

Curcumin attenuates dimethylnitrosamine-induced liver injury in rats through Nrf2-mediated induction of heme oxygenase-1

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Abstract Curcumin (diferuloylmethane 姜黄素), a yellow colouring agent present in the rhizome of *Curcuma longa* Linn (Zingiberaceae), has been reported to possess anti-inflammatory, antioxidant, antimutagenic and anticarcinogenic activities. Curcumin exerts its chemoprotective and chemopreventive effects via multiple mechanisms. It has been reported to induce expression of the antioxidant enzymes in various cell lines. Heme oxygenase-1 (HO-1) is an important antioxidant enzyme that plays a pivotal role in cytoprotection against noxious stimuli of both endogenous and exogenous origin. In the present study, we found that oral administration of curcumin at 200 mg/kg dose for four consecutive days not only protected against dimethylnitrosamine (DMN)-induced hepatic injury, but also resulted in more than three-fold induction of HO-1 protein expression as well as activity in rat liver. Inhibition of HO-1 activity by zinc protoporphyrin-IX abrogated the hepatoprotective effect of curcumin against DMN toxicity. NF-E2-related factor 2 (Nrf2) plays a role in the cellular protection against oxidative stress through antioxidant response element (ARE)-directed induction of several phase-2 detoxifying and antioxidant enzymes including HO-1. Curcumin administration resulted in enhanced nuclear translocation and ARE-binding of Nrf2. Taken together, these findings suggest that curcumin protects against DMN-induced hepatotoxicity, at least in part, through ARE-driven induction of HO-1 expression.

Keywords: Curcumin; Tetrahydrocurcumin; Heme oxygenase-1; Nrf2; Hepatoprotection; ARE

姜黄素通过 Nrf2 介导血红素加氧酶-1 产生 减轻二甲基亚硝胺诱导的大鼠肝脏损伤

摘要: 姜黄素 (diferuloylmethane), 一种黄色色素, 是从药用辅料姜黄的根茎中提炼而出的主要有效成分, 主要药理作用包括抗炎、抗氧化、抗突变、抗肿瘤等方面作用。姜黄素通过复杂的作用机制发挥化学保护和预防作用, 已有报道表明, 它能在各种细胞系中诱导抗氧化酶的表达。血红素加氧酶-1(HO-1)是一种重要的抗氧化酶, 它在内源性和外源性伤害性刺激的细胞保护作用中发挥了关键作用。本研究中, 我们发现连续四天给予大鼠姜黄素灌胃 (200 mg/kg) 不仅可以保护二甲基亚硝胺(DMN)诱导的肝损伤, 而且导致肝脏HO-1和活性和蛋白表达量增加三倍以上。通过锌原卟啉IX抑制HO-1的活性, 姜黄素对DMN诱导肝损伤的保护作用消失。NF-E2相关因子2(Nrf2)是细胞抗氧化损伤的中枢调节者, Nrf2通过与抗氧化反应元件(ARE)的结合从而诱导包括HO-1在内的抗氧化酶和二相解毒酶的表达。给予姜黄素激发Nrf2转位进入细胞核增加并与ARE结合。总之, 这些研究提示姜黄素对DMN诱导肝损伤的保护作用, 在一定程度上是通过ARE驱动诱导HO-1的表达来实现的。

关键词: 姜黄素; 二甲基亚硝胺; 血红素加氧酶-1; NF-E2 相关因子 2; 肝保护作用; 抗氧化反应元件