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Temoporfin in cyclodextrin in liposome nanoparticles for tumor targeting

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Application of meta-tetra(hydroxyphenyl)chlorin (mTHPC), one of the most potent photosensitizer (PS), in the photodynamic therapy (PDT) of solid tumors encounters several complications originating from its poor solubility in aqueous medium. It requires low light doses and concentrations to be photoactive; however mTHPC aggregation results in reduced photodynamic activity, moderate selectivity and skin photosensitivity. To improve the transport of mTHPC to target tissue and to strengthen its intra-tissue accumulation, the coupling of two independent delivery systems by encapsulating cyclodextrin/mTHPC inclusion complexes into liposomes to achieve drug-in-cyclodextrin-in-liposome (DCL) nanoparticles has been proposed. Liposomes offer an excellent opportunity to achieve selective drug targeting which is expected to optimize the pharmacokinetic parameters, prevent local irritation, and reduce drug toxicity. In its turn, cyclodextrin-based inclusion complexes have been already utilized as independent carriers for improvement of mTHPC delivery into the tumor tissue. Thus, the aim of this study was to evaluate the effect of DCLs on mTHPC distribution *in vitro* tumor models. After optimization of DCL composition, we choose TDCL double loaded nano construct including trimethyl- β -cyclodextrin/mTHPC inclusion complexes in the inner aqueous core and mTHPC molecules in lipid compartment.

We studied mTHPC accumulation and localization in 3D tumor multicellular spheroid model. We demonstrated that the application of TDCL resulted in homogeneous distribution of mTHPC across the whole spheroid. Such efficient intra-tissue delivery is related to the extremely high binding of trimethyl- β -cyclodextrin to mTHPC that was confirmed by means of exclusion gel-chromatography.

Biography

Ilya Yakavets is a co-directed PhD student in Belarussian State University (Minsk, Belarus) and in the Université de Lorraine (Nancy, France). He defended his Master's degree in Belarussian State University (Minsk, Belarus) in 2016 in the field of Biophysics. Currently, his PhD research focuses on the application of hybrid nanosized photosensitizer carrier based on liposomes and cyclodextrins in photodynamic therapy. The current abstract describes a part of the results of his PhD study related to the development and application of drug-in-cyclodextrin-in-liposome nanoparticles for improved delivery of mTHPC to the tumor targets. The presentation of this PhD project at BioSE Doctoral School (Nancy, France) was awarded by the first prize in 2017. He has published his results in 6 articles in international peer-review journals. His main research interests include: photodynamic therapy, photoactive drugs, multicellular tumor spheroids, cyclodextrin inclusion complexes.

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