LIPOSOMES WITH HIGH ENCAPSULATION CAPACITY FOR PACLITAXEL: PREPARATION, CHARACTERISATION AND IN VIVO ANTICANCER EFFECT AGAINST B16F10 MOUSE MELANOMA

Koudelka, Š., Turánek-Knotigová, P., Mašek, J. & Turánek, J.

VÚVeL, Brno, Czech Republic

Abstract

Paclitaxel (PTX) is approved for the treatment of ovarian and breast cancer. The commercially available preparation of PTX, Cremophor EL is associated with hypersensitivity reactions in spite of a suitable premedication. The developed liposomal PTX formulations are known to be troubled with low PTX encapsulation capacity (maximal content, 3 mol %) and often accompanied by PTX crystallisation. The application of “pocket forming” lipids significantly increased the entrapment capacity of PTX in the liposomes up to 10 mol %. Stable lyophilised preparation of PTX (7 mol %) encapsulated in the liposomes composed of SOPC/POPG/MOPC (molar ratio, 60:20:20) doped with 5 mol % vitamin E had the size distribution of 180-190 nm (PDI, 0.1) with ζ-potential of -31mV. Sucrose was found to be a suitable cryoprotectant at the lipid:sugar molar ratios of 1:5 – 1:10. This liposomal formulation did not show any evidence of toxicity in C57Bl/6 mice treated with the highest doses of PTX (100 mg/kg administered as a single dose and 150 mg/kg as a cumulative dose applied in 3 equivalent doses in 48-hour intervals). A dose-dependent anticancer effect was found in both hollow fibre implants and syngenic B16F10 melanoma mouse tumour models. This new formulation demonstrated very useful safety and efficacy profiles and could be favourable for clinical applications.

Acknowledgement: This work was supported by grants: grant No. MZE 0002716202 and KAN 200520703 AVČR

Author did not supply full text of the paper/poster