摘要

Acetaminophen (APAP) overdose causes severe liver damage. APAP-induced liver injury (AILI) represents the most frequent cause of drug-induced liver failure. APAP is relatively insoluble and can only be taken orally; however, its pro-drug, propacetamol is water-soluble and can be injected directly. We previously established novel AILI mouse model using a single intraperitoneally propacetamol injection. Kaempferol (K), is a flavonoid found in many edible plants and in herbals. K was investigated to have anti-inflammation and anti-oxidation effects in previous studies, but the effect and mechanism of K on AILI is unknown. Male BALB/c mice were randomly divided into six groups including WT group, only propacetamol (600 mg/kg) injection group (P only), kaempferol (250 mg/kg orally) only group (K250 only), and three groups of mice received different doses of kaempferol 1 hour before propacetamol injection (P+K62.5, P+K125, P+K250). After analyzing the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities and liver histopathology, we demonstrated that the optimal protective dosage of kaempferol is 125 mg/kg, which significantly attenuates AILI in mice. To decipher the protective mechanism(s) of kaempferol, kaempferol pretreatment significantly decreased hepatic microsomal CYP2E1 levels and oxidative stress, and increased the hepatic glutathione level of AILI mice. Furthermore, pretreatment of kaempferol reduced hepatic TNF-α and IL-6 levels. These finding suggest that pretreatment of kaempferol can ameliorate AILI through its anti-oxidative and anti-inflammation effect. Thus, we demonstrated that kaempferol has a great protective effect against AILI in model mice and may develop as a hepatic protective drug for human.

關鍵詞: Propacetamol-induced Acetaminophen-overdose, Kaempferol, Protective Effect and Mechanisms

參考文獻

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