

Protective effects of silymarin against isotretinoin induced liver and kidney injury in mice

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Isotretinoin (ISR), the common therapeutic agent for acne vulgaris, when used long term, leads to various side effects *viz.*, oxidative toxicity, renal and hepatic dysfunction, depression, congenital abnormalities, aortic art defects, microcephaly, etc. Here, we explored the effects of silymarin (SLY), a flavonolignan from the seeds of the milk thistle *Silybum marianum* (L.) which has potential to protect the liver against chemical and environmental toxins and increase proliferation rate of tubule cells, against ISR induced liver and kidney injury. Thirty-two male Balb/c mice (3 months of age) were divided into four groups: control, isotretinoin (ISR, 40 mg/kg/day), silymarin (SLY, 200 mg/kg/day), and ISR+SLY group. We investigated liver and kidney injury by histopathological scoring system, and apoptotic cells labelled by TUNEL method. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured in serum samples biochemically. ALT and AST levels were increased in ISR group ($P = 0.025$, $P = 0.003$, respectively). SLY decreased those levels in ISR+SLY group ($P = 0.002$, $P = 0.013$, respectively). Liver tissues of ISR group showed interstitial edema and necrosis, alteration in shape and size of nuclei, mononuclear and kuppfer cell infiltration. Kidney tissues of ISR group showed tubular degeneration, necrosis, glomerular collapse, mononuclear cell infiltration, and hemorrhage. SLY improved those histopathological changes and suppressed apoptotic cell death. We suggest that silymarin might be beneficial to some extent by preventing the side effects induced by chronic ISR therapy in patients with acne vulgaris.

Keywords: 13-cis-Retinoic acid, Acne vulgaris, Apoptosis, Milk thistle, Oxidative stress, *Silybum marianum*