Cucurbitacin D suppresses benzo[a]pyrene-induced liver injury by modulating Nrf2 signaling

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Abstract

Background: Accumulating studies have shown strong correlation of HCC and co-morbidity factors including smoking. Tobacco smoke contains benzo[a]pyrene, which is extremely carcinogenic and contributes to liver damage. Cucurbitacin, a triterpene, has a wide range of biological activities, including antioxidant, anti-inflammatory, and anti-cancer properties. However, their hepatoprotective effects remain poorly understood. In the current study, we examined the hepatoprotective activity of cucurbitacin D, a novel analog of cucurbitacin, against benzo[a]pyrene-induced liver injury in human HepG2 cells.

Method: To investigate the hepatoprotective effect of cucurbitacin D against benzo[a]pyrene-induced liver damage, proliferation, clonogenicity, migration, invasion, Western blotting, and qPCR analyses were performed. The DCFDA assay was performed to determine the level of intracellular reactive oxygen species (ROS) in liver cells.

Results: Functional assays showed that cucurbitacin D exhibited cytoprotective effects against dose-dependent growth inhibition by benzo[a]pyrene in human HepG2 cells. This protective effect was likely associated with antioxidant potential of cucurbitacin D, as evidenced by the attenuation of ROS observed by fluorimeter and fluorescence microscopy. Western blotting analysis demonstrated Cucurbitacin D targets Nrf-2 signaling pathway and associated effector proteins including HO-1 and LC3A in protecting liver cells against benzo[a]pyrene induce oxidative damage. Further studies are underway to understand the underlying molecular mechanism of action.

Conclusion: These findings demonstrate the hepatoprotective effects of cucurbitacin D against benzo[a]pyrene-induced liver damage, making it a promising ingredient for nutritional supplements.