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FLUORESCENCE ANALYSIS OF META-TETRA(HYDROXYPHENYL)CHLORINE COMPLEXATION WITH MONOMERIC AND POLYMERIC CYCLODEXTRINS

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Spectral methods have been developed for analyzing the equilibrium and kinetics of the complexation process of the known photosensitizer, meta-tetrakis(hydroxyphenyl)chlorine (mTHPC), with monomeric and polymeric derivatives of β-cyclodextrin (β-CD). The study of the binding isotherms showed that mTHPC has a higher affinity for the polymeric derivatives of β-CD studied, namely, carboxymethyl-β-cyclodextrin polymer (CM-β-CDPD) and β-cyclodextrin polymer (β-CDPD), than for monomeric methyl-β-cyclodextrin (M-β-CDMD). Profiles for the change in the relative content of mTHPC inclusion complexes with β-CDs in solution with and without the presence of lipid vesicles were obtained and the dissociation constants of the photosensitizer (PS) molecules were calculated from the content of the inclusion complexes with cyclodextrins. The dissociation of mTHPC from the inclusion complexes with M-β-CDMD takes 1–2 min, while this process takes more than one hour with polymeric CDs, (CM-β-CDPD and β-CDPD). These findings suggest that the complexation of the title chlorine with polymeric and monomeric cyclodextrins may play an essential role in the delivery of photosensitizer to cellular/tissue structures.

Keywords: *meta-tetra(hydroxyphenyl)chlorin, β-cyclodextrin, inclusion complexes, polymer, lipid vesicles.*

Introduction. Photodynamic therapy (PDT) has developed rapidly in recent decades for the treatment of oncological and other diseases [1]. The essence of PDT is the use of specialized photosensitizers (PS) capable of accumulating and remaining in tumor cells and tissues. Upon laser irradiation, PS molecules initiate photochemical reactions by generating singlet oxygen and free radical products, which then cause damage to pathological cells and tissues.

In order to compare the efficiency of various photosensitizers in clinical practice, we use the photodynamic activity parameter, which is defined as the inverse product of the PS concentration and the light dose yielding a therapeutic effect. Relative to this term, meta-tetra(hydroxyphenyl)chlorine (mTHPC) (Fig. 1) now appears to be the most efficient photosensitizer. A major problem in the use of this photosensitizer is its poor solubility in water leading to its aggregation upon introduction into the organism. This behavior affects the biodistribution of these molecules, thereby reducing their bioaccessibility and, as a consequence, their therapeutic effectiveness [2]. This problem can be overcome by using specialized pharmacological species, usually employed for the introduction of nonpolar pharmacological compounds. Foscan® is a preparation approved for treating head and neck tumors as well as gastrointestinal and respiratory tract cancer, which is a solution of mTHPC in a mixture of ethanol and propylene glycol [2, 3]. Pharmacological formulations Fospeg® and Foslip® containing mTHPC immersed in ordinary and sterically-stabilized liposomes have similarly been proposed [2, 4]. Feasibility has also been demonstrated for the use of carbon nanotubes, protein nanoparticles, polymer containers, and dendrimers as nanocarriers for mTHPC molecules [5–8].

Promise for the introduction of mTHPC has been found using preparations containing cyclodextrins (CD) [5, 9], which can solubilize poorly soluble compounds by forming inclusion complexes. The mechanisms for the insertion and release of porphyrin molecules from such systems have been examined in detail by several workers [10–12]. The experimental results indicate that mTHPC efficiently forms inclusion complexes with CD derivatives (mTHPC/CD) due to the insertion of the phenyl side-groups into the CD cavity (Fig. 1). The type of the mTHPC complexes formed with either 1:1 or 1:2 stoichiometry depends on the cyclodextrin chemical structure. A characteristic feature of the inclusion complexes

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