levels. Ginsenoside F1 (GF1) is a metabolite of ginsenoside Rg1 that increases the production of interleukin 13 (IL-13) from human epidermal γδ T cells. Then, IL-13 significantly reduces the expression of mRNA and proteins of both tyrosinase and dopachrome tautomerase and reduces melanin synthesis in normal human epidermal melanocytes (NHEMs), leading to the visible brightening of the NHEM pellet. GF1 inhibits melanogenesis via inducing cell body enlargement and dendrite retraction in B16F10 cells. It leads to the accumulation of pigment granules in melanocyte cell bodies, which notably influences their transfer from melanocytes and thus decreases visible pigmentation. Interestingly, GF1 increases the expression of intracellular melanin and tyrosinase. Chang-Seok Lee et al found that GF1 has whitening effects in the human epidermis containing melanocytes and keratinocytes. They demonstrated that GF1 inhibits α-MSH-induced dendrite formation, leading to the inhibition of melanosome transfer to keratinocytes in human cell cocultures. GF1 disrupts melanin transfer from melanocytes in the basal layer to keratinocytes in the upper layer, indicating a whitening function in a human skin equivalent. Dan-Dan Wang et al synthesized ginsenoside 1a, a new ginsenoside derivative from F1. Ginsenoside 1a largely decreases melanin synthesis and suppresses tyrosinase activity at 100 μm, indicating that it has greater efficacy than ginsenoside F1 and arbutin at the same concentration. Cinnamic acid is mainly found in *Cinnamomum cassia* BLUME and *P. ginseng*. Melan-a cells treated with 100 ppm of cinnamic acid can lead to decreased melanin, have an effective inhibitory influence on tyrosinase activity, decrease the expression of tyrosinase in melan-a cells, and have depigmenting activity on UV-B-induced hyperpigmentation of brown guinea pig skin. The ethyl acetate extract of *P. ginseng* C. A. Meyer (PG-2) has the strongest influence on depressing melanogenesis, and its key constituents are polyphenolic compounds, which may inhibit melanogenesis through restraining oxidative stress.

**Scutellaria baicalensis**

According to component analyses, baicalin, wogonoside, baicalein, wogonin, and oroxylin A are the main components of *S. baicalensis*. The effects of every fraction of antimelanogenesis have been investigated. The results showed that among these 5 flavones, wogonin and wogonoside exhibit high resistance to melanin production in both B16F10 melanoma cells and primary melanocytes. Wogonin clearly inhibits melanin production and evidently lightens the color of skin equivalents, possibly due to the calpain/proteosomal pathway promoting proteolytic degradation of melanophilin. SOX9 is a potential target for the effect of these *S. baicalensis* flavones. Additionally, wogonin and 2 wogonin analogs, mono-O-methyl flavones, considerably suppress melanosome transport. The structural specificities of the mono-O-methyl group in the flavone A-ring and the aglycone form play important roles in decreasing melanosome. It has been reported that Rab27A, synaptotagmin-like protein (SLP) 2A/synaptotagmin 2, a melanophilin (MLPH)/SLP homolog lacking C2 domains-A, and myosin Va are involved in the regulation of melanosome transport. The o-methyl-positioned flavones inhibit melanosome transport through downregulating the level of MLPH. Baicalin decreases MITF protein levels and also decreases the protein level of tyrosinase, which is transcriptionally regulated by MITF. Furthermore, the baicalin-induced hypopigmenting effect is related to the PI3K/Akt signaling pathway. However, in a study by Xiaohong Li et al, baicalin was shown to lead to phosphorylation of ERK and decrease the MITF protein level, tyrosinase activity and melanin level.

**Ssanghwa-tang**

Herbal cocktails containing a myriad of phytochemicals simultaneously affect multiple biological and pathological processes via synergistic and reciprocal actions. Appropriately formulated herbal cocktails may act in concert to amplify the therapeutic efficacy of their components while minimizing adverse effects. These combined actions are known as pharmacological or pharmaceutical combinatorial effects. Ssanghwa-tang (SHT) is a traditional herbal medicine and has been widely used for years in Korea, China, and Japan. In a study by Aeyung Kim et al, the ability of SHT to inhibit melanin synthesis was evaluated. SHT significantly inhibits cAMP-induced melanin synthesis in B16F10 cells via repression of the PKA and p38 MAPK signaling pathways and subsequently reduces the level of CREB phosphorylation, MITF, and melanogenic enzymes. Some single herbs in SHT have already been shown to suppress melanogenesis through inhibiting tyrosinase activity, but the effective doses are much higher and potentially cytotoxic compared with the dose used in SHT.
| Name                          | Active components | Biological activities                                                                 | Reference   |
|-------------------------------|-------------------|---------------------------------------------------------------------------------------|-------------|
| *Angelica keiskei*            | Chalcones         | Inhibit melanin formation                                                              | 115         |
| *Alpinia zerumbet*            |                   | Reduce the melanin content                                                             | 116         |
| *Astragalus membranaceus*     | PG2               | Inhibit the melanin production                                                          | 117         |
| *Aunostachys roxburghii*      | Alcohol extracts  | Inhibit melanogenesis                                                                  | 118         |
| *Arctostaphylos uva-ursi*     | Arbutin           | Inhibit the biosynthesis of melanin and tyrosinase activity                             | 119         |
| *Arctium lappa*               | Artigenin         | Inhibit tyrosinase activity                                                             | 120         |
| *Artocarpus communis*         |                   | Decrease melanin content and tyrosinase activity                                        | 121         |
| CM                            |                   | Reduce cellular tyrosinase activity and melanin formation                               | 109,110     |
| *Cinnamomum osmophloeum*      | Kanethira         | Inhibit tyrosinase activity                                                             | 122         |
| *Cassia auriculata*           | Methanol extract  | Inhibit melanogenesis                                                                  | 123         |
| *Cassulina sappan* Linn       | Methanol extract  | Inhibit melanin synthesis                                                               | 124         |
| CE                            |                   | Suppress tyrosinase activity by inhibiting ANGPTL 2 expression                         | 111         |
| CBM                           |                   | Have antimelanogenic activities                                                        | 112         |
| *Cyrtomium fortunei* J. Smith|                   | Inhibit tyrosinase activity and melanin production                                      | 125         |
| Crocetin                      |                   | Anti-tyrosinase properties                                                              | 126         |
| *Cnidium monieri* Cusson      | Osthol            | Inhibit melanin content                                                                 | 127         |
| *Eupatorium lindleyanum*      |                   | Suppress melamine production                                                            | 128         |
| ES                            |                   | Regulate the expression of tyrosinase and MITF                                         | 129         |
| *Heracleum moellendorffii* Hance|               | Inhibit melanogenic enzymes and melanin                                               | 17          |
| *Glycyrriza uralenisi*        | Flowers           | Suppress tyrosinase activity                                                            | 130         |
| Gentiana                      |                   | Suppressed melanin production through down-regulation of tyrosinase, tyrosinase related proteins, MITF and inhibiting CREB phosphorylation | 86          |
| *Ganoderma lucidum*           | GLP               | Inhibit UVB-induced skin pigmentation                                                   | 88          |
| Ginseng                       | Panax ginseng berry extract (Gb-AuNPs) | Suppress cellular tyrosinase and melanin                                               | 84,85       |
|                              | Ginsenoside Rh23, Rb2, and Rh6; vina-ginsenoside R13; vina-ginsenoside R4; picrionside A; 20-O-β-d-glucopyranosyl-3β, 6α, 12β, and 20ß; and 25-pentahydammar-23-ene | Inhibit melanin biosynthesis | 83,131–133 |
|                              | A-Rh4             | Decrease the melanin content and tyrosinase activity via downregulation of cAMP levels | 89          |
|                              | GF1               | Reduce the expression of tyrosinase and dopachrome tautomerase and inhibit melanin synthesis by increasing the production of IL-13; decreases visible pigmentation by inhibiting melanosome transport; | 90-92       |
|                              | Ginsenoside Ia    | Decreases melatin synthesis and suppresses tyrosinase activity                          | 93          |
|                              | Cinnamic acid     | Reduce melanin and tyrosinase activity                                                 | 134         |
|                              | PG-2              | Inhibit melanogenesis                                                                  | 72          |
| *Garvinia mangostana*         | Mangosenone F     | Inhibit production of melanin                                                          | 135         |
| *Kaempferia galanga*          | Ethyl p-methoxycinnamate | Inhibit tyrosinase activity                                                            | 136         |
| *Limoniastrum gyninianum*     | The aqueous gall extract | Inhibit melanin synthesis and tyrosinase activity                                       | 137         |
| *Lepidium apetalum* (ELA)     |                   | Decrease melanin content via an ELA-mediated increase in keratino-cyte IL-6 production | 138         |
| *Morus alba* L. Leaves        | Ethyl acetate fraction | Decrease the activity of tyrosinase                                                  | 139         |
| *Magnolia grandiflora*        |                   | Decrease the expression of tyrosinase and TRP-1,                                        | 140         |
| *Michelia alba*               | (-)-N-formylanonaine | Inhibit mushroom tyrosinase                                                           | 141         |
| *Phylo nodiflora* Greene      |                   | Suppress melanogenesis                                                                 | 20          |
| *Polygonum cuspidatum*        | Piccid            | Inhibit melanogenesis                                                                  | 142         |

(Continued)
ERK pathways.106,107 probably through modulating the PI3k/Akt and MAPK/ERK pathways.105 Activation of the PI3K/Akt and MAPK/ERK pathways results in the expression of MITF, tyrosinase, TRP-1, and TRP-2, which have been shown to reduce melanin production by reducing N and 1-

Furthermore, gomisin N has been shown to reduce melanin production by reducing N and 1-

GLP can greatly relieve erythema reactions in guinea pig skin caused by high-dosage UVB irradiation.88 Downregulation of tyrosinase expression and the expression of MITF, tyrosinase, TRP-1, and TRP-2, have been shown to reduce melanin production by reducing N and 1-

Gomisin N has been shown to reduce melanin production by reducing N and 1-

| Table 1. Continued |
|-------------------|
| **Name**               | **Active components** | **Biological activities**               | **Reference** |
| Pistacia atlantica subsp. mutica | Methanol and ethylacetate extracts | Inhibit tyrosinase activity | 143 |
| Rhodiola rosea | Aqueous alcohol extract | Inhibit tyrosinase activity | 99 |
| Santellaria baicalensis | Wogonin | Inhibit melanogenesis and melanosomal transport | 96,97 |
|                     | The 6-methyl-positioned flavones | Inhibit melanosomal transport | 98 |
|                     | Baicalin | Decrease tyrosinase activity and melanin level | 109,144 |
| SHT                  |                     | Inhibit melanin synthesis | 94 |
| Schisandra chinensis (Turcz.) Baillon | Gomisin N | Inhibit melanogenesis through the MC1R pathway | 106 |
|                     | 1-O-MFF | Reduce melanin production | 107 |
| Sophora flavescens | Phenolic diterpenes | Inhibit the Rab27a protein | 114 |
| Salvia officinalis | Downregulation of tyrosinase expression | 146 |
| Sauromorus chinensis | Inhibit melanogenesis | 147 |
| Sauropus androgynus L. Merr. | p-Coumaric acid | Inhibit tyrosinase expression | 148 |
| Sasa quelpaertensis Nakai | The Chinese herb Paeonia suffruticosa Andrews, commonly called Cortex Moutan, significantly reduces not only cellular tyrosinase activity but also melanin formation in B16 cells, which may result in the downregulation of the protein levels of MC1R, MITF, and TRP-1.108,109 Angiopoietin-like protein (ANGPTL) 2 is an inflammatory mediator produced in sun-exposed skin areas that can accelerate pigment production in keratinocytes and melanin-producing cells. Chrysanthemum indicum×Erigeron annuus suppresses ANGPTL 2 expression, thereby inhibiting tyrosinase activity in melanocytes.110 The yields and components of essential oils extracted from Chrysanthemum boreale MANKINO (CBM) (CBMEOs) are different at each stage, but CBMEOs have antimelanogenic activities in all CBM harvesting stages, resulting in skin-whitening biological activities though phosphorylation of ERK 1/2 and p38 MAPK.111 Euphorbia supina (ES) is an annual herbaceous plant and is largely used in traditional herbal formulations. ES extract weakens α-MSH-stimulated melanin synthesis by regulating the expression of tyrosinase and MITF. These activities might be due to gallic acid and protocatechuic acid, which have been detected in ES extract.112 Rab27a is essential for melanosome transport to the dendrite tips in human melanocytes.113 Sauropus androgynus L. Merr. | 110 |
| Saururus chinensis | Methanol and ethylacetate extracts | Inhibit melanogenesis | 150 |
| Xanthium strumarium | Inhibit the melanin production | 151 |

**Others**

The Chinese herb Paeonia suffruticosa Andrews, commonly called Cortex Moutan, significantly reduces not only cellular tyrosinase activity but also melanin formation in B16 cells, which may result in the downregulation of the protein levels of MC1R, MITF, and TRP-1.108,109 Angiopoietin-like protein (ANGPTL) 2 is an inflammatory mediator produced in sun-exposed skin areas that can accelerate pigment production in keratinocytes and melanin-producing cells. Chrysanthemum indicum×Erigeron annuus suppresses ANGPTL 2 expression, thereby inhibiting tyrosinase activity in melanocytes.110 The yields and components of essential oils extracted from Chrysanthemum boreale MANKINO (CBM) (CBMEOs) are different at each stage, but CBMEOs have antimelanogenic activities in all CBM harvesting stages, resulting in skin-whitening biological activities though phosphorylation of ERK 1/2 and p38 MAPK.111 Euphorbia supina (ES) is an annual herbaceous plant and is largely used in traditional herbal formulations. ES extract weakens α-MSH-stimulated melanin synthesis by regulating the expression of tyrosinase and MITF. These activities might be due to gallic acid and protocatechuic acid, which have been detected in ES extract.112 Rab27a is essential for melanosome transport to the dendrite tips in human melanocytes.113 Sauropus androgynus L. Merr. extract weakens α-MSH-stimulated melanin synthesis by regulating the expression of tyrosinase and MITF. These activities might be due to gallic acid and protocatechuic acid, which have been detected in ES extract.112 Rab27a is essential for melanosome transport to the dendrite tips in human melanocytes.113
Heracleum moellendorfii-treated melan-a cells exhibit increased pERK levels and subsequently decrease the expression of MITF, leading to the inhibition of melanogenic enzymes and melanin. Table 1 summarizes the key properties and activities in relation to the botanical extracts described in this section.

Conclusions

The biological activities of Chinese herbal medicines that are potentially useful for treating skin hyperpigmentation are summarized in this text. The active components of Chinese herbal medicines and their biological activities are provided in Table 1. In recent years, herbal medicines have become an important approach in drug discovery programs for developing potent melanogenesis inhibitors. This method has several advantages, including being milder, safer, and less irritating than traditional methods. However, the skin-whitening effects of a single Chinese herbal medicine with a skin-whitening active ingredient are relatively limited, and they do not meet the needs of the majority of women. The development of new skin-whitening agents should search for more effective compound formulas with multiple orientations, multiple targets, and multiple levels, from reducing melanocyte formation to inhibiting tyrosinase activity to the process of migration to the epidermis to the reduction of melanin formation at the genetic level and others. Different skin-whitening active ingredients produce synergistic effects without a mutual reaction and exert a stronger whitening effect.

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