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Influence of the surface properties of nanoliposomes on protein corona formation

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One of the biggest problems upon nanoparticles' administration *in vivo* is their interaction with blood proteins and the formation of the protein corona (PC), followed by the rapid recognition and uptake of the particles by the mononuclear phagocyte cells, thus leading to quick removal from the circulation. Therefore, understanding of the particle–PC complex formation is a prerequisite for successful development of drug carrier system and proper characterization is essential.
This problem could be partially overcome by the decoration of the particles' surface with polyethylene glycol (PEG) [1]. In order to investigate the effect of PEG on the PC formation, as well as to characterize the interaction, two formulations of nanoliposomes (NLs) (lechitin:cholesterol:PEG = 8.7:1:1.7 and 9:1:0.17 for *sample 1* and *2*, respectively) loaded with rosmarinic extract (RE) were prepared by the modified lipid film hydration technique [2]. Blank samples were prepared for comparison. The mean size of the prepared NLs was ~120 nm, with unimodal narrow size distribution and high encapsulation efficiency (~90%). *In vitro* release studies showed that the prepared vesicles had prolonged drug release properties (26 and 46% for 24h, for *sample 1* and *2*, respectively). The slower release of RE from *sample 1* could be probably due to the fast hydration process of the higher amount of PEG present on the surface of the vesicles. NLs–PC complex formation was confirmed using SDS-PAGE. Our previous investigations using Bratford assay confirmed that the PEG increases the hydrophilicity of the NLs surface thus resulting in reduced PC formation. These results were confirmed using FTIR and quantitative information of protein–NLs interactions was gained. From the obtained spectra it could be concluded that NLS-protein interaction was mainly due to the hydrogen bonds formed between C = O...N-H or C = O...H-OH. These interactions were stronger between the NLs prepared with lower PEG amount and the protein. Incorporation of RE into the NLs did not affect the intensity of the interactions.

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2. Lj. Cambuleva, D. Shalabalija, I. Cvetkovikj, M. Simonoska Crcarevska, M. Glavas Dodov, *Maced. Pharm. Bull.*, **2016** , *62(suppl),* 641.