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Preparation and characterization of valspodar loaded nanoliposomes as a potential adjuvant therapy for drug-resistant tumors

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Background and Aims: Valspodar, an analogue of cyclosporin, is more active than the first generation agents such as verapamil and cyclosporin A in reversing P-gp mediated multidrug resistance. In spite of high potency and specificity, a major confounding factor in its use is the pharmacokinetic interaction and increase in cytotoxicity of anticancer drugs. A great deal of these shortcomings may be tackled by administering these agents using nanoparticulate delivery systems. Therefore, the present work was undertaken to develop a liposomal formulation of valspodar.
Methods: In attempt to increase the encapsulation efficiency of the drug, different methods for liposome preparation such as thin-film hydration technique followed by either extrusion or probe sonication, ethanol injection method, and remote film loading were tested and the effects of different parameters such as drug to lipid molar ratio, cholesterol mole percent and lipid compositions, were investigated. Liposomes were extensively characterizied in terms of entrapment efficiency (%EE), size, zeta potential, and release profile.
Results: The remote film loading method was proved to be the most effective method for valspodar liposomal entrapment. It was found that the amount of drug associated with vesicles was always higher for the greater lipid/drug ratios, lower cholesterol mol% and the more fluid lipid compositions. The best formulation (EPC:DSPE-PEG2000:CHOL 60:5:30 %mol) showed a narrow size distribution with average diameter of 91.3 ± 0.2 nm, zeta potential of -6 ± 1.2 and EE of 65%. The drug release profiles proved the efficacy of the optimized liposome in controlling the drug release in such a way that percent drug release up to 72 hours was recorded as approximately 40%.
Conclusions: In this study, valspodar nanoliposomes were successfully prepared and characterized as a potential adjuvant therapy for enhancing delivery of anticancer drugs in multidrug resistance tumor cells.

Keywords: Valspodar; Nanoliposome; Preparation methods; Remote film loading