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7-ethyl-10-hydroxy-camptothecin (sn38)

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Objective: 7-Ethyl-10-hydroxy-camptothecin (SN38) is the most biologically active member of camptothecins but the usage of drug was restricted because of its poor solubility in pharmaceutical solvents. Irinotecan as a prodrug of SN38 is the only commercially available formulation of this group but individual differences induce different metabolism rate of Irinotecan to SN38. In this study, we investigated the effect of aptamer functionalization on therapeutic efficiency of PAMAM dendrimers containing SN38.

Methods and Materials: AS1411 aptamer conjugated formulation of PEGylated PAMAM containing SN38 was prepared. Nanoparticles were characterized for drug loading and PEGylation efficiency. In vitro cytotoxicity and cellular uptake of SN38 in prepared formulations after 3 hours of exposure to murine colon carcinoma (C-26) cell line were investigated. Then in vivo anti-tumor efficacy and survival analysis were studied in C-26 mice bearing tumor during 54 days.

Result: In vitro evaluations revealed significantly higher cytotoxicity and much lower IC50 for all preparations compared to SN38 solution. Cellular uptake studies showed a higher values of uptake for aptamer conjugated formulations after 3 hours of exposure. Regarding to in vivo results, all prepared formulations improved survival of animal model. All PEGylated formulations conjugated with aptamer in dose of 1 mg/Kg and 2 mg/Kg and formulation conjugated with aptamer in dose of 2 mg/Kg indicated significantly better tumor growth inhibition compared to Irinotecan (25 mg/Kg).

Conclusion: The results of this study showed that encapsulation of SN38 in dendrimer and modification of dendrimer by A1411 aptamer improved the anti-tumor effect of drug.

Keywords: 7-Ethyl-10-hydroxycamptothecin (SN38), Irinotecan, Camptothecins, Chemotherapy, Poly (amidoamine) (PAMAM) dendrimer, AS1411 aptamer.

Biography

Kiana Sherkat Sadi did Ph.D. in the field of pharmacy from Mashhad University of Medical Sciences, Iran. She published lot of papers related to the field of pharma.