IN VITRO EVALUATION OF ANTISENSE OLIGONUCLEOTIDE FUNCTIONALIZED CORE-SHELL NANOPARTICLES LOADED WITH A-TOCOPHEROL SUCCINATE

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Abstract- Antisense oligonucleotide (ASO)-conjugated-α-tocopherol succinate (TCS)-loaded-poly(lactic acid)-g-poly(ethylene glycol) nanoparticles (ASO-TCS-PLA-PEG NPs), with the ratio of polymer/ TCS of 10:1.25 10:5 10:7 (w/w) were prepared for targeting cancer therapy. The amphiphilic PLA, amino terminated PEG graft copolymers were synthesized by ring opening polymerization reaction. Nanoparticles were produced by using double emulsion (w/o/w) solvent evaporation method. ASO-TCS-PLA-PEG NPs demonstrated satisfactory encapsulation and loading efficiency and size distribution. The short term stability studies were carried out at 4 °C and 25 °C for 30 days to assess their mean particle size, polydispersity index and zeta potential. The cellular uptake and extended cytoplasmic retention of the NPs in A549 human lung carcinoma cells were examined by fluorescence microscopy. In human lung cancer cells, ASO-TCS-PLA-PEG NPs exhibited better cellular internalization, cytotoxicity and apoptotic and necrotic effects. These findings showed that ASO-modified with nanoparticles could serve as a promising nanocarrier for targeted tumor cells.

Keywords- PLA-PEG; antisense oligonucleotide; α-tocopherol succinate; drug delivery; human lung cancer cells.