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Thymoquinone Suppresses Cellular Proliferation, Inhibits VEGF Production and Obstructs Tumor Progression and Invasion in the Rat Model of DMH-Induced Colon Carcinogenesis

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Author(s)

Wasfi Asfour, Sawsan Almadi, Lina Haffar

ABSTRACT

A myriad of medicinal effects has been attributed to Thymoquinone (TQ), the major biological-active component of *Nigella sativa*. TQ has been shown to exhibit potent anti-tumor activities. The present work was undertaken to further explore TQ's chemopreventive efficacy against 1, 2-dimethylhydrazine (DMH)-induced colon carcinogenesis in the rat model through a two-phase study (initiation and post-initiation) and to evaluate its potential impact on tumor progression and invasion in vivo. TQ treatment in the initiation phase significantly reduced tumor incidence, multiplicity and mean tumor volume. However, although mean tumor volume and multiplicity were decreased upon TQ treatment in the post-initiation phase, TQ did not reduce incidence significantly. Cellular proliferation, as assessed by expression of colonic PCNA, was shown to be inhibited in consequence to TQ treatment in both phases, with a more pronounced reduction in the initiation phase. In addition, our results demonstrated an appreciable negative impact of TQ on vascular endothelial growth factor (VEGF) production in tumor-bearing rats. Furthermore, we provided evidence that TQ-treatment, in both phases, tended to considerably suppress tumor progression and invasion. Taken together, the present study demonstrated that TQ, at an orally daily dose of 10 mg/kg, has a chemopreventive effect in the initiation phase, and has the potential to attenuate tumor burden, suppress progression of pre-neoplastic lesions and to inhibit tumor growth in the post-initiation phase of DMH-induced colon carcinogenesis. We surmise that such effects of TQ may be due to suppression of cellular proliferation and inhibition of VEGF production. The results could provide an effective chemopreventive approach in the primary prevention of colon cancer in humans in the next future, and illuminate a promising horizon to combat progression of benign colonic pre-neoplastic lesions into malignant metastatic tumors and to manage colon cancer.

KEYWORDS

Thymoquinone; PCNA-LI; VEGF Serum Levels; Tumor Progression; Invasion; Rat; DMH-Induced Colon Carcinogenesis; Initiation; Post Initiation Phase; Modified Duke's Classification; Chemoprevention

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