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Identification and validation of natural anti-drug resistant and anticancer stem cell agents in TNBC stem cells

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Statement of the problem: Cancer drug resistance reduces the effect of the drug(s) in cancer cells. Triple-negative breast cancer (TNBC) is an aggressive disease with a poor therapy outcome. Drug resistance and self-renewal properties of stem cells make it an attractive target for anticancer drug discovery. ABC transporter and stemness markers are positively involved in stem cell drug resistance. Nowadays natural remedies are of interest due to lesser side effects and cost-effective. Taken together, there is an urgent need to identify novel natural anti-drug resistant and anticancer agents against TNBC stem cells.

Methodology & Theoretical Orientation: Different scientific literature database were used to prepare the list of phytochemicals present in Bulbine spp. Molecular docking and simulation approach was used to identify the ABC transporter inhibitor from the enlisted phytochemicals. Literature shows that the enlisted phytochemicals are soluble in the polar solvent. Thus, we prepared the methanolic (polar) extract of Bulbine spp. Anti-drug resistance and anticancer activity of the extract was examined by using MTT, drug efflux, and colony formation assay. Further, the therapeutic potential of the extract was studied in terms of apoptosis induction and reduction in stemness markers (Oct4, Sox2, Nanog, and Myc) at the transcriptional level.

Findings: In silico study revealed potent phytochemical showing better binding affinity with ABC transporter in comparison to standard inhibitors. Extract inhibited the mammosphere formation and reduced colony formation in TNBC cells. Treatment showed reduced drug efflux activity, down-regulated stem cell markers and induced apoptosis in the cells.

Conclusion & Significance: Present in silico and *in vitro* study suggest that Bulbine spp. phytochemicals have anti-drug resistance and anti-cancer stem cell potential. The phytochemicals may act as the lead candidate for drug development against triple negative breast cancer stem cells.

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