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Gene Expression Profiling and Protein Analysis Reveal Suppression of the C-Myc Oncogene and Inhibition JAK/STAT and PI3K/AKT/mTOR Signaling by Thymoquinone in Acute Myeloid Leukemia Cells

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Abstract

Background: Overexpression of c-Myc plays an essential role in leukemogenesis and drug resistance, making c-Myc an attractive target for cancer therapy. However, targeting c-Myc directly is impossible, and c-Myc upstream regulator pathways could be targeted instead.

Objective: This study investigated the effects of thymoquinone (TQ), a bioactive constituent in *Nigella sativa*, on the activation of upstream regulators of c-Myc: the JAK/STAT and PI3K/AKT/mTOR pathways in HL60 leukemia cells. Method: Next-generation sequencing (NGS) was performed for gene expression profiling after TQ treatment. The expression of c-Myc and genes involved in JAK/STAT and PI3K/AKT/mTOR were validated by quantitative reverse transcription PCR (RT-qPCR). In addition, Jess assay analysis was performed to determine TQ's effects on JAK/STAT and PI3K/AKT signaling and c-Myc protein expression.

Results: The results showed 114 significant differentially expressed genes after TQ treatment ($p < 0.002$). DAVID analysis revealed that most of these genes' effect was on apoptosis and proliferation. There was downregulation of c-Myc, PI3K, AKT, mTOR, JAK2, STAT3, STAT5a, and STAT5b. Protein analysis showed that TQ also inhibited JAK/STAT and PI3K/AKT signaling, resulting in inhibition of c-Myc protein expression.

Conclusion: the findings suggest that TQ potentially inhibits proliferation and induces apoptosis in HL60 leukemia cells by downregulation of c-Myc expression through inhibition of the JAK/STAT and PI3K/AKT signaling pathways.

Keywords: thymoquinone, leukemia, c-Myc, JAK/STAT, PI3K/AKT, signaling, apoptosis

Biography

I have over three years of experience in cell culture laboratories, and experience in working as a laboratory supervisor in Mutah university for ten years until now gave me a chance to increase my qualification by teaching student hematology and parasitology and others. Furthermore, I have studied the effectiveness of natural compounds against leukemia in my PhD degree.