PHYTOL, A DITERPENE ALCOHOL, INHIBITS THE INFLAMMATORY RESPONSE BY REDUCING CYTOKINE PRODUCTION AND OXIDATIVE STRESS

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Introdução: Many drugs used as treatment for inflammatory process are associated with significant adverse effects and as alternative therapy many natural compounds with different mechanisms of action may be used to treat this process. Investigate the effect anti-inflammatory of phytol in mice. Materiais e Métodos: The present study was approved by the local ethics committee (protocol no. 0066/10). The anti-inflammatory activity of phytol was evaluated using several inflammatory agents (carrageenan, compound 48/80, serotonin, histamine, and prostaglandin E2) to induce paw edema. Peritonitis was induced intraperitoneally (i.p) by carrageenan and analyzed 4 h later. Samples of the paw tissue and peritoneal fluid were removed to determine myeloperoxidase (MPO) activity or TNF-? IL-1 ?, GSH and MDA levels respectively. Resultados e Discussão: In models of paw edema (n = 6), the pre-treatment of mice with phytol significantly and dose-dependently reduced carrageenan-induced paw edema (0.061 ± 0.003 ml), with maximal inhibitory effect at a dose of 75 mg/kg (0.026 ± 0.002 ml). Phytol 75 mg/kg inhibited edema induced by compound 48/80 (0.108 ± 0.011 ml) to (0.038 ± 0.008 ml), histamine (0.082 ± 0.003 ml) to (0.030 ± 0.010 ml), serotonin (0.084 ± 0.008 ml) to (0.028 ± 0.005 ml), bradykinin (0.070 ± 0.009 ml) to (0.018 ± 0.06 ml) and PGE2 (0.069 ± 0.003 ml) to (0.030 ± 0.007 ml). For evaluation of neutrophil migration (n = 6), phytol 75 mg/kg, i.p., injected thirty minutes before of carrageenan, produced a significantly reduced the leukocyte recruitment (2.39 ± 0.62 x 103 cells/ml) and neutrophil migration (0.42 ± 0.45 × 103 cells/ml) to the peritoneal cavity, as compared to carrageenan group (total leukocyte 4.83 ± 0.99 × 103 cells/ml and neutrophil recruitment 3.55 ± 0.32 × 103 cells/ml). The levels of TNF- ? and IL-1 ? were evaluated using the ELISA (n = 6), and the pre-treatment with phytol 75 mg/kg i.p significantly reduced TNF - ? (106.8 ± 32.81 pg/ml), IL-1 ? (607.1 ± 147.6 pg/ml) as compared to carrageenan group (TNF- ?, 208.7 ± 39.22 pg/ml and IL1- ?, 1073 ± 180.1 pg/ml). The levels of GSH, MDA and MPO were measured by spectrophotometry (n = 6). The administration of carrageenan induced an increase in MDA (25.17 ± 4.47 nmol/ml) and decreased GSH levels (59.73 ± 8.19 ?g/ml) concentrations in peritoneal fluid and also increased MPO activity (9.85 ± 0.96 U/mg) in paw tissue.
The pre-treatment with phytol 75 mg/kg i.p significantly reduced MDA (10.73 ± 1.75 nmol/ml) concentrations, MPO activity (3.21 ± 0.82 U/mg) and increased GSH levels (94.05 ± 17:17 / ml).

**Conclusão:** Phytol reduces the inflammatory response and oxidative stress in mice by reducing neutrophil migration.