Anticancer activity of thymoquinone in breast cancer cells: possible involvement of PPAR-γ pathway.


Source

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Abstract

Thymoquinone (TQ), an active ingredient of Nigella sativa, has been reported to exhibit anti-oxidant, anti-inflammatory and anti-tumor activities through mechanism(s) that is not fully understood. In this study, we report the anticancer effects of TQ on breast cancer cells, and its potential effect on the PPAR-γ activation pathway. We found that TQ exerted strong anti-proliferative effect in breast cancer cells and, when combined with doxorubicin and 5-fluorouracil, increased cytotoxicity. TQ was found to increase sub-G1 accumulation and annexin-V positive staining, indicating apoptotic induction. In addition, TQ activated caspases 8, 9 and 7 in a dose-dependent manner. Migration and invasive properties of MDA-MB-231 cells were also reduced in the presence of TQ. Interestingly, we report for the first time that TQ was able to increase PPAR-γ activity and down-regulate the expression of the genes for Bcl-2, Bcl-xL and survivin in breast cancer cells. More importantly, the increase in PPAR-γ activity was prevented in the presence of PPAR-γ specific inhibitor and PPAR-γ dominant negative plasmid, suggesting that TQ may act as a ligand of PPAR-γ. Also, we observed using molecular docking analysis that TQ indeed formed interactions with 7 polar residues and 6 non-polar residues within the ligand-binding pocket of PPAR-γ that are reported to be critical for its activity. Taken together, our novel observations suggest that TQ may have potential implication in breast cancer prevention and treatment, and show for the first time that the anti-tumor effect of TQ may also be mediated through modulation of the PPAR-γ activation pathway.

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