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Modified glycol chitosan nanocarriers carry hydrophobic materials into tumours

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Development of an efficient delivery system for hydrophobic drugs remains a major concern in chemotherapy. The objective of the current study is to develop a polymeric drug-delivery system for etoposide from amphiphilic derivatives of glycol chitosan, capable to improve the pharmacokinetics and to reduce the adverse effects of etoposide due to various organic solvents used in commercial formulations for solubilization of etoposide. As a promising carrier, amphiphilic derivatives of glycol chitosan were synthesized by chemical grafting of palmitic acid N-hydroxysuccinimide and quaternization glycol chitosan backbone. To this end, a 7.9 kDa glycol chitosan was modified by palmitoylation and quaternization into 13kDa. Nano-sized micelles prepared from this amphiphilic polymer had the capability to encapsulate up to 3mg/ml etoposide. The pharmacokinetic results indicated that GCPQ based etoposide formulation transformed the biodistribution pattern. AUC 0.5-24 hr 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. 30, $p<0.05$) and brain (19 vs. 9,$p<0.001$)Using the hydrophobic fluorescent dye Nile red, we showed that micelles efficiently delivered their payload to MCF7 and A2780 cancer cells *in-vitro* and to A431 xenograft tumor *in-vivo*, suggesting these systems could deliver hydrophobic anticancer drugs such as etoposide to tumors. The pharmacokinetic results indicated that the GCPQ micelles transformed the biodistribution pattern and increased etoposide concentration in the brain significantly compared to the free drug after intravenous administration. GCPQ based formulations not only reduced side effects associated with currently available formulations but also increased their transport through the biological barriers, thus making it a good delivery system.

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