Anti-inflammatory effects of the Nigella sativa seed extract, thymoquinone, in pancreatic cancer cells - Chehl - 2009 - HPB

- Hwyda A. Arafat

- First published: 22 July 2009Full publication history
- DOI: 10.1111/j.1477-2574.2009.00059.xView/save citation
- Cited by: 45 articles

- Presented at the 9th Annual Meeting of the American Hepato-Pancreato-Biliary Association, 12–15 March 2009, Miami, FL, USA.

Hwyda A. Arafat, Department of Surgery, Thomas Jefferson University, 1015 Walnut Street, Suite 618, Curtis, Philadelphia, PA 19107, USA. Tel: + 1 215 955 6383. Fax: + 1 215 955 2878. E-mail: hwyda.arafat@jefferson.edu

Abstract

Background: Both hereditary and sporadic forms of chronic pancreatitis are associated with an increased risk of developing pancreatic ductal adenocarcinoma (PDA). Inflammation has been identified as a significant factor in the development of solid tumour malignancies. We have recently shown that thymoquinone (Tq), the major constituent of *Nigella sativa* oil extract, induced apoptosis and inhibited proliferation in PDA cells. Tq also increased p21 WAF1 expression, inhibited histone deacetylase (HDAC) activity, and induced histone hyperacetylation. HDAC inhibitors have been shown to ameliorate inflammation-associated cancer. In this study, we evaluated the anti-inflammatory potential of Tq in PDA cells in comparison with that of a specific HDAC inhibitor, trichostatin A (TSA).

Methods: PDA cells were treated with or without Tq (25–75 μM), with or without pre-treatment of tumour necrosis factor (TNF)-α (25 ng/ml). The effect of Tq on the expression of different proinflammatory cytokines and chemokines was analysed by real-time polymerase chain reaction (PCR). Luciferase-labelled promoter studies evaluated the effect of Tq on the transcription of monocyte chemoattractant protein-1 (MCP-1) and nuclear factor-κB (NF-κB). The effect of Tq on the constitutive and TNF-α-induced activation and nuclear translocation of NF-κB was examined by ELISA and immunohistochemistry.

Results: Tq dose- and time-dependently significantly reduced PDA cell synthesis of MCP-1, TNF-α, interleukin (IL)-1β and Cox-2. At 24 h, Tq almost completely abolished the expression of these cytokines, whereas TSA had a less dramatic effect. Tq, but not TSA, significantly and dose-dependently reduced the intrinsic activity of the MCP-1 promoter. Tq also inhibited the constitutive and TNF-α-mediated activation of NF-κB in PDA cells and reduced the transport of NF-κB from the cytosol to the nucleus.

Conclusions: Our data demonstrate previously undescribed anti-inflammatory activities of Tq in PDA cells, which are paralleled by inhibition of NF-κB. Tq as a novel inhibitor of proinflammatory pathways provides a promising strategy that combines anti-inflammatory and proapoptotic modes of action.