PAMAM Dendrimer Based Targeted Nano-Carrier for Therapeutic agents: synthesis, characterization and application *in vitro*

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Abstract: In this article, interleukin-6 (IL-6)-conjugated with anionic generation 4.5 (G4.5) poly (amidoamine) (PAMAM) dendrimer was synthesized through EDC/NHS coupling chemistry, and the conjugation was confirmed using Fourier-transformed infrared spectroscopy (FT-IR) and 2-dimensional nuclear magnetic resonance (2D NMR). After IL-6 conjugation, nanoparticle size was confirmed to approximately 70 nm and zeta potential increased from -56.5 ± 0.2 to -19.1 ± 2.4 mV due to neutralization of G4.5 PAMAM. Furthermore, the cellular uptake of the conjugates by HeLa cells was significantly enhanced in comparison to free G4.5, in which the complex has a potential bio-imaging probe *in vitro*. For further, the anti-cancer drug doxorubicin was physically loaded onto G4.5-IL6 with the loading content and encapsulation efficiency of 9.8 wt% and 51.3%, respectively. The cellular internalization and uptake efficiency of G4.5-IL6/DOX complexes was observed and compared by confocal microscopy and flow cytometry using HeLa cells, respectively. The lower IC50 value of G4.5-IL6/DOX was obtained, this is due to the higher drug loading and faster drug release rate corresponded with greater cytotoxicity. The cytotoxic effect was also further verified by increment in late apoptotic/necrotic cells due to delivery of drug through receptor-mediated endocytosis. Based on these results, G4.5-IL6 is a better suited carrier for targeted drug delivery of DOX to cervical cancer cells.

Keywords: PAMAM dendrimer, Interleukin-6 (IL-6), Bio-imaging, *in vitro*, HeLa cells, DOX, Drug delivery.