Effects of Silymarin on the Pro-inflammatory Cytokine-Induced MCP-1, NF-κB and ROS in Human Mesangial Cells

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Background : Monocyte chemoattractant protein-1 (MCP-1), nuclear factor-κB (NF-κB), and reactive oxygen species (ROS) play an important role during glomerular inflammation. Silymarin, a polyphenolic flavonoid antioxidant, is known to have anti-inflammatory effects. However, underlying mechanisms have not been fully understood. We investigated the effects of silymarin on the pro-inflammatory cytokine- induced MCP-1 expression, NF-κB activation, and intracellular ROS production in human mesangial cells.

Methods : Cells were pretreated with or without silymarin for 1 h, and then stimulated with tumor necrosis factor-α (TNF-α) or interleukin-1β (IL-1β). MCP-1 mRNA and protein expression were measured by Northern blot analysis and ELISA respectively. NF-κB binding activity was determined by electrophoretic mobility shift assay and nuclear translocation of p65 subunit of NF-κB was demonstrated using confocal microscope. Intracellular ROS production was determined by flow cytometry, using 2'7'-dichlorofluorescin diacetate.

Results : Silymarin inhibited TNF-α- or IL-1β- induced MCP-1 mRNA expression dose dependently (50-200 μM) and also MCP-1 protein expression. Silymarin also partially suppressed TNF-α- or IL-1β- induced NF-κB activation. Confocal microscope demonstrated that silymarin partially inhibited TNF-α-induced nuclear translocation of p65 subunit of NF-κB. PDTC, a NF-κB inhibitor, dose dependently inhibited the TNF-α-induced MCP-1 mRNA expression. Intracellular ROS produced by phorbol myristate acetate (PMA) was inhibited by silymarin as well.

Conclusion : Silymarin exerts anti-inflammatory effects on pro-inflammatory cytokine-stimulated mesangial cells, at least in part, by inhibiting MCP-1expression via suppression of NF-κB and also reduces PMA-induced intracellular ROS production.