



# Thymoquinone Rescues T Lymphocytes from Gamma Irradiation-Induced Apoptosis and Exhaustion by Modulating Pro-Inflammatory Cytokine Levels and PD-1, Bax, and Bcl-2 Signaling.

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## Abstract:

**BACKGROUND/AIMS:** Recent studies have shown that thymoquinone (TQ) exerts protective effects against ionizing radiation-induced cataracts in lens after total cranium irradiation of rats. Nevertheless, there is no published work investigated the effects of TQ on T cell development and biology in animal models exposed to gamma radiation. Therefore, in the present study we focused on determining the effects of TQ on radiation damage in the thymus, radiation-induced T cell imbalance, and on immune dysfunction induced by gamma-rays. **METHODS:** Three groups of rats were used: a control group, a gamma-irradiated group, and a gamma-irradiated group that was orally supplemented with TQ. Serum lipid profiles, malondialdehyde (MDA) levels, and pro-inflammatory cytokine levels were measured to assess gamma irradiation-induced oxidative stress and inflammatory capacity. T cell apoptosis was evaluated by annexin V/propidium iodide staining followed by flow cytometry analysis. The expression of pro-apoptotic proteins such as Bax and caspase-3, the anti-apoptotic protein Bcl-2, and an exhaustion marker of T cells (PD-1) in CD4+ and CD8+ T cell populations was evaluated using flow cytometry analysis. The T cell architecture of the thymus gland was evaluated by histological analysis. **RESULTS:** Exposure to gamma radiation increased triglyceride, cholesterol, LDL-C, MDA, TNF- $\alpha$  and IL-6 levels and decreased HDL-C levels. The altered lipid profile and MDA and pro-inflammatory cytokine (TNF- $\alpha$  and IL-6) levels induced by exposure to gamma radiation were significantly restored in TQ-treated gamma-irradiated rats. Rats exposed to gamma radiation exhibited increased exhaustion of T lymphocytes via down-regulation of Bcl-2 expression and upregulation of PD-1, Bax, and caspase-3 expression, which sensitized these cells to apoptosis. Interestingly, treatment of gamma-irradiated rats with TQ decreased T cell exhaustion and apoptosis by modulating the expression of Bcl-2, PD-1, Bax, and caspase-3. **CONCLUSIONS:** Our results provide evidence for the beneficial effects of TQ as an effective radioprotective candidate that enhances cellular immunity.

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