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Anthocyanins from *Hibiscus syriacus* L. Inhibit Oxidative Stress-mediated Apoptosis by Activating the Nrf2/HO-1 Signaling Pathway

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Hibiscus syriacus L. is widely distributed throughout Eastern and Southern Asia and its root bark has been used as a traditional remedy. Recently, the extracts of *H. syriacus* L. exerts anti-cancerous, anti-microbial, and anti-inflammatory activities. However, the effect of anthocyanin-rich fraction of *H. syriacus* L. petals (PS) has not been studied under excessive oxidative stress. In this study, we evaluated the cellular protective effect of PS in HaCaT human skin keratinocytes under hydrogen peroxide (H_2O_2)-induced oxidative stress conditions. PS at below 400 μg/ml did not show any cell death; however, over 800 μg/ml of PS gradually increased cell death. PS at below 400 μg/ml significantly inhibited H_2O_2-induced apoptosis in HaCaT cells concomitant with downregulation of Bax and upregulation of pro-PARP and p-Bcl-2. Additionally, PS remarkably reversed H_2O_2-induced excessive reactive oxygen species (ROS) production and apoptosis, and also significantly inhibited mitochondrial ROS production concomitant with suppression of H_2O_2-induced mitochondrial depolarization. H_2O_2-mediated ratio of Bax to Bcl-2, and caspase-3 activation were markedly abolished in the presence of PS. Moreover, the inhibition of HO-1 function using zinc protoporphyrin, an HO-1 inhibitor, significantly attenuated the cellular protective effects of PS against H_2O_2, indicating the significance of HO-1 in PS mediated cytoprotective effect, which was mediated by activating nuclear factor erythroid 2-related factor-2 (Nrf2). Taken together, our results suggest that cytoprotective effect of PS in HaCaT keratinocytes against oxidative stress-induced apoptosis is mediated by inhibiting cellular and mitochondrial ROS production, which is downregulated by activating Nrf2/HO-1 axis.

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