In-silico analysis of Thymoquinone as anti-cancer agent against chemoresistance associated proteins in ovarian cancer

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Abstract:
Thymoquinone (TQ) is a polyphenol obtained from *Nigella sativa* and is known to play a fundamental role in controlling homeostasis. It possesses anti-cancer, anti-oxidant, anti-microbial, anti-inflammatory, and analgesic properties. It has shown anti-cancer properties in several cancers such as prostate, pancreatic, breast, lymphoma, leukemia, medulloblastoma, and ovarian cancer (OvCa). OvCa is one of the lethal malignancies worldwide having distinct symptoms and a poor prognosis. One of the reasons for treatment failure in OvCa is the resistance to cisplatin leading to the reoccurrence of tumors. Since chemoresistance has been reported to affect multiple factors, combination therapies along with polyphenol can help to overcome the drug resistance. TQ has been used for targeted drug delivery systems and is capable of altering molecular and signaling pathways. It has been proven to enhance cisplatin response. Certain apoptotic proteins like Bcl-2, Bax, STAT3, p53, and caspase-3/9 are regulated during cancer progression and are involved in signaling chemoresistance. In this study, TQ interactions with chemoresistance proteins have been observed and desired output has been noted. TQ is docked with the mentioned proteins to check the efficiency in OvCa and as a potential anti-cancer agent. The 3D structure prediction was carried out using Phyre2 and SWISS-MODEL. The molecular docking of protein targets and TQ was done using the PatchDock server. The docked results were then visualized using Discovery Studio. This study helps us to understand the interactions between TQ and apoptotic proteins that help in the augmentation of conventional therapy. This knowledge will also help in developing a new approach and alternate therapeutic strategies using polyphenols like TQ, even in resistant cells.

Keywords: Thymoquinone, Ovarian cancer, Chemoresistance, Cisplatin, Proteins