Thymoquinone inhibits prostate cancer progression by modulating Cytochrome P450 (CYPs)

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Background: Prostate cancer (PCa) incidence and mortality remain high in African American (AA) than Caucasian American (CA) men. Multiple factors contribute to this critical disease disparity, androgen receptors (AR), and differences among variants of the genes such as Cytochrome P450 (CYP) are involved in androgen biosynthesis and metabolism that may switch to gene regulation for prostate growth. However, inhibitors have been approved for CYP genes, the major pitfall, undesirable side effects, and quality of life in those patients. Therefore, targeting CYPs with a natural compound, Thymoquinone (TQ), a constituent of Nigella sativa (black seed), potentially safe and curative option for PCa patients. **Methods:** Cell viability assay (MTT) was performed to determine IC_{50} value in PCa cells (MDAPCa2b (AA) and LNCaP (CA) with varying concentrations of TQ for different time intervals. Further, Live/Dead cell assay, 3D invasion, migration, immunofluorescence (IF), qRT-PCR, and western blots were used to detect the role of TQ for the expression of CYPs gene. **Results:** Cell viability assay determines the optimal IC_{50} value of TQ in both cell lines. We showed overexpression of CYP3A4 and CYP17A1 stimulates proliferative, migratory, and invasive potential of PCa cells. However, treatment with TQ significantly downregulated the expression of these genes in PCa cells. Further, TQ exhibits high specificity for MDAPCa2b compared to LNCaP cells, confirmed by IF and immunoblots. **Conclusions:** These results demonstrate TQ could be the potent inhibitor of the active sites of the Cytochrome P450 enzymes and be used as potential therapeutics for men of African descent.