

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

**Authors :** Nahid Eskandari, Marjan Ghagozolo, Ehsan Almasi

**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 200µM) 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  $3 \times 10^{-5}$  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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