Directed Enzyme Prodrugs Therapy (DEPT) as an alternative method against conventional cancer treatments

Abstract

Directed Enzyme Prodrugs Therapy (DEPT) as an alternative method against conventional cancer treatments, in which the non-toxic prodrugs is converted to highly cytotoxic derivative, has attracted an ample attention in recent years for cancer therapy studies. Nitroreductase enzymes (NTR) catalyze the conversion of the nitro group of prodrugs via hydroxylamine to amine group and the active drug inhibits tumor formation by binding to DNA. E. coli nitroreductase/CB1954 (5-aziridinyl-2,4-dinitrobenzamide) is the best known combination for different cancer types. For this purpose, more effective NTR/prodrug combinations should be investigated for cancer therapies.

Our group synthesized and characterized various type of aromatic and heterocyclic prodrugs containing nitro group and investigated the enzymatic interaction of these potential prodrugs with our two novel nitroreductases (Ssap-NtrB and Gk-Ntr). Metabolite profiles were determined by HPLC analysis, and kinetic parameters were calculated. The prodrugs were evaluated by MTT and SRB assay in different cancer cell lines and healthy cell. Also, biological data was supported with in silico studies. According to the results, our promising enzyme/prodrug combinations may use NTR based cancer therapy.