

## **PRETREATMENT WITH SILYMARIN MODIFIES THE LEVEL OF ENDOTOXIN-INDUCED NEUTROPHIL MIGRATION AND LIVER INJURY**

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Endotoxin, which is generated by gram-negative, microbial pathogens such as *Escherichia coli* (*E. coli*), is a persistent environmental contaminate that can cause lethality. Recent studies have indicated that urban communities demonstrate a higher occurrence of endotoxin-induced lethality the compared to non-urban communities. The speculation is that exposure risk is higher in urban environments. Exposure can occur through microfloral translocation, environmental contact, ingestion of contaminated food products, and infection after invasive surgical procedures. In humans and animals, the liver is one the primary targets of endotoxemic infection. The hepatotoxicity of endotoxin includes elevated plasma levels of hepato-specific enzymes such as gamma-glutamyltranspeptidase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Also, exposure to endotoxin causes hepatic edema, peroxidation and cellular necrosis. In addition, this exposure to endotoxin causes hepatic edema, peroxidation and cellular endotoxemia is treated with antibiotic therapy. More recently, clinicians and research have become interested in the therapeutic effectiveness (e.g. hepato-protective) of natural products such as flavonoids. Silymarin, the natural polyphenolic flavonoid extract of the milk thistle, has been well documented for its anti-inflammatory, anti-oxidant and hepato-protective activity. Recent studies have suggested that Silymarin pretreatment protects against endotoxin-induced liver injury. Male Sprague Dawley rats were treated for 5 consecutive days with 25-50 mg/kg/day Silymarin (orally). On day 6, the Silymarin treated rats received 0.5-3.0 mg/kg of endotoxin (i.p.). After a 6 hour exposure period, liver samples were collected for histological analysis of liver injury and plasma samples were collected for analysis of enzymatic markers (AST, ALT and GGT) of hepatotoxicity. Pretreatment with Silymarin decreased hepato-cellular injury, prevented elevations of plasma enzyme markers, decreased hepato-cellular injury, prevent elevation so plasma enzymes markers, decreased neutrophil accumulation and expression of adhesion molecules. These data suggest that Silymarin pretreatment alters neutrophil activity and reduces the severity of endotoxin-induced liver injury. (NIH Grant RR11606-05)