Silybin, a component of sylimarin, exerts anti-inflammatory and anti-fibrogenic effects on human hepatic stellate cells

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Source:

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BACKGROUND/AIMS: Hepatic fibrogenesis, a consequence of chronic liver tissue damage, is characterized by activation of the hepatic stellate cells (HSC). Silybin has been shown to exert antifibrogenic effects in animal models. However, scant information is available on the fine cellular and molecular events responsible for this effect. The aim of this study was to assess the mechanisms regulating the anti-fibrogenic and anti-inflammatory activity of Silybin.

METHODS: Experimentswere performed on HSC isolated from human liver and activated by culture on plastic.

RESULTS: Silybin was able to inhibit dose-dependently (25-50 microM) growth factor-induced pro-fibrogenic actions of activated human HSC, including cell proliferation ($P < 0.001$), cell motility ($P < 0.001$), and de novo synthesis of extracellular matrix components ($P < 0.05$). Silybin (25-50 microM), inhibited the IL-1-induced synthesis of MCP-1 ($P < 0.01$) and IL-8 ($P < 0.01$) showing a potent anti-inflammatory activity. Silybin exerts its effects by directly inhibiting the ERK, MEK and Raf phosphorylation, reducing the activation of NHE1 (Na+/H+ exchanger, $P < 0.05$) and the IkBalpha phosphorylation. In addition, Silybin was confirmed to act as a potent anti-oxidant agent.

CONCLUSION: The results of the study provide molecular insights into the potential therapeutic action of Silybin in chronic liver disease. This action seems to be mostly related to a marked inhibition of the production of pro-inflammatory cytokines, a clear anti-oxidant effect and a reduction of the direct and indirect pro-fibrogenic potential of HSC.