Modulatory effects of curcumin, silybin-phytosome and alpha-R-lipoic acid against thioacetamide-induced liver cirrhosis in rats

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Highlights
• Curcumin, silybin-phytosome and alpha-R lipoic acid protect against the hepatotoxic effects of thioacetamide.
• These dietary supplements prevented the development of chemically induced liver cirrhosis.
• The beneficial effects of these supplements are mediated via their antioxidant and antifibrotic potentials.

Abstract
Liver cirrhosis is the final consequence of a progressive fibrotic process characterized by excessive collagen deposition and destruction of the normal liver architecture. This study aimed to investigate the protective effects of curcumin, silybin-phytosome and alpha-R-lipoic acid against thioacetamide-induced cirrhosis. Male rats were allocated into five groups of which one group received saline and served as normal control. Animals from groups 2–5 were treated with thioacetamide administered intraperitoneally at a dose of 200 mg/kg 3 times per week for 7 weeks. Group 2 was left untreated while groups from 3 to 5 were given a daily oral dose of curcumin, silybin-phytosome or alpha-R-lipoic acid simultaneously with thioacetamide. Increases in hepatic levels of malondialdehyde (MDA) and protein carbonyls (Pr Co) associated with thioacetamide administration were partially blocked in those groups receiving supplements. Glutathione (GSH) depletion, collagen deposition, matrix metalloproteinase-2 (MMP-2) activity, transforming growth factor-β1 (TGF-β1) level as well as α-smooth muscle actin (α-SMA) and heat shock protein-47 (HSP-47) gene expressions were also decreased in response to supplements administration. Serological analysis of liver function and histopathological examination reinforced the results. In conclusion, the present study highlights the antioxidant and the antifibrotic potentials of these supplements against chronic liver diseases caused by...
ongoing hepatic damage.

**Graphical abstract**

Abbreviations

ALT, alanine aminotransferase; ALP, alkaline phosphatase; ANOVA, analysis of variance; ARE, antioxidant response element; AST, aspartate aminotransferase; CYP2E1, cytochrome P450 2E1; DHLA, dihydrolipoic acid; ECM, extracellular matrix; ELISA, enzyme-linked immunosorbent assay; GGT, γ-glutamyl transferase; GSH, glutathione; H&E, hematoxylin and eosin; HMG-COA reductase, 3-hydroxy-3-methylglutaryl coenzyme A reductase; HRP, horseradish peroxidase; HSCs, hepatic stellate cells; HSE, heat shock promoter element; HSF1, heat shock factor 1; HSP-47, heat shock protein 47; Keap1, Kelch-like ECH-associated protein 1; LDH, lactate dehydrogenase; MDA, malondialdehyde; MMP-2, matrix metalloproteinase-2; MMPs, matrix metalloproteinases; M-MuLV, moloney murine leukemia virus; Nrf2, nuclear factor-erythroid-2-related factor 2; PAI-1, plasminogen activator inhibitor; PC, phosphatidylycholine; PPAR-γ, peroxisome proliferator-activated receptor-γ; Pr Co, protein carbonyls; RT-PCR, real time polymerase chain reaction; TAA, thioacetamide; TGF-β1, transforming growth factor-β1; TG, triglycerides; α-SMA, α-smooth muscle actin

**Keywords**

Liver cirrhosis; Thioacetamide; Curcumin; Silybin-phytosome; Alpha-R-lipoic acid; Oxidative stress

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