

Abstract:

Hesperidin is a flavanone glycoside that is found in the Citrus species and showed antioxidant, hepatoprotective as well as anticancer activity. This study investigated the effect of hesperidin on the PI3K/Akt pathway as a possible mechanism for its protective effect against diethylnitrosamine (DEN)-induced hepatocellular carcinoma (HCC). Adult Wistar rats were divided into Control group (received drug vehicle); DEN group (received 100 mg/L of DEN solution for 8 weeks), and hesperidin + DEN group (received 200 mg/kg body weight of hesperidin/day orally for 16 weeks + DEN solution as DEN group). Our findings showed that the administration of hesperidin significantly decreased the elevation in liver function enzymes, serum AFP level, and oxidative stress markers. Moreover, hesperidin administration suppressed DEN-induced upregulation of PI3K, Akt, CDK-2 protein expression, and preserved the integrity of the liver tissues from HCC formation. In conclusion, the hepatoprotective activity of hesperidin is mediated via its antioxidation and downregulation of the PI3K/Akt pathway.