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Hepatoprotective activity of Silymarin against Acetaminophen involves an enhancement of the Glutathione-dependent detoxification capacity

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We previously showed that silymarin was capable of increasing hepatic glutathione (GSH) levels via a modification of the transsulfuration reactions in liver. To investigate its pharmacological significance we determined the effects of silymarin pretreatment on the acetaminophen (APAP)-induced hepatotoxicity. Male mice were treated with silymarin (200 mg/kg, po) every 12 h for a total of 3 doses prior to APAP challenge (500 mg/kg, ip). Silymarin pretreatment attenuated the liver injury significantly as determined by inhibition of the increase in plasma enzyme activities, lipid peroxidation and formation of nitrotyrosine protein adducts in liver. Concentrations of APAP, APAP-glucuronide or APAP-sulfate were not changed, but thiol-conjugates of APAP, such as APAP-GSH, APAP-cysteine and APAP-N-acetylcysteine, were elevated in plasma. However, silymarin treatment did not induce protein expression of Cyp2e1, Cyp1a2, and Cyp3a11, the major isoforms involved in metabolic activation of APAP. Comparable results were obtained with hepatic microsomal activities measured using p-nitrophenol, ethoxyresorufin and erythromycin, indicating that the increased generation of APAP-thiol conjugates should be attributed to an augmentation of the GSH conjugation capacity. It is suggested that silymarin may prevent the APAP-induced hepatotoxicity by increasing GSH availability which enhances the detoxifying capacity of liver cell against the toxic electrophile generated from this analgesic-antipyretic

Biography

Young Chul Kim is a Professor of Toxicology at Seoul National University, College of Pharmacy since 1986. He received his MS and from Purdue University, and completed Postdoctoral studies at the National Institute of Environmental Health Sciences (NIEHS), NIH, USA. He has published more than 100 papers in reputed journals. He is a recipient of several prestigious international and national awards including the Thieme Most Innovative Original Paper Award at GA and the Korean Teachers' Award.

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