

An In-vitro Investigation of Surface Modified Hemo-Compatible Nano Structured Lipid Carriers for MDR Modulation and CD-44 Targeting in Colon Adenocarcinoma

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ABSTRACT

Colon adenocarcinoma arises from the glandular origin in colon and leads to high degree of mortality in patients. Although a number of chemotherapeutic agents are available for this condition, but regular treatment failures as well as toxic effects of the anticancer agents warrant for a more targeted drug delivery system along with better diagnostic tools. In present work, we developed a novel hyaluronated cationic nanostructured lipid carrier (NLCs) which contains CPT-11/irinotecan (the first line drug for colon cancer) as well as coumarin-6 (the fluorescent probe) to target CD44 biomarker which commonly overexpresses on colon cancer. The cationic core NLCs was developed by using Capmule MCM and Compritol ATO888 as lipid phase with a particle size of 150 ± 2.5 nm and entrapment efficiency 93.98 ± 2.5 %. Coumarin-6 was also encapsulated into these particles with final concentration of $15 \mu\text{g/mL}$. The cationic core NLCs were coated with hyaluronic acid by ionic conjugation. The hyaluronated CNLCs were having a particle size of 255 ± 4.2 nm. In-vitro drug release studies revealed a slow and sustain release of the drug as well practically no leaching of coumarin-6. The confocal laser microscopy studies were performed with developed CNLCs in two CD44 overexpression cell lines (HT-29 and Colo-320). The studies revealed marked uptake of the CNLCs by both the cell lines in just two hours. The results were comparable to the FITC conjugated CD44 antibodies. Therefore, the developed dual purpose CNLCs were found to be highly specific for CD44 biomarker and can be utilized to deliver the cytotoxic payload to the concerned cancer cells. The developed formulations were found to be compatible with blood components. The MTT assay revealed that the developed particles had enhanced cytotoxicity against both non-MDR as well MDR cancer cells.