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Inhibitory effects of thymoquinone, the major component of *Nigella sativa* L. seeds, on spontaneous and evoked contractions of guinea pig isolated ileumParvardeh, S.^a, Fatehi, M.^b^a Department of Pharmacology, Faculty of Medicine, Ahwaz Jundishapour University of Medical Sciences, Ahwaz, Iran^b Department of Pharmacology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

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Background: It has been recently shown that essential oil of *Nigella sativa* seeds and its major constituent, thymoquinone (TQ), possess relaxant activity on isolated trachea and ileum. Several mechanisms have been suggested to explain the smooth muscle relaxant effects of the essential oil of *Nigella sativa* seeds. But, only in one study, it has been shown that TQ exerts its relaxant activity probably through the inhibition of histaminergic and serotonergic receptors. Objective: This study was carried out in order to further evaluating the mechanism(s) of muscle relaxant activity of TQ. Methods: Tension recording technique using an isometric transducer connected to a physiograph in an organ bath set up was used. The spontaneous contractions of isolated ileum and contractile responses evoked by acetylcholine (ACh), histamine (His), potassium chloride (KCl), and repetitive electrical field stimulation (EFS), were recorded. ACh (10 μ M), His (100 μ M), KCl (10 mM), and EFS (20 Hz, 0.2 ms, 130 V), were applied before and after adding TQ (10, 20, 40, 80, 100 μ M). Moreover, in order to evaluate the role of Ca^{2+} -channels in TQ-induced relaxation of ileum, the amplitude of contractions evoked by EFS were recorded in the presence and absence of TQ (80 μ), in Ca^{2+} -free Krebs solution, as well as following adding of cumulative concentrations of $CaCl_2$ (0.1, 0.2, 0.4, 1, 2 mM). Results: The results showed that TQ at the minimum concentration of 20 μ M decreased the amplitude of spontaneous contractility ($p < 0.01$) and His- and EFS- evoked contractions ($p < 0.05$). Also, the amplitude of ACh- and KCl - evoked contractions were decreased by TQ at the minimum concentration of 40 μ M ($p < 0.01$ and $p < 0.001$, respectively). The maximum inhibitory effects of TQ against ileum contractility were achieved by the concentration of 100 μ M. Furthermore, the cumulative concentrations of $CaCl_2$ in the presence of TQ (80 μ M), failed to increase the amplitude of contractions induced by EFS, which were suppressed in Ca^{2+} -free medium. Conclusion: These findings indicated that TQ possesses inhibitory effects on contractility of guinea pig isolated ileum, and that effects may be responsible for the smooth muscle relaxant activity of *Nigella sativa* seeds. The mechanism by which TQ relaxes ileum contractility was exerted, at least in part, through an antagonistic activity on calcium channels in guinea pig ileum smooth muscle cells.

Author keywords

Calcium channels; Guinea pig ileum; Tension recording; Thymoquinone

Indexed Keywords

EMTREE drug terms: acetylcholine; calcium channel; calcium chloride; histamine; *Nigella sativa* extract; potassium chloride; thymoquinone

EMTREE medical terms: animal tissue; article; black cummin; citric acid cycle; controlled study; electrostimulation; evoked muscle response; guinea pig; ileum contraction; nonhuman; plant seed; smooth muscle contractility; smooth muscle relaxation; transducer

Species Index: *Cavia*; *Nigella sativa*

Chemicals and CAS Registry Numbers: acetylcholine, 51-84-3, 60-31-1, 66-23-9; calcium chloride, 10043-52-4; histamine, 51-45-6, 56-92-8, 93443-21-1; potassium chloride, 7447-40-7; thymoquinone, 490-91-5

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