Melanogenic inhibition and toxicity assessment of flavokawain A and B on B16/F10 melanoma cells and zebrafish (Danio rerio)

ABSTRACT

Excessive production of melanin implicates hyperpigmentation disorders. Flavokawain A (FLA) and flavokawain B (FLB) have been reported with anti-melanogenic activity, but their melanogenic inhibition and toxicity effects on the vertebrate model of zebrafish are still unknown. In the present study, cytotoxic as well as melanogenic effects of FLA and FLB on cellular melanin content and tyrosinase activity were evaluated in α-MSH-induced B16/F10 cells. Master regulator of microphthalmia-associated transcription factor (Mitf) and the other downstream melanogenicrelated genes were verified via quantitative real time PCR (qPCR). Toxicity assessment and melanogenesis inhibition on zebrafish model was further observed. FLA and FLB significantly reduced the specific cellular melanin content by 4.3-fold and 9.6-fold decrement, respectively in α-MSH-induced B16/F10 cells. Concomitantly, FLA significantly reduced the specific cellular tyrosinase activity by 7-fold whilst FLB by 9-fold. The decrement of melanin production and tyrosinase activity were correlated with the mRNA suppression of Mitf which in turn downregulate Tyr, Trp-1 and Trp-2. FLA and FLB exhibited non-toxic effects on the zebrafish model at 25 and 6.25 μM, respectively. Further experiments on the zebrafish model demonstrated successful phenotype-based depigmenting activity of FLA and FLB under induced melanogenesis. To sum up, our findings provide an important first key step for both of the chalcone derivatives to be further studied and developed as potent depigmenting agents.

Keyword: α-MSH; B16/F10 melanoma; Chalcone; Flavokawain; Melanogenesis; Zebrafish