Regulation of low-density lipoprotein receptor and 3-hydroxy-3- methylglutaryl coenzyme a reductase gene expression by thymoquinone-rich fraction and thymoquinone in HepG2 cells.

ABSTRACT

Background and Aim: Nigella sativa and its active constituent thymoquinone (TQ) have been exploited for their various health benefits. This work was aimed to investigate the regulatory effects of TQ-rich fraction (TQRF) and commercial TQ on the low-density lipoprotein receptor (LDLR) and 3-hydroxy-3- methylglutaryl-coenzyme A reductase (HMGCR) genes in HepG2 cells. Methods and Results: TQRF was extracted from N. sativa seeds using supercritical fluid extraction. The regulatory effects of TQRF at 80 μg/ml and TQ at 2 μg/ml on LDLR and HMGCR gene expression were investigated in HepG2 cells using quantitative real-time PCR. The TQ content in TQRF was 2.77% (w/w) and was obtained at a temperature of 40°C and a pressure of 600 bar. Treatment of cells with TQRF and TQ resulted in a 7- and 2-fold upregulation of LDLR mRNA level, respectively, compared with untreated cells. The mRNA level of HMGCR was downregulated by 71 and 12%, respectively, compared with untreated cells. Conclusion: TQRF and TQ regulated genes involved in cholesterol metabolism by two mechanisms, the uptake of low-density lipoprotein cholesterol via the upregulation of the LDLR gene and inhibition of cholesterol synthesis via the suppression of the HMGCR gene.

Keyword: 25-Hydroxycholesterol; 3-Hydroxy-3-methyl-glutaryl-coenzyme A reductase; HepG2 cells; Low-density lipoprotein receptor; Nigella sativa; Supercritical fluid extraction; Thymoquinone; Thymoquinone-rich fraction.