

## In vitro P-Glycoprotein Modulation: Combinatorial Approach Using Natural Products

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**Abstract :** Context: Over-expression of P-glycoprotein (P-gp) plays critical role in absorption of many drug candidates which results into lower bioavailability of the drug. P-glycoprotein also over expresses in many pathological conditions like diabetes, affecting the drug therapy. Modulation of P-gp expression using inhibitors can help in designing novel formulation enhancing the bioavailability of the drug in question. Objectives: The main focus of the study was to develop advanced glycation end products (AGEs) induced P-gp over expression in Caco-2 cells. Curcumin, piperine and epigallocatechin gallate were used to evaluate their P-gp inhibitory action using combinatorial approach. Materials and methods: Methylglyoxal (MG) induced P-gp over expression was checked in Caco-2 cells using real time PCR. P-gp inhibitory effects of the phytochemicals were measured after induction with MG alone and in combination of any two compounds. Cytotoxicity of each of the phytochemical was evaluated using MTT assay. Results: Induction with MG (100mM) significantly induced the over expression of P-glycoprotein in Caco-2 cells after 24 hr. Curcumin, piperine and epigallocatechin gallate alone significantly reduced the level of P-gp within 6 hr of treatment period monitored by real time PCR. The combination of any two phytochemical also down regulated the expression of P-gp in cells. Combinations of Curcumin and epigallocatechin gallate have shown significant down regulation when compared with other two combinations. Conclusions: Combinatorial approach for down regulating the expression of P-gp, in pathological conditions like diabetes, has demonstrated promising approach for therapeutic purpose.

**Keywords :** p-glycoprotein, curcumin, piperine, epigallocatechin gallate, p-gp inhibition

**Conference Title :** ICFSN 2016 : International Conference on Food Security and Nutrition

**Conference Location :** Vienna, Austria

**Conference Dates :** June 16-17, 2016