CYTOTOXIC SURFACES FOR REGIONAL CHEMOTHERAPY

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Introduction

Regional chemotherapy, in contrast to conventional approaches, enables local delivery of anti-cancer compounds limitting the side-effects of the treatment [1]. Among a wide range of possible drug carriers, conducting polymers are unique materials allowing highly controlled, electrostatic immobilization and release of a variety of biologically active compounds (FIG. 1). One of the most stable polymers exhibiting biocompatibility and high conductivity is PEDOT – this is why this polymer was selected to serve as a platform for the immobilization of betulin (FIG. 2) – one of the most often occurring triterpene presenting a broad range of biological properties, i.e. anti-cancer, anti-bacterial, anti-inflammatory, anti-fugal and anti-viral activities [2].

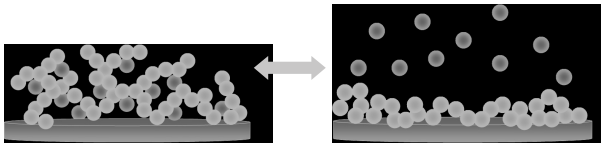

FIG. 1. The schematic representation of ion-exchange properties of conducting polymers.

Materials and Methods

The process of drug incorporation was performed by means of the three-step procedure that is described in details in [3]. In this procedure, the monomer is electrochemically polymerized in the presence of the primary dopant, then the doping ions are removed from the polymer matrix via application of reduction potential, and drug is immobilized via the re-oxidation of the matrix in the presence of drug. The drug-loaded PEDOT matrix was characterized by means of Raman and IR spectroscopies, as well as SEM. The process of drug release was triggered by means of cyclic voltammetry, and the cytotoxic activity of released drug was verified against KB and MCF-7 cancer cell lines.

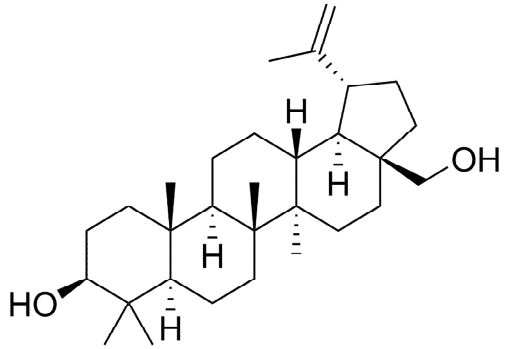

FIG. 2. Chemical structure of betulin.

Results and Discussion

The proposed immobilization procedure was proven to be an efficient method of drug incorporation resulting in the formation of betulin/PEDOT composite. The release of betulin immobilised in conjugated polymer matrix was performed under spontaneous (passive) and electro-assisted (active) modes in PBS. The range of applied reduction potentials was optimized – low enough to start the process of release but not too low, to prevent the process of matrix degradation.

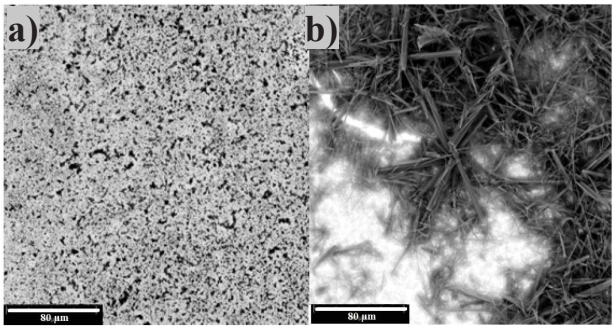

FIG. 3. SEM images of PEDOT (a) and betulin/PEDOT (b) matrix.

In vitro studies conducted with human oral carcinoma (KB) and human breast adenocarcinoma (MCF-7) cancer cell lines showed that for both types of cancer cell lines the solutions obtained as a result of active release exhibited the lowest IC_{50} values (13.34 ± 0.88 µg/ml and 12.57 ± 1.81 µg/ml for KB and MCF-7, respectively), hence they possessed the highest cytotoxic activity among all investigated samples. For comparison, the IC_{50} values for the samples released by means of spontaneous mode were equal to 19.25 ± 0.15 µg/ml and 20.05 ± 3.12 µg/ml for KB and MCF-7, respectively.

Conclusions

Betulin/PEDOT composite was shown to be a promising material for the surface modification for the needs of regional chemotherapy. The IC_{50} values of released drug were found to be comparable with the results of cytotoxic activity of betulinic acid against MCF-7 cancer cell lines [4], showing that the processes of electrochemical drug immobilization and release had no adverse effects on its biological activity.

Acknowledgments

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