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Kaempferol Protects Against Acetaminophen-Induced Acute Liver Injury by Inhibiting Oxidative Stress, Inflammation and Apoptosis in Mice

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SUMMARY. **Acetaminophen (APAP) is a widely used analgesic and antipyretic drug in the clinic, but excessive amounts of APAP can result in liver damage. However, APAP-induced acute liver injury lacks effective treatment. In this study, acetaminophen-treated mice were used as a model to explore the efficacy of kaempferol as an antioxidation, anti-inflammatory and anti-apoptotic agent and to explore its efficacy in the treatment of APAP-induced acute liver injury. In this study, 50 mice were randomly divided into 5 groups: group I, the negative control, was fed hydroxymethyl cellulose sodium; group II was treated with 300 mg/kg acetaminophen; group III was intraperitoneally injected with 20 mg/kg kaempferol; groups IV and V were injected and fed 20 mg/kg kaempferol, respectively, 1 h after receiving a dose of 300 mg/kg acetaminophen. We found that kaempferol could significantly inhibit the increase in ALT and AST in the serum and TNF-α and IL-6 in the liver. In addition, kaempferol up-regulated the mRNA expression levels of antioxidant factors SOD2 and Nrf2 and down-regulated the mRNA expression levels of TNF-α, IL-6 and TLR4 in the liver injury model. In addition, we found that kaempferol could reduce bax and increase bcl-2 and procaspase-3. These results suggest that kaempferol can protect against APAP-induced liver toxicity by inhibiting oxidative stress, inflammatory response, and apoptosis pathways.**

RESUMEN. El acetaminofeno (APAP) es un analgésico y antipirético ampliamente utilizado en la clínica. Sin embargo, la lesión hepática aguda inducida por APAP carece de un tratamiento eficaz. En este estudio, se utilizaron ratones tratados con paracetamol como agente antioxidante, antiinflamatorio y antiapoptótico y con lesión hepática aguda inducida por APAP. Cincuenta ratones se dividieron al azar en 5 grupos: el grupo I, el control negativo, se alimentó con hidroximetilcelulosa sódica; el grupo II fue tratado con 300 mg/kg de acetaminofeno; al grupo III se inyectó por vía intraperitoneal con 20 mg/kg de kaempferol; los grupos IV y V se inyectaron y se alimentaron con 20 mg/kg de kaempferol, respectivamente, 1 h después de recibir una dosis de 300 mg/kg de paracetamol. Encontramos que el kaempferol podría inhibir significativamente el aumento de ALT y AST en el suero y TNF-α e IL-6 en el hígado. Además, el kaempferol aumentó los niveles de expresión del ARNm de SOD2 y Nrf2 y redujo los niveles de expresión del ARNm de TNF-α, IL-6 y TLR4 en el modelo de lesión hepática. Además, encontramos que el kaempferol podría reducir bax y aumentar bcl-2 y procaspase-3. Estos resultados sugieren que el kaempferol puede proteger contra la toxicidad hepática inducida por APAP mediante la inhibición del estrés oxidativo, la respuesta inflamatoria y las vías de apoptosis.

KEY WORDS: acetaminophen, acute liver injury, apoptosis, inflammation, kaempferol, oxidative stress

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