Morin induces melanogenesis via activation of ERK and JNK signaling pathways in B16F10 melanoma cells

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Morin은 B16F10 흑색 종 세포에서 ERK 및 JNK 신호 전달 경로의 활성화를 통해 멜라닌 생성을 유도

요 약
Morin is a well-known flavonoid. Previous studies have reported anti-apoptotic, antioxidant, and anti-inflammatory properties of morin. Although morins have been studied for their biochemical and biological actions, the melanogenesis effects and mechanism of action remains unknown. In this study, we found the effect of morin on melanogenesis and its molecular mechanisms in B16F10 melanoma cells. Morin exhibited no cytotoxicity at concentration ranges of 5–100 μM. The results showed that morin significantly increased intracellular tyrosinase activity and intracellular melanin content without cytotoxicity. Also, morin increased the protein levels of TRP-1, TRP-2 and MITF which were related on melanogenesis. Additional results identified that morin promote the phosphorylation of ERK and JNK. These results indicated that morin stimulated melanogenesis via the ERK and JNK signaling pathways in B16F10 melanoma cells. Taken together, the present study suggested that morin will help potential therapeutic implications for depigmentation disorder.

1. Introduction

Vitiligo is a skin depigmentation disorder [1]. This skin disease characterized by depigmented of skin, and occurs when cutaneous melanocytes are destroyed or non-functional. Melanin is produced by the melanosomes of melanocytes and is scattered in the basal layer of the epidermis. Melanin is an essential component of skin pigmentation that plays an important role in preventing UV damage [2-3]. Melanogenesis is regulated by melanogenic enzymes such as tyrosinase (TYR), tyrosinase-related protein 1 (TRP 1) and tyrosinase-related protein 2 (TRP 2). Microphthalmia-associated transcription factor (MITF) is a major regulator that regulates the transcription of genes involved in melanin synthesis. There are several signaling pathways mediating melanogenesis. In this signal pathway the c-Jun N-terminal kinase mitogen-activated protein kinase (JNK MAPK) and p38 mitogen-activated protein kinase (p38 MAPK) pathway may upregulate melanogenesis by increasing MITF expression. The extracellular signal-regulated kinase mitogen-activated protein kinase (ERK MAPK)-dependent MITF expression pathway is also involved in melanogenesis [1]. Morin (2′,3′,4′,5,7-pentahydroxyflavone) is a well-known flavonoid that is naturally found in various frui ts, mulberries, almonds, red wines, and many Chinese medicinal herbs [4]. Previous studies have reported anti-apoptotic, antioxidant, and anti-inflammatory properties of morin [5]. Although morins have been studied for their biochemical and biological actions, the melanogenesis effects and mechanism of action remains unknown [6]. In this study, we investigated the effect of morin on melanin biosynthesis and its molecular mechanisms in B16F10 melanoma cells [7].

2. Material & Method

Morin was purchased from Sigma-Aldrich. Antioxidant experiment measured DPPH and ABTS radical scavenging activity. Cell viability was examined using the MTT (3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Melanin content was measured as described previousl...
Cellular tyrosinase activity was estimated by measuring the rate of L-DOPA oxidation. Western blot analysis was conducted by separating cell lysates by SDS-gel electrophoresis. The gels were transferred on PVDF membranes, and exposed to the appropriate antibodies. Statistical analysis of the experimental data points was performed using an SPSS test and Duncan.

3. Results & Discussion

Morin increased DPPH and ABTS radical scavenging activity in a dose-dependent manner. At the concentration of 250 μg/ml, radical scavenging activity of DPPH and ABTS increased to 90% and 100% respectively, which was similar to ascorbic acid (Fig. 1, 2). Morin exhibited no cytotoxicity at concentration ranges of 5-100 μM (Fig. 3). Morin significantly increased tyrosinase activity and melanin synthesis in a dose-dependent manner (Fig. 4, 5). Morin induced melanogenesis was accompanied by increased expressions of TRP-1, TRP-2 and MITF (Fig. 6, 7, 8). Morin also increased p-JNK expression and decreased p-ERK expression (Fig. 9). In conclusion, the present study suggested that morin promoted melanogenesis in B16F10 melanoma cells by activating the regulating ERK and JNK signaling pathways. Taken together, the present study suggested that morin may be a useful agent for treating skin hypopigmentation disorders.
in B16F10 melanoma cells for 72h. α-MSH (100μM) was used as a positive control.

[Fig. 6] Effects of morin on melanogenesis–related protein TRP–1 expression in B16F10 melanoma cells for 48h.

[Fig. 7] Effects of morin on melanogenesis–related protein TRP–2 expression in B16F10 melanoma cells for 72h.

[Fig. 8] Effects of morin on melanogenesis–related protein MITF expression in B16F10 melanoma cells for 24h.

[Fig. 9] Effects of morin on melanogenesis–related protein p–ERK, p–JNK, p–p38 expression in B16F10 melanoma cells.

참고문헌


