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Research article

Anti-melanogenic activity of rice bran extracts for development of cosmeceutical ingredients

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Abstract: Rice bran is rich in bioactive compounds, but its potential for cosmeceutical applications remains insufficiently explored. In this study, we investigated the anti-melanogenic effects of a 70% ethanol extract of rice bran prepared by ultrasonication in distilled water. The extract was evaluated for DPPH radical scavenging activity, cytotoxicity, tyrosinase inhibition, melanin production, and associated signaling pathways in B16F10 murine melanoma cells. The rice bran extract exhibited DPPH radical scavenging activity and showed no cytotoxicity in B16F10 cells. It also inhibited tyrosinase activity in a dose-dependent manner and suppressed melanin synthesis in B16F10 cells. Mechanistically, the extract reduced the TRP1, TRP2, and MITF protein levels, while increasing the phosphorylation of Erk and Akt in B16F10 cells. In addition, treatment with PD98059 or LY294002 attenuated the extract-induced downregulation of MITF and altered MITF phosphorylation. These findings suggest that rice bran extract may serve as a potential cosmeceutical ingredient for controlling melanogenesis, warranting further cosmeceutical investigation.

Keywords: *Oryza sativa*; cosmetics; melanosis; microphthalmia-associated transcription factor; tyrosinase-related protein 1; tyrosinase-related protein 2

1. Introduction

Rice bran is a by-product of the rice milling process, consisting of the outer layers of the rice grain that are removed when brown rice is processed into white rice [1–3]. This layer includes the seed coat, germ, and broken grains. Rice bran is rich in nutrients, containing proteins, fats, ash, crude fiber,

and various bioactive compounds such as phenolic acids, flavonoids, tocopherols, tocotrienols, and phytic acid, many of which are known to have antioxidant and anti-cancer properties [4–6]. Despite its high nutritive value, rice bran is often underutilized and primarily used as livestock feed or boiler fuel due to challenges in stabilization, which can lead to rancidity from its high oil content. Recent advancements in stabilization techniques have expanded its applications, including extraction of rice bran oil, which is a high-quality vegetable oil, and the use of rice bran derivatives in cosmetic products [4,7,8]. However, there is not enough research on the anti-melanogenic activity and working mechanisms of rice bran extract for cosmeceutical ingredients.

The melanogenesis signaling pathway involving Akt- or Erk-mediated microphthalmia-associated transcription factor (MITF) regulation is a complex process that plays a crucial role in skin pigmentation [9–11]. MITF is a master regulator of melanocyte development and melanin production [12]. MITF is involved in the cellular response to ultraviolet (UV) exposure, which is a key environmental factor influencing skin pigmentation [13]. It controls the expression of key melanogenic enzymes such as tyrosinase, tyrosinase-related protein 1 (TRP1), and tyrosinase-related protein 2 (TRP2). Akt is activated by various growth factors and hormones. Activated Akt can phosphorylate and inactivate glycogen synthase kinase-3 β (GSK3β), which normally phosphorylates and destabilizes MITF [14]. By inhibiting GSK3β, Akt indirectly stabilizes MITF, promoting melanogenesis. Erk is part of the mitogen-activated protein kinase (MAPK) signaling cascade. Erk can have both positive and negative effects on MITF through degradation of MITF [15]. This complex interplay of signaling pathways in melanogenesis highlights the intricate regulation of skin pigmentation and offers multiple potential targets for therapeutic interventions in pigmentation disorders.

A cosmeceutical is a type of cosmetic product that is claimed to have medicinal or drug-like benefits [16–18]. These products are marketed as cosmetics but reputedly contain biologically active ingredients that can provide therapeutic effects on the skin [19−21]. The term "cosmeceutical" combines "cosmetic" and "pharmaceutical" and was coined in the 1980s by Dr. Albert Kligman. These products serve both cosmetic and therapeutic purposes, aiming to improve appearance while also delivering health benefits. They commonly contain ingredients like antioxidants, peptides, vitamins, and botanical extracts that are believed to have beneficial effects on the skin [22]. They often claim to address issues such as wrinkles, aging, hyperpigmentation, acne, and inflammation [23]. Several cosmeceutical products and natural compounds exhibit anti-melanogenic activity, which can help reduce hyperpigmentation and promote skin lightening. However, it is necessary to continue to study novel cosmeceutical ingredients with anti-melanogenic activity due to the ongoing demand for more effective and safer skin lightening and anti-aging products.

In this study, we evaluated the potential of rice bran ethanol extract as a cosmeceutical ingredient with a focus on its anti-melanogenic properties. The rice bran extract demonstrated anti-melanogenic effects by inhibiting tyrosinase and regulating Akt or Erk-mediated MITF in B16F10 cells. Consequently, our ongoing research indicates that rice bran extract could be a promising agent for treating skin melanogenesis and supporting skin tissue maintenance.

2. Materials and methods

2.1. Rice bran extract preparation

Rice bran was obtained from Sejong city in South Korea and thoroughly washed with fresh water before being air-dried. Due to variability in the quality of rice bran depending on the cultivation region, we used rice bran obtained from a specific local source to ensure consistency in the starting material.

The dried rice bran was then ground and passed through a 30-mesh sieve (600 μm particle size) [24]. Subsequently, the ground material was mixed with 70% ethanol (EtOH; Sigma, St. Louis, MO, USA) and subjected to ultrasonication (20 KHz, 500 Watt ± 2, Sonic & Materials, CT, USA) for 1 h. The resulting supernatant was filtered using 110 nm filter paper (No. 2, Advantec, Tokyo, Japan), and excess ethanol was removed via rotary evaporation (Eyela, Tokyo, Japan). Finally, the sample was dried using a vacuum freeze dryer (Labogene, Lillerød, Denmark) for 72 h. The extract was dissolved in DMSO (100 mg/mL) and stored at −20 °C. The final 0.5% DMSO concentration was used for all in vitro cell experiments.

2.2. Cell culture

B16F10 murine melanoma cell lines (Korean Cell Line Bank, Seoul, Korea) were maintained in Dulbecco's modified Eagle's medium (Thermo Fisher, Waltham, MA, USA) supplemented with 10% fetal bovine serum and 1% streptomycin/penicillin at 37 °C in a humidified incubator containing 5% CO_2 [9,10].

2.3. Free radical scavenging assay

Free radical scavenging activity of rice bran extract was assessed using 2,2-diphenyl-1-picrylhydrazyl (DPPH; Sigma) [9,10]. DPPH powder was dissolved in methanol (0.2 mM solution). Various concentrations of rice bran extract or ascorbic acid (1 μM, Sigma) were then placed in 96-well plates, followed by the addition of the DPPH solution (a final DPPH concentration of 0.1 mM) to each well. The plates were incubated in the dark at room temperature for 30 min. Absorbance was measured at 517 nm using a multi-well microplate reader (Molecular Devices, Mountain View, CA, USA).

2.4. WST-1 assay

B16F10 cells were seeded in 96-well plates at a density of 1×10^3 cells per well and incubated for 24 h in a humidified environment (37 °C, 5% CO_2) [10]. Following incubation, the cells were treated with various concentrations of rice bran extract or retinoic acid (1 μM, Sigma) for 24 h. Subsequently, 10 μL of EZ-CYTOX (DoGenBio, Seoul, South Korea) was added to each well. After 1 h incubation at 37 °C in the dark, the absorbance was measured at 570 nm using a multi-well microplate reader (Molecular Devices).

2.5. Tyrosinase activity assay

B16F10 cells were seeded in 6-well plates at a density of 1×10^5 cells per well and incubated for 24 h in a humidified environment (37 °C, 5% CO_2) [10]. Following incubation, the cells were treated with various concentrations of rice bran extract or kojic acid (Sigma) for 24 h. Subsequently, the cells were lysed using lysis buffer (Cell Signaling Technology, Danvers, USA) and centrifuged at 18,000 × g for 30 min at 4 °C. The supernatant was collected to assess tyrosinase activity. The reaction mixture, including 60 mM phosphate-buffered saline (PBS, pH 6.8), 10 mM L-DOPA (Sigma) solution, and the supernatant, was incubated at 37 °C. Following incubation, dopachrome formation was measured at 475 nm using a multi-well microplate reader (Molecular Devices).

2.6. Melanin content analysis

B16F10 cells were seeded in 6-well plates at a density of 1×10^5 cells per well and incubated for 24 h in a humidified environment (37 °C, 5% CO_2) [10]. Following incubation, cells were stimulated with α-melanocyte-stimulating hormone (α-MSH, Sigma) and treated with various concentrations of rice bran extract or kojic acid for 72 h. Subsequently, the cells were harvested and washed with PBS. The total melanin content in the cell pellets was visualized, and their image was captured. The color density of the cell pellet was photographed and analyzed using ImageJ software and presented in graph form.

2.7. Western blotting analysis

B16F10 cells were seeded in 6-well plates at a density of 1×10^5 cells per well and incubated for 24 h in a humidified environment (37 °C, 5% CO_2) [10]. Following incubation, the cells were treated with various concentrations of rice bran extract for 24 h. Subsequently, cells were lysed using lysis buffer (Cell Signaling Technology). The extracted proteins were separated on SDS-polyacrylamide gels and transferred to polyvinylidene difluoride membranes (Merck Millipore, Burlington, MA, USA). The membranes were then blocked with 5% bovine serum albumin (BSA, Sigma). Primary antibodies (1: 1000 dilution) were applied to the membranes and incubated overnight at 4 °C. Antibodies for MITF, phospho-MITF (pMITF), Akt, phospho-Akt (pAkt), Erk, and phospho-Erk (pErk) were purchased from Cell Signaling Technology. Antibodies for TRP1, TRP2, and β-actin were obtained from Santa Cruz Biotechnology (Santa Cruz, CA, USA). Following primary antibody incubation, the membranes were incubated with HRP-conjugated anti-mouse or anti-rabbit secondary antibodies (1: 10,000 dilution, Cell Signaling Technology) for 1 h at room temperature. Protein detection was achieved using enhanced chemiluminescence (ECL; GE Healthcare, Little Chalfont, UK) and visualized with a Chemidoc system (Bio-Rad, Hercules, CA, USA).

2.8. Statistical analysis

All experiments were conducted with biological and technical triplicates. The results are presented as the mean ± standard deviation (SD). Significant differences between the control and the experimental group were assessed using a Student's t-test, with a significance threshold set at $P < 0.05$.

3. Results

3.1. Rice bran extract shows antioxidant activity

The ethanol extraction method combined with ultrasonication offers several advantages for preparing plant extracts, particularly in enhancing the efficiency and quality of the extraction process. To determine the most effective extraction condition for rice bran using EtOH, the DPPH assay was performed. As shown in Figure 1A, it was confirmed that the 70% and 90% EtOH rice bran extract showed the strongest DPPH scavenging activity. Since 70% EtOH costs less than 90% EtOH, 70% EtOH extraction condition was adapted for economical production and because it

yielded the highest antioxidant activity, suggesting efficient extraction of both hydrophilic and moderately lipophilic bioactive compounds. Importantly, the melanin inhibition and tyrosinase activity assays were conducted independently to experimentally validate anti-melanogenic effects, rather than assuming them from antioxidant results alone. Thus, antioxidant activity was used as a screening parameter for extract selection, while melanin inhibition was confirmed through dedicated biological assays. The overall extraction process was schematically described in Figure 1B. Then, different concentrations (125, 250, and 500 μg/mL) of the 70% EtOH extract of rice bran were used to examine the free radical scavenging activity. As shown in Figure 2A, 70% EtOH extract of rice bran reduced absorbance in a dose-dependent manner, suggesting that this extract decreased free radicals. A concentration of 500 μg/mL of 70% ethanol extract of rice bran reduced absorbance by approximately 45% compared to the control. Ascorbic acid (1 μM), as the positive control, reduced absorbance to approximately 35% compared to the control group. In addition, we examined the effect of 70% EtOH extract of rice bran on the growth of B16F10 murine melanoma cell lines, which are derived from a murine melanoma, making them an appropriate in vitro model for studying melanoma and melanogenesis. B16F10 cells were treated with 70% EtOH extract of rice bran, and their growth rate was assessed using the WST-1 assay. As shown in Figure 2B, 500 μg/mL of 70% EtOH extract of rice bran appeared to induce only a slight increase in cell growth, which was comparable to the effect of 1 μM retinoic acid as the positive control. These findings suggest that 70% EtOH extract of rice bran may reduce free radicals without causing cell toxicity.

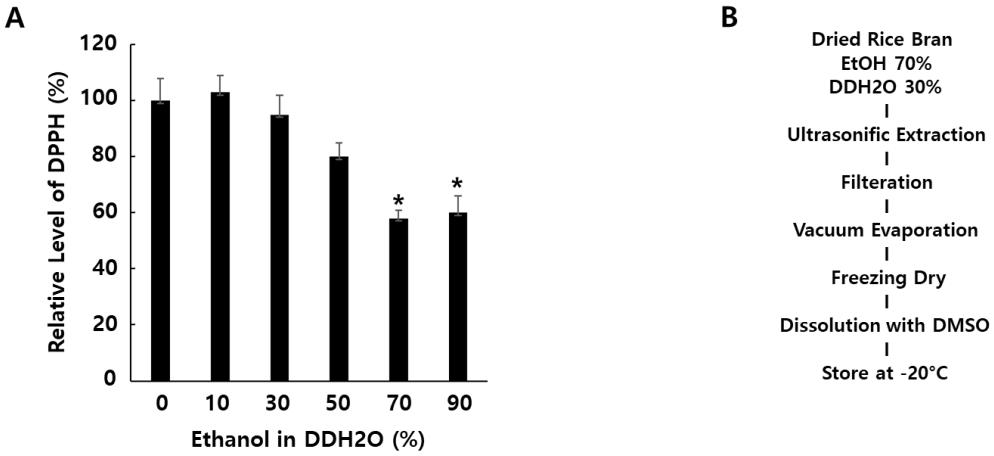

Figure 1. Preparation of rice bran extract. (A) DPPH assay result showing free-radical scavenging ability of rice bran extract using various concentrations of EtOH in ddH_2O. Data from three independent experiments, presented as average ± SD (*$p < 0.05$ compared to the control). (B) Ultrasonification preparation diagram of rice bran extract using 70% EtOH in ddH_2O.

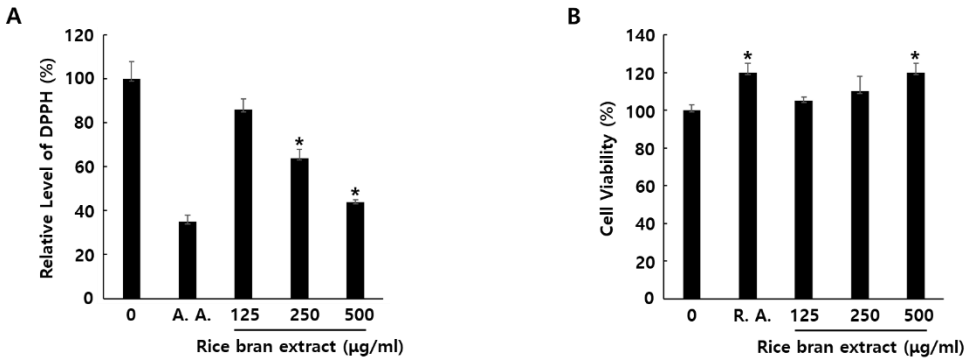

Figure 2. Antioxidant activity and activation of B16F10 cell proliferation by rice bran extract. (A) DPPH assay result showing free-radical scavenging ability of 70% EtOH rice bran extract (125, 250, and 500 μg/mL). 1 μM of ascorbic acid (A.A.) was adopted as the positive control. Data from three independent experiments, presented as average ± SD (*$p < 0.05$ compared to the control). (B) WST-1 assay result showing activation of B16F10 cell proliferation by 70% EtOH rice bran extract (125, 250, and 500 μg/mL). 1 μM of retinoic acid (R.A.) was adopted as the positive control. Data from three independent experiments, presented as average ± SD (*$p < 0.05$ compared to the control).

3.2. Rice bran extract displays anti-melanogenesis activity

Tyrosinase is activated by exposure to ionizing and UV radiation. This activation triggers the process of melanogenesis, which occurs within specialized organelles called melanosomes found in melanocytes. The stimulation of tyrosinase by these forms of radiation leads to increased melanin production, a natural protective response of the skin to potentially damaging radiation. 70% EtOH extract of rice bran was used to determine the inhibitory effect on tyrosinase activity in B16F10 cells by the Tyrosinase Inhibitor Assay kit. As shown in Figure 3A–B, 70% EtOH extract of rice bran (125, 250, and 500 μg/mL) showed a dose-dependent inhibitory effect on the tyrosinase in B16F10 cells. Kojic acid (75, 150, and 300 μM), as the positive control, was also observed to inhibit tyrosinase in a dose-dependent manner. A concentration of 500 μg/mL of 70% ethanol extract of rice bran inhibited tyrosinase activity by approximately 50% compared to the control. For comparison, 300 μM of kojic acid, used as a positive control, demonstrated about 50% inhibition of tyrosinase activity. To measure the anti-melanogenic effect of 70% ethanol extract of rice bran in B16F10 cells, a melanin content assay was performed. To stimulate melanin production, 1 μM of α-MSH was added to B16F10 cells, except for the control group. Subsequently, kojic acid (75, 150, and 300 μM) or 70% EtOH extract of rice bran (125, 250, and 500 μg/mL) was added to cells for 72 h. After incubation, the color density of the cell pellet was analyzed. As shown in Figure 4A–B, the results showed that kojic acid or 70% EtOH extract of rice bran reduced melanin content in a dose-dependent manner. Due to the stimulation by α-MSH, the melanin content in B16F10 cells increased by approximately 30%. 500 μg/mL of 70% EtOH extract of rice bran showed a statistically significant ($P < 0.05$) reduction (35%) in melanin content, which was comparable to the effect (40%) of 300 μM kojic acid as the positive control. These results indicate that 70% EtOH extract of rice bran has the potential to inhibit melanogenesis in B16F10 cells.

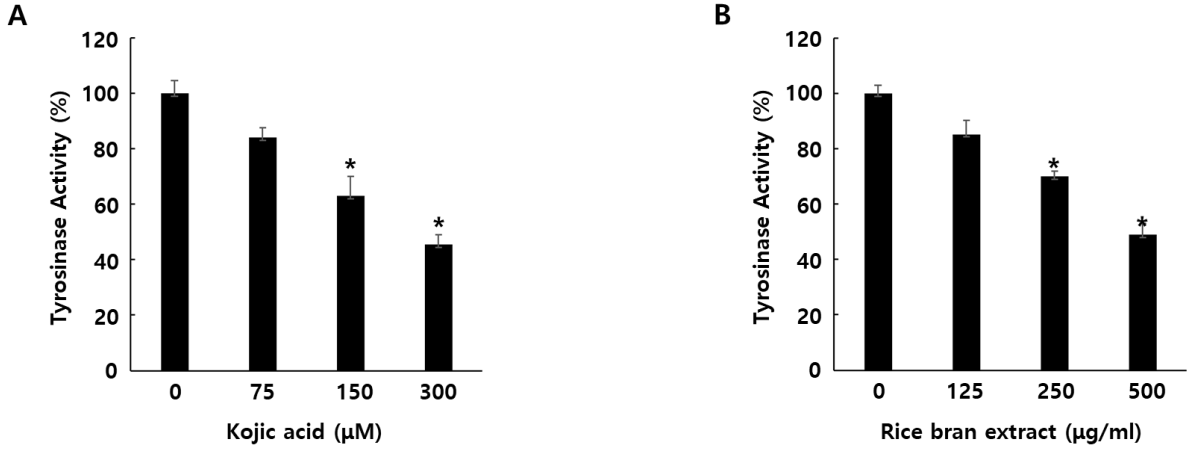

Figure 3. Anti-tyrosinase activity of 70% ethanol extract of rice bran. The same number of B16F10 cells were exposed to various concentrations of (A) kojic acid (75, 150, and 300 μM) or (B) 70% ethanol extract of rice bran (125, 250, and 500 μg/mL), following the protocol outlined in the materials and methods section. Kojic acid was used as the positive control. Data from three independent experiments, presented as average ± SD (*p < 0.05 compared to the control).

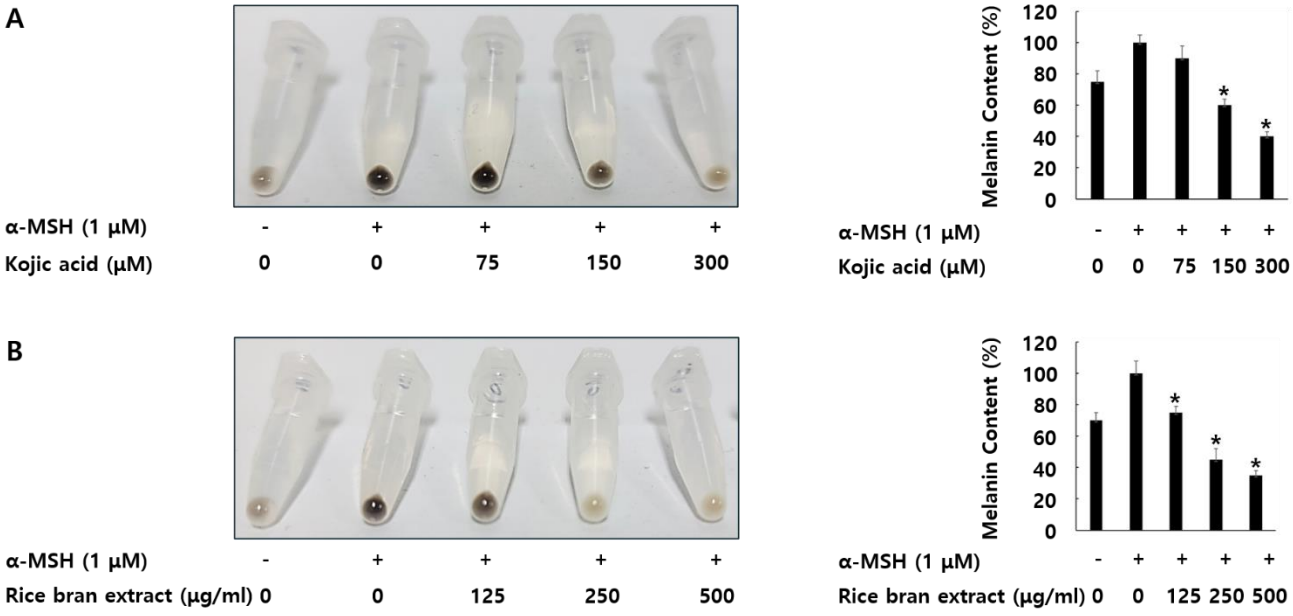

Figure 4. Anti-melanogenic activity of 70% ethanol extract of rice bran. The same number of B16F10 cells were exposed to various concentrations of (A) kojic acid (75, 150, and 300 μM) or (B) 70% ethanol extract of rice bran (125, 250, and 500 μg/mL), following the protocol outlined in the materials and methods section. Kojic acid was used as the positive control. Data from three independent experiments, presented as average ± SD (*p < 0.05 compared to the control).

3.3. Rice bran extract decreases the expression of MITF and TRP1/2 in B16F10 cells

The relationship between MITF and TRP1/TRP2 is crucial for the regulation of melanogenesis in skin cells. MITF is considered the master regulator of melanocyte development and melanogenesis. It controls the expression of several genes involved in melanin production, including TRP1 and TRP2. This transcriptional control allows MITF to upregulate the expression of TRP1 and TRP2 when melanin production needs to be increased. To investigate the mechanistic role of 70% ethanol extract of rice bran in B16F10 cells, these were treated with rice bran extract at concentrations of 0, 250, and 500 μg/mL, and the expression level of TRP1, TRP2, and MITF protein was measured using western blot analysis. As shown in Figure 5A, 70% ethanol extract of rice bran significantly reduced the expression levels of TRP1, TRP2, and MITF. These findings suggest that 70% ethanol extract of rice bran could inhibit melanin production in B16F10 cells by suppressing the protein expression of MITF and its downstream targets. We further explored whether the reduction of MITF by 70% ethanol extract of rice bran was linked to the phosphorylation of Akt and Erk. Previous studies have shown that activation of Akt and Erk signaling pathways can inhibit melanogenesis. Both Akt and Erk activation can lead to the phosphorylation of MITF, followed by proteasome-mediated ubiquitination, resulting in decreased MITF protein stability and increased degradation. To elucidate the specific mechanism by which 70% ethanol extract of rice bran inhibits melanin synthesis, we examined its effect on Akt and Erk phosphorylation in B16F10 melanoma cells using western blot analysis. As shown in Figure 5A, 70% ethanol extract of rice bran significantly increased the levels of phosphorylated Akt and Erk in a dose-dependent manner. These results suggest that 70% ethanol extract of rice bran could inhibit melanogenesis by activating Erk and Akt pathways, leading to the suppression of MITF. Then, to investigate the relationship between phosphorylation of MITF and phosphorylation of Erk or Akt in B16F10 cells, we treated cells with 70% ethanol extract of rice bran in the presence of either MEK/Erk-specific inhibitor (PD98059) or PI3K/Akt-specific inhibitor (LY294002). The addition of PD98059 or LY294002 prevented the downregulation of MITF and phosphorylation of MITF induced by 70% ethanol extract of rice bran (Figure 5B–C). These results suggest that the inhibitory effects of 70% ethanol extract of rice bran on melanogenesis could be linked to the activation of Erk and Akt pathways and MITF downregulation.

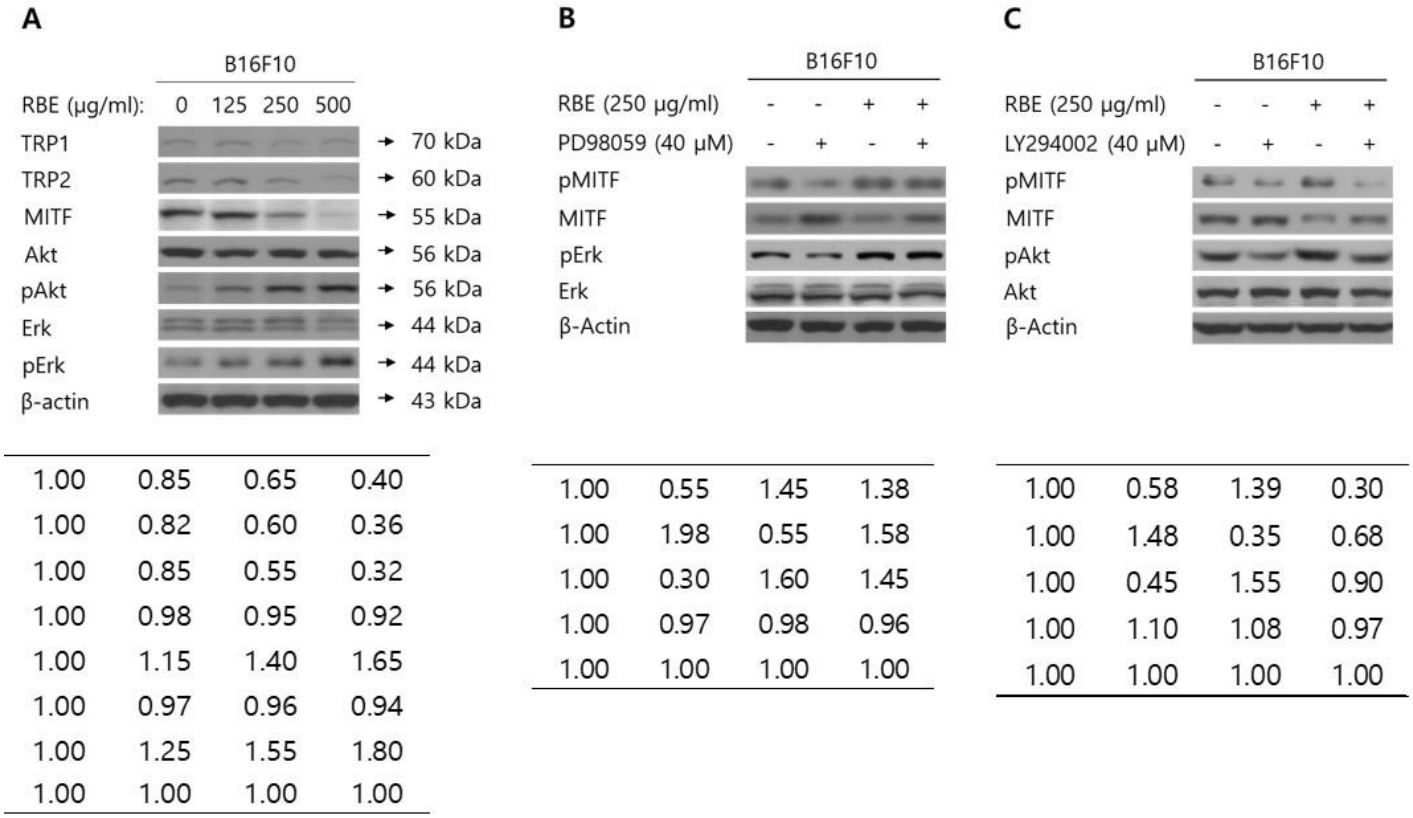

Figure 5. Regulation of melanin synthesis-related protein expression by 70% ethanol extract of rice bran in the same number of B16F10 cells. (A) B16F10 cells were exposed to various concentrations of 70% ethanol extract of rice bran (125, 250, and 500 μg/mL); the indicated protein expression level was analyzed by western blotting, as outlined in the materials and methods section. β-actin was used as a loading control. Activation of Erk (B) and Akt (C) by 70% ethanol extract of rice bran in B16F10 cells. B16F10 cells were exposed to 70% ethanol extract of rice bran (250 μg/mL) in the presence of PD98059 (40 μM) or LY294002 (40 μM); the indicated protein expression level was analyzed by western blotting, as outlined in the materials and methods section. β-actin was used as a loading control. The band density was quantified by the ImageJ software.

4. Discussion

Rice bran is the outer layer of the rice grain, which is removed during the milling process to produce white rice. It is a by-product of rice processing and is rich in nutrients, making it a valuable source of various bioactive compounds [2]. Several research works have shown the health benefits of rice bran extract. A review paper highlighted multiple health benefits of phytosterols found in rice bran oil, including anti-cancer, anti-inflammatory, anti-allergic, anti-bacterial, cholesterol-lowering, skin protection, anti-obesity, anti-diabetic, neuroprotective, gastroprotective, and immune-enhancing properties [25]. A study found that cycloartenyl trans-ferulate, a component of rice bran extract, inhibited mammalian DNA polymerase and suppressed inflammation [26]. Another work has shown that rice bran polysaccharides exhibited anti-tumor, immune-enhancing, and blood glucose-lowering effects [27,28]. A study showed that rice bran oil contains substances that might decrease cholesterol absorption in the body [29]. Other studies indicated that rice bran has beneficial biochemical and antioxidant effects on various diseases, including dementia, cardiovascular disease, and Alzheimer's disease [30−32]. These studies collectively suggest that rice bran extract has a wide range of potential health benefits, particularly in the areas of cardiovascular health, diabetes management, cancer prevention, and immune system support.

Rice bran extract has demonstrated significant anti-melanogenic effects, which means it can inhibit or reduce melanin production in skin cells. Glucosylceramides and elasticamide derived from rice oil by-products have shown potent anti-melanogenic activities [33]. In a study using B16 melanoma cells, glucosylceramides and elasticamide significantly suppressed melanin production. Especially, elasticamide, a ceramide found in rice bran, demonstrated anti-melanogenic effects in human 3D-cultured melanocytes and suppressed the expression of TRP1 in normal human melanocytes. In addition, a clinical trial using rice bran extract containing 1.2 mg/day of glucosylceramides and 56 μg/day of elasticamide showed significant suppression of UV-B-induced skin pigmentation after 8 weeks of ingestion. Another study showed that rice bran protein hydrolysates contain tyrosinase inhibitory peptides, which can contribute to the anti-melanogenic effect [34]. Rice bran ash extract, which contains soluble minerals, including orthosilicic acid, has shown potential to promote melanogenesis through increasing MITF phosphorylation [35]. While this may seem contradictory, it suggests that different components of rice bran can have varied effects on melanin production. Fermented rice bran has been shown to downregulate MITF expression and inhibit α-MSH-induced melanogenesis in B16F1 melanoma cells, indicating that the fermentation process may enhance the anti-melanogenic properties of rice bran [36,37]. These findings suggest that rice bran extract and its components have significant potential as ingredients in skin-lightening products or treatments for hyperpigmentation disorders. The anti-melanogenic effects are attributed to various compounds present in rice bran, including glucosylceramides, elasticamide, and other bioactive molecules. Further research is ongoing to fully understand the mechanisms of action and to develop more effective formulations for skincare applications. In this study, we were also able to confirm the inhibitory activity of rice bran extract on melanin pigment production in B16F10 murine melanocytes. We also demonstrated that rice bran extract activates Akt and Erk, which are involved in signaling pathways that can influence MITF activity and stability.

Both Akt and Erk pathways play crucial roles in melanogenesis, allowing for a focused

research strategy. Insights gained from studying these pathways could be applicable to various skin conditions involving hyperpigmentation. There is already a substantial body of research on Akt and Erk pathways in cancer and other cellular processes, providing a strong foundation for melanogenesis studies. These pathways offer several potential targets for developing anti-melanogenic agents, increasing the chances of finding effective treatments. Many plant extracts have shown anti-melanogenic effects through Akt or Erk inhibition, opening avenues for natural product research. In fact, there are lots of works dealing with plant extracts that prevent melanogenesis through activation of Akt or ERK pathways, leading to down-regulation of MITF. *Nymphaea nouchali* flower extract was found to stimulate MAPK phosphorylation, including Erk, which led to the degradation of tyrosinase and MITF, suppressing melanin production [38]. The study showed that selective inhibitors of Erk attenuated *Nymphaea nouchali* flower extract's inhibitory effects on melanogenesis. Both leaf and root extracts of *Patrinia villosa* were found to have anti-melanogenic effects through the induction of Erk and autophagy [39]. The activity of phosphorylated Erk was enhanced when exposed to *Patrinia villosa* extract. *Daphne odora* extract inhibited tyrosinase activity and α-MSH-induced melanin biosynthesis in B16F10 melanoma cells [40]. *Daphne odora* extract activated Akt and Erk signaling pathways, leading to decreased phosphorylation and reduced MITF expression. This inhibition of the melanogenesis signaling cascade resulted in a significant depigmenting effect. While in vitro studies may show promising results, translating these findings into effective and safe in vivo treatments can be challenging. Researching Akt and Erk pathways for anti-melanogenic activity offers promising avenues for developing targeted treatments, but researchers must carefully consider the complex roles these pathways play in cellular function and potential long-term effects of their modulation.

5. Conclusions

In conclusion, this study demonstrates that rice bran extract may suppress melanogenesis in B16F10 cells, potentially through the modulation of Akt/Erk-associated MITF signaling. However, it is important to note that the mechanisms can be complex and often involve multiple signaling pathways. Thus, additional investigations are necessary to uncover precise molecular pathways, perform in silico network pharmacology analysis, and identify the key active ingredients responsible for the observed effects, such as an increase in cell proliferation and a decrease in melanogenic activity. This deeper exploration will help clarify the underlying mechanisms and pinpoint the specific compounds that contribute to the observed activity.

Use of generative-AI tools declaration

The author declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The author declares no conflict of interest.

Author contributions

PSH: Conceptualization, Investigation, Supervision, Writing – original draft, review, and editing.

Data availability

The data of this study is available from the corresponding author upon request.

References

1. Sharif MK, Butt MS, Anjum FM, et al. (2014) Rice bran: a novel functional ingredient. *Crit Rev Food Sci Nutr* 54: 807–816. https://doi.org/10.1080/10408398.2011.608586
2. Tan BL, Norhaizan ME, Chan LC (2023) Rice bran: from waste to nutritious food ingredients. *Nutrients* 15: 2503. https://doi.org/10.3390/nu15112503
3. Das PP, Gul MZ, Weber AM, et al. (2025) Rice bran extraction and stabilization methods for nutrient and phytochemical biofortification, nutraceutical development, and dietary supplementation. *Nutr Rev* 83: 692–712. https://doi.org/10.1093/nutrit/nuae174
4. Sahini MG, Mutegoa E (2023) Extraction, phytochemistry, nutritional, and therapeutical potentials of rice bran oil: a review. *Phytomedicine Plus* 3: 100453. https://doi.org/10.1016/j.phyplu.2023.100453
5. Manzoor A, Pandey VK, Dar AH, et al. (2023) Rice bran: nutritional, phytochemical, and pharmacological profile and its contribution to human health promotion. *Food Chem Adv* 2: 100296. https://doi.org/10.1016/j.focha.2023.100296
6. Yu Y, Zhang J, Wang J, et al. (2019) The anti-cancer activity and potential clinical application of rice bran extracts and fermentation products. *RSC Adv* 9: 18060–18069. https://doi.org/10.1039/C9RA02439E
7. Punia S, Kumar M, Siroha AK, et al. (2021) Rice bran oil: emerging trends in extraction, health benefit, and its industrial application. *Rice Sci* 28: 217−232. https://doi.org/10.1016/j.rsci.2021.04.002
8. Huang W, Liu B, Shi D, et al. (2024) Research progress on the quality, extraction technology, food application, and physiological function of rice bran oil. *Foods* 13: 3262. https://doi.org/10.3390/foods13203262
9. Im DS, Lee JM, Lee J, et al. (2017) Inhibition of collagenase and melanogenesis by ethanol extracts of *Orostachys japonicus* A. Berger: possible involvement of Erk and Akt signaling pathways in melanoma cells. *Acta Biochim Biophys Sin* 49: 945−953. https://doi.org/10.1093/abbs/gmx090
10. Lee J, Ji J, Park SH (2018) Antiwrinkle and antimelanogenesis activity of the ethanol extracts of Lespedeza cuneata G. Don for development of the cosmeceutical ingredients. *Food Sci Nutr* 6: 1307−1316. https://doi.org/10.1002/fsn3.682

11. Jang EJ, Shin Y, Park HJ, et al. (2017) Anti-melanogenic activity of phytosphingosine via the modulation of the microphthalmia-associated transcription factor signaling pathway. *J Dermatol Sci* 87: 19−28. https://doi.org/10.1016/j.jdermsci.2017.03.011
12. Kawakami A, Fisher DE (2017) The master role of microphthalmia-associated transcription factor in melanocyte and melanoma biology. *Lab Invest* 97: 649−656. https://doi.org/10.1038/labinvest.2017.9
13. Pillaiyar T, Manickam M, Jung SH (2017) Recent development of signaling pathways inhibitors of melanogenesis. *Cell Signal* 40: 99−115. https://doi.org/10.1016/j.cellsig.2017.09.004
14. Choi H, Yoon JH, Youn K, et al. (2022) Decursin prevents melanogenesis by suppressing MITF expression through the regulation of PKA/CREB, MAPKs, and PI3K/Akt/GSK-3β cascades. *Biomed Pharmacother* 147: 112651. https://doi.org/10.1016/j.biopha.2022.112651
15. Lv J, Fu Y, Cao Y, et al. (2020) Isoliquiritigenin inhibits melanogenesis, melanocyte dendricity and melanosome transport by regulating ERK-mediated MITF degradation. *Exp Dermatol* 29: 149−157. https://doi.org/10.1111/exd.14066
16. Morganti P, Coltelli MB (2019) A new carrier for advanced cosmeceuticals. *Cosmetics* 6: 10. https://doi.org/10.3390/cosmetics6010010
17. Lee CM (2016) Fifty years of research and development of cosmeceuticals: a contemporary review. *J Cosmet Dermatol* 15: 527−539. https://doi.org/10.1111/jocd.12261
18. Omidian H, Akhzarmehr A, Bertol CD (2026) Natural-based antioxidants in cosmeceuticals: extraction, bioavailability and skin ageing applications. *Int J Cosmet Sci* 48: 394–427. https://doi.org/10.1111/ics.70039
19. Abdullah B, Nasreen R, Ravichandran N (2012) A comprehensive review of consumption pattern and strategies in cosmeceutical market with a focus on dermaceuticals in Indian market. *Int J Sci Res Publ* 2: 176–179.
20. Femenia A (2007) High-value co-products from plant foods: cosmetics and pharmaceuticals, *Handbook of Waste Management and Co-Product Recovery in Food Processing*, Elsevier, 470−501. https://doi.org/10.1533/9781845692520.4.470
21. Crespi O, Rosset F, Pala V, et al. (2025) Cosmeceuticals for anti-aging: mechanisms, clinical evidence, and regulatory insights—a comprehensive review. *Cosmetics* 12: 209. https://doi.org/10.3390/cosmetics12050209
22. Goyal A, Sharma A, Kaur J, et al. (2022) Bioactive-based cosmeceuticals: an update on emerging trends. *Molecules* 27: 828. https://doi.org/10.3390/molecules27030828
23. Milam EC, Rieder EA (2021) An approach to cosmeceuticals, *Essential Psychiatry for the Aesthetic Practitioner*, 42−48. https://doi.org/10.1002/9781119680116.ch4
24. Lee CM, Kang MA, Lee J, et al. (2023) Hibiscus syriacus L. extract by ultrasonic assistance displays anti-inflammatory and pro-apoptotic activity in LPS-stimulated raw 264.7 cells. *Arab J Chem* 16: 105168. https://doi.org/10.1016/j.arabjc.2023.105168
25. Liu Z, Liu X, Ma Z, et al. (2023) Phytosterols in rice bran and their health benefits. *Front Nutr* 10: 1287405. https://doi.org/10.3389/fnut.2023.1287405
26. Mizushina Y, Kuriyama I, Yamazaki A, et al. (2013) Cycloartenyl trans-ferulate, a component of the bran byproduct of sake-brewing rice, inhibits mammalian DNA polymerase and suppresses inflammation. *Food Chem* 141: 1000−1007. https://doi.org/10.1016/j.foodchem.2013.04.048

27. Wang L, Li Y, Zhu L, et al. (2016) Antitumor activities and immunomodulatory of rice bran polysaccharides and its sulfates in vitro. *Int J Biol Macromol* 88: 424−432. https://doi.org/10.1016/j.ijbiomac.2016.04.016
28. Oluwajuyitan TD, Ijarotimi OS, Fagbemi TN, et al. (2021) Blood glucose lowering, glycaemic index, carbohydrate-hydrolysing enzyme inhibitory activities of potential functional food from plantain, soy-cake, rice-bran and oat-bran flour blends. *J Food Meas Charact* 15: 3761−3769. https://doi.org/10.1007/s11694-021-00954-2
29. Lei L, Chen J, Liu Y, et al. (2018) Dietary wheat bran oil is equally as effective as rice bran oil in reducing plasma cholesterol. *J Agric Food Chem* 66: 2765−2774. https://doi.org/10.1021/acs.jafc.7b06093
30. Behl T, Kumar S, Sehgal A, et al. (2021) Rice bran, an off-shoot to newer therapeutics in neurological disorders. *Biomed Pharmacother* 140: 111796. https://doi.org/10.1016/j.biopha.2021.111796
31. Saji N, Francis N, Schwarz LJ, et al. (2019) Rice bran derived bioactive compounds modulate risk factors of cardiovascular disease and type 2 diabetes mellitus: an updated review. *Nutrients* 11: 2736. https://doi.org/10.3390/nu11112736
32. El-Din SS, Abd Elwahab S, Rashed L, et al. (2021) Possible role of rice bran extract in microglial modulation through PPAR-gamma receptors in Alzheimer's disease mice model. *Metab Brain Dis* 36: 1903−1915. https://doi.org/10.1007/s11011-021-00741-4
33. Miyasaka K, Manse Y, Yoneda A, et al. (2022) Anti-melanogenic effects of glucosylceramides and elasticamide derived from rice oil by-products in melanoma cells, melanocytes, and human skin. *J Food Biochem* 46: e14353. https://doi.org/10.1111/jfbc.14353
34. Ochiai A, Tanaka S, Tanaka T, et al. (2016) Rice bran protein as a potent source of antimelanogenic peptides with tyrosinase inhibitory activity. *J Nat Prod* 79: 2545−2551. https://doi.org/10.1021/acs.jnatprod.6b00449
35. Jang HJ, Seo YK (2016) Pigmentation effect of rice bran extracted minerals comprising soluble silicic acids. *Evid Based Complement Alternat Med* 2016: 3137486. https://doi.org/10.1155/2016/3137486
36. Jamaluddin A, Yusof N, Abdul Rahman S, et al. (2023) Effect of Aspergilus oryzae-fermented broken rice, brewers' rice and rice bran on melanogenesis in highly pigmented human melanoma, MNT-1. *Food Res* 6: 81−89. https://doi.org/10.26656/fr.2017.6(S4).011
37. Nguyen HT, Gu M, Choi CW, et al. (2022) Enhanced anti-melanogenic effect of adlay bran fermented with *Lactobacillus brevis* MJM60390. *Appl Microbiol* 2: 502−515. https://doi.org/10.3390/applmicrobiol2030039
38. Alam MB, Ahmed A, Motin MA, et al. (2018) Attenuation of melanogenesis by N*ymphaea nouchali* (Burm. f) flower extract through the regulation of cAMP/CREB/MAPKs/MITF and proteasomal degradation of tyrosinase. *Sci Rep* 8: 13928. https://doi.org/10.1038/s41598-018-32303-7
39. Jeong D, Park SH, Kim MH, et al. (2020) Anti-melanogenic effects of ethanol extracts of the leaves and roots of *Patrinia villosa* (thunb.) Juss through their inhibition of CREB and induction of ERK and autophagy. *Molecules* 25: 5375. https://doi.org/10.3390/molecules25225375

40. Eom YS, Jeong D, Ryu AR, et al. (2022) *Daphne odora* exerts depigmenting effects via inhibiting Creb/Mitf and activating Akt/Erk-signaling pathways. *Curr Issues Mol Biol* 44: 3312−3323. https://doi.org/10.3390/cimb44080228

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