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The Immunosuppressive Effects of Silymarin with Rapamaycin on the Proliferation and Apoptosis of T Cell

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Abstract : Introduction: Silymarin, as a polyphenolic flavonoid derived from milk thistle (Silybum marianum), is known to have antioxidant, immunomodulatory, antiproliferative, antifibrotic, and antiviral effects. The goal of this study was to determine immunosuppressive effect of Silymarin on proliferation and apoptosis of human T cells in comparison with Rapamycin and FK506. Methods: Peripheral Blood Mononuclear Cells (PBMCs) from healthy individuals were activated with Con A (5µg/ml) and then treated with Silymarin, Rapamycin and FK506 in various concentrations (0.001, 0.01, 0.1, 1, 10,100 and 200□M) for 5 days. PBMCs were examined for proliferation using CFSE assay and the concentration that inhibited 50% of the cell proliferation (IC50) was determined for each treatment. For apoptosis assay using flow cytometry, PBMCs were activated with Con A and treated with IC50 dose of Silymarin, Rapamycin and FK506 for 5 days, then cell apoptosis was analysed by FITC-annexin V/PI staining and flow cytometry. The effects of Silymarin, Rapamycin and FK506 on the activation of PARP (poly ADP ribose polymerase) pathway in PBMCs stimulated with Con A and treated with IC50 dose of drugs for 5 days evaluated using the PathScan cleaved PARP sandwich ELISA kit. Results: This study showed that Silymarin had the ability to inhibit T cell proliferation in vitro. Moreover, our results indicated that 100 µM ($P < 0.001$) and 200 µM ($P < 0.001$) of Silymarin has more inhibitory effect on T cells proliferation than FK506 and Rapamycin. Our data showed that the effective doses (IC50) of Silymarin, FK506 and Rapamycin were 3×10-5 µM, 10-8 µM and 10-6 µM respectively. Data showed that the inhibitory effect of Silymarin, FK506 and Rapamycin on T cell proliferation was not due to cytotoxicity and none of these drugs at IC50 concentration had not affected the level of cleaved PARP. Conclusion: Silymarin could be a good candidate for immunosuppressive therapy for certain medical conditions with superior efficacy and lesser toxicity in comparison with other immunosuppressive drugs.

Keywords : silymarin, immunosuppressive effect, rapamycin, immunology
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