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INHIBITION OF INDUCIBLE NITRIC OXIDE SYNTHASE EXPRESSION BY SILYMARIN IN LPS-STIMULATED MACROPHAGES

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Silymarin, a polyphenolic flavonoid antioxidant, has been shown to have anti-inflammatory, hepatoprotective, and anticarcinogenic effects. In the present study, we report the inhibitory effect of silymarin on nitric oxide (NO) production and inducible nitric oxide synthase (iNOS) mRNA expression in macrophages. *In vivo* administration of silymarin attenuated NO production of peritoneal macrophages in lipopolysaccharide (LPS)-treated mice. Silymarin also produced dose-dependent suppression of LPS-stimulated production of NO in isolated mouse peritoneal macrophages and macrophage cell line RAW264.7. Moreover, treatment of RAW264.7 with silymarin inhibitied LPS-stimulated expression of iNOS mRNA in a dose-related manner. To further investigate the mechanism responsible for reduced iNOS gene expression, we investigated the effect of silymarin on LPS-stimulated activation of NF-κB/REL, which regulates various genes involved in immune and inflammatory response. LPS-stimulated DNA binding of NF-κB/REL was inhibited by silymarin, and this effect was mediated through inhibition of phosphorylation and degradation of IκBα. NF-κB/REL-dependent reporter gene expression was also suppressed by silymarin. Collectively, these data suggest that silymarin may inhibit NO production and iNOS mRNA expression via inhibition of NF-κB/REL activation.