Targeting Drug Resistant Cancer Cells by Plant Based Bio-Active Compounds

Moazzam, Manahil (School: Lahore Grammar School, OPF Senior Girls Campus)

Development of drug resistance is a great challenge in cancer treatment as existing chemotherapeutics become ineffective after some time. For this project, human breast cancer cells MCF-7 Wt (drug sensitive) and MCF-7 gemR (gemcitabine resistant) were studied to find bioactive compounds that show selective toxicity towards gemcitabine resistant cells (collateral sensitivity). Cells were treated with several flavonoids; myricetin, quercetin, baicalein, hesperetin and other chemotherapeutics and bioactive compounds like gemcitabine, vincristine, oxaliplatin, cytarabine, doxorubicin, paclitaxel, and curcumin in increasing drug concentrations to find out which compounds had the most potent effect on MCF-7 gemR. Results of MTT cytotoxicity assay confirmed the resistant nature of MCF-7 gemR as they continued to thrive even at 800uM gemcitabine. Next, the quantification of toxicity of the bioactive compounds towards the cells was carried out using MTT assay. The results showed that MCF-7 gemR cells showed collateral sensitivity towards baicalein, quercetin, doxorubicin, and paclitaxel. For baicalein, MCF-7 gemR showed 17 times more sensitivity at 200uM and for quercetin it showed 5 times more sensitivity at 100uM; for doxorubicin and paclitaxel resistant cells showed approximately 4 times more sensitivity for various concentrations of drugs. The compounds showing collateral sensitivity were tested in combinations and 100 uM baicalein was found to be most effective when used in combination with 0.25 uM doxorubicin or paclitaxel. Further experiments would be quantification of expression of genes involved to better understand the mechanism behind collateral sensitivity.

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