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Pharmacokinetic and Tissue Distribution of Etoposide Loaded Modified Glycol Chitosan Nanoparticles

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Abstract : The development of efficient delivery systems remains a major concern in cancer chemotherapy as many efficacious anticancer drugs are hydrophobic and difficult to formulate. Nanomedicines based on drug-loaded amphiphilic glycol chitosan micelles offer potential advantages for the formulation of drugs such as etoposide that may improve the pharmacokinetics and reduce the formulation-related adverse effects observed with current formulations. Amphiphilic derivatives of glycol chitosan were synthesized by chemical grafting of palmitic acid N-hydroxysuccinimide and quaternization to glycol chitosan backbone. To this end, a 7.9 kDa glycol chitosan was modified by palmitoylation and quaternization, yielding a 13 kDa amphiphilic polymer. Micelles prepared from this amphiphilic polymer had a size of 162nm and were able to encapsulate up to 3 mg/ml etoposide. Pharmacokinetic results indicated that the GCPQ micelles transformed the biodistribution pattern and increased etoposide concentration in the brain significantly compared to free drugs after intravenous administration. AUC 0.5-24h showed statistically significant difference in ETP-GCPQ vs. Commercial preparation in liver (25 vs.70, $p<0.001$), spleen (27 vs.36, $p<0.05$), lungs (42 vs.136,$p<0.001$),kidneys(25 vs.70,$p< 0.05$),and brain(19 vs.9,$p<0.001$). ETP-GCPQ crossed the blood-brain barrier, and 4, 3.5, 2.6, 1.8, 1.7, 1.5, and 2.5 fold higher levels of etoposide were observed at 0.5, 1, 2, 4, 6, 12, and 24hrs; respectively suggesting these systems could deliver hydrophobic anticancer drugs such as etoposide to tumors but also increased their transport through the biological barriers, thus making it a good delivery system

Keywords : glycol chitosan, micelles, pharmacokinetics, tissue distribution
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