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In vitro evaluation of nanoliposomal doxorubicin modified with tat peptide developed by post-insertion method on C-26 colon carcinoma cell line

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Background and Aims: Doxil is PEGylated liposome of doxorubicin (PLD) which unlike conventional solution of doxorubicin has reduced the side effects of drug delivery. Since its anti cancer activity is limited to the time the drug is released and penetrated to the cell, TAT peptide modified liposomes were formulated to enhance cellular uptake. TAT is a peptide of HIV which facilitates the translocation of virus into cytoplasm. Also it is one of the members of cell penetrating peptides which facilitate the translocation of large cargos such as liposomes.
Methods: PLD was prepared by solvent evaporation /extrusion and the doxorubicin was remote loaded into these liposomes. Then TAT peptide attached to mPEG DSPE 2000 was post inserted into PLDs to form 25, 50, 100 and 200 tat per liposome. Cell interaction and MTT test was carried out in order to evaluate the rate of cellular uptake and the cytotoxicity of TAT formulations.
Results: Cell interaction results after 3hr incubation showed significant cellular uptake of TAT modified liposomes in comparison with PLDs. Also, TAT3 formulations were capable to deliver higher amount of doxorubicin to C-26 cells than TAT1 and TAT2.Cellular uptake results at 4°C incubation showed that intracellular drug delivery of TAT is not energy dependent. Hence, the Tat peptide could preserve its drug delivery properties even at lower temperature. Furthermore, the results indicated that formulations with higher TAT density were capable to deliver more doxorubicin into tumoral cells.
Conclusions: Tat modified liposomes of doxorubicin are more efficient intracellular drug delivery formulations than PLDs which release the drug after decomposition by acidic pH and lipase of the tumor site.

Keywords: TAT; Cell penetrating peptide; Doxorubicin; C-26 colon carcinoma cell line; Liposome