Surface Modified Polyamidoamine Dendrimer with Gallic Acid Overcomes Drug Resistance in Colon Cancer Cells HCT-116

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Abstract: Cancer cells can develop resistance to conventional therapies especially chemotherapeutic drugs. Resistance to chemotherapy is another challenge in cancer therapeutics. Therefore, it is important to address this issue. Gallic acid (GA) is a natural plant compound that exhibits various biological properties including anti-proliferative, anti-inflammatory, anti-oxidant and anti-bacterial. Despite of the wide spectrum biological properties GA has cytotoxic response and low bioavailability. To overcome this problem, GA was conjugated with the Polyamidoamine(PAMAM) dendrimer for improving the bioavailability and efficient delivery in drug-resistant HCT-116 Colon Cancer cells. Gallic acid was covalently linked to 4.0 G PAMAM dendrimer. PAMAM dendrimer is well established nanocarrier but has cytotoxicity due to presence of amphiphilic nature of amino group. In our study we have modified surface of PAMAM dendrimer with Gallic acid and examine their anti-proliferative effects in drug-resistant HCT-116 cells. Further, drug-resistant colon cancer cells were established and thereafter treated with different concentration of PAMAM-GA to examine their anti-proliferative potential. Our results show that PAMAM-GA conjugate induces apoptotic cell death in HCT-116 and drug-resistant cells observed by Annexin-PI staining. In addition, it also shows that multidrug-resistant drug transporter P-gp protein expression was downregulated with increasing the concentration of GA conjugate. After that we also observed the significant difference in Rh123 efflux and accumulation in drug sensitive and drug-resistant properties in Rh123 efflux and accumulation in drug sensitive and drug-resistant property and cytotoxic response to treatment of cancer.

Keywords : drug resistance, gallic acid, PAMAM dendrimer, P-glycoprotein

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