

Silibinin promotes melanogenesis through the PKA and p38 MAPK signaling pathways in melanoma cells

Abstract

Silibinin is a flavonolignan isolated from milk thistle (*Silybum marianum*). Silibinin has been reported to possess multiple biological activities; however, its effect on melanogenesis remains unclear. This study investigated the effect of silibinin on melanogenesis in melanoma cells and the associated molecular mechanism. Our findings demonstrated that silibinin markedly increased melanin content in murine B16-F1 and human HMV-II melanoma cells. Silibinin activated intracellular tyrosinase activity and expression of tyrosinase, tyrosinase-related protein (TRP)-1, TRP-2, and microphthalmia-associated transcription factor (MITF). Furthermore, silibinin enhanced the phosphorylation of cyclic AMP-responsive element-binding protein (CREB), protein kinase A (PKA), and p38 mitogen-activated protein kinase (MAPK) but not of Akt and extracellular signal-regulated kinase (ERK). The specific PKA (H-89) and p38 (SB203580) inhibitors significantly attenuated silibinin-mediated melanin synthesis. These results suggest that silibinin is an effective stimulator of melanogenesis through upregulation of the protein expression of melanogenic enzymes activated by the PKA and p38 pathways, leading to CREB phosphorylation and MITF expression. Therefore, silibinin may have potential for use in the treatment of hypopigmentation disorders.