OPTIMIZATION OF TEMOPORFIN BIODISTRIBUTION BY CYCLODEXTRINS-BASED NANOSTRUCTURES

Yakavets I.[1,2,3], Lassale H.-P.[1,2], Bezdetnaya L.[1,2], Zorin V.[3,4]

[1] Centre de Recherche en Automatique de Nancy (CRAN), CNRS UMR 7039, Université de Lorraine, Vandoeuvre-lès-Nancy, France;
[2] Institut de Cancérologie de Lorraine, Vandoeuvre-lès-Nancy, France;
[3] Belarusian State University, Minsk, Belarus;
[4] International Sakharov Environmental Institute, Minsk, Belarus

Temoporfin (*meta*-tetrakis(3-hydroxyphenyl)chlorin, mTHPC) is one of the most potent clinically approved photosensitizer (PS) for the photodynamic therapy (PDT) of head and neck cancers. mTHPC molecules are highly hydrophobic and are prone to strong aggregation in biological media, resulting in decreased photodynamic efficacy, moderate selectivity and prolonged skin photosensitivity. Various attempts are being made to use special drug delivery forms for mTHPC introduction in order to prevent aggregation and improve pharmacokinetic properties of the PS.

Cyclic oligosaccharides such as β-cyclodextrins (β-CDs) are also promising delivery systems for different nonpolar drugs including aryl-substituted porphyrins. β-CDs readily interact with mTHPC incorporating side groups of drug molecule in the inner hydrophobic cavity. The formation of inclusion complexes increases mTHPC solubilization and recovers its photophysical properties. According to our data, β-CDs significantly modify mTHPC *in vitro* and *in vivo* biodistribution in particular inhibiting mTHPC aggregation and accelerating PS transportation to target tissue. We have obtained convincing evidence that the β-CDs strongly effect on mTHPC transport mechanism in blood and solid tissues and accelerate its molecules transfer among the various serum proteins and cells.

Additional possibilities in PDT with mTHPC are related to the use of β-CDs-based nanoscale structures. Encapsulation of CD/PS inclusion complex into liposomes (drug-in-cyclodextrin-in-liposome, DCL) allows significantly increase entrapment of hydrophobic PS in the aqueous core of liposomes. Application of DCL delays the dissociation of drug-CD complexes, avoid rapid drug release and, as a result, improve the pharmacokinetics of the PSs in vivo.

This work was supported by Belarusian Republican Foundation for Fundamental Research (BRFFR) (grant numbers M17MC-028, Б17-106).