SONOCHEMICAL SYNTHESIS OF DRUG MOLECULES NANOPARTICLES: TOWARDS CONTROLLED DRUG RELEASE

PAULINA CHYTROSZ*, MONIKA GOLDA-CEPA, ANDRZEJ KOTARBA

FACULTY OF CHEMISTRY, JAGIELLONIAN UNIVERSITY, POLAND
*E-MAIL: PAULINA.CHYTROSZ@STUDENT.UJ.EDU.PL

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Introduction

Nanotechnology is rapidly spreading across all fields of science such as electronic, aerospace and medicine. At the nanoscale, physical, chemical, and biological properties differ from the properties of individual atoms and molecules of bulk matter. Therefore, it provides a possibility to develop new, advanced materials which meet the demands of high-tech applications, e.g. in-site controlled drug delivery systems (DDS). Advanced studies of the strategies for drug anchoring and hence, controlled elution kinetics are vividly investigated. For controlled drug delivery systems, numerous approaches are used i.e. micelles, hydrogels, biodegradable polymeric matrix [1]. Sonochemical synthesis is found to be a new, effective method to produce DDS. This technique has been successfully utilized for the synthesis of inorganic nanoparticles [2], while for organic ones, only a few literature reports are available [3-5]. The study aimed to explore one-step sonochemical approach to produce fluorouracil and diclofenac sodium salt nanoparticles and their simultaneous embedding into oxygen plasma modified parylene C surface.

Materials and Methods

Parylene C films were obtained using CVD technique (ParaTech Coating Scandinavia AB). Polymer surfaces were modified using oxygen plasma (FEMTO system, Diener Electronics) to generate oxygen-containing functional groups and nanotopography.
The nanoparticles of fluorouracil and diclofenac sodium salt (Sigma-Aldrich) were formed and subsequently deposited during the one-step process at the surface of plasma-modified parylene C using an ultrasonic generator with the following parameters: frequency 20 kHz, amplitude 30%, and time 6 min. Solutions of drugs in deionized water were 2.5 mg/ml and 15 mg/ml for fluorouracil and diclofenac, respectively. The developed system was thoroughly characterized in terms of particle size (NTA, TEM), surface dispersion (IR-image) and drug release kinetics (UV-Vis).

Results and Discussion

Nanoparticles obtained via sonochemical synthesis were about 100 nm (diclofenac) and 50-100 nm (fluorouracil). In order to get more in-depth insight into the nanoparticles size, TEM observations were conducted. The obtained nanoparticles were amorphous with spherical shape (FIG. 1).
Test of the drugs' stability in ultrasounds was carried out using ATR – IR spectroscopy. There were no significant changes between the spectra of reference samples and those subjected to ultrasound.
The presence of the sonochemically obtained nanoparticles was confirmed using ART – IR technique. The collected spectra revealed characteristic bands at 1644 and 745 cm^{-1} for fluorouracil and diclofenac, respectively. An apparent increase in the absorbance was observed for drug–containing samples when compared to the parent samples of oxygen plasma modified parylene C, indicating the presence and fairly uniform distribution of the NPs. For the average sample (2 cm^2) drug load was estimated to be ~4 μg and 70 μg for fluorouracil and diclofenac, respectively.
The elution studies revealed the strong burst effect of the fluorouracil/parylene C system, where the drug was completely eluted in 30 min. In contrast, the diclofenac/parylene C system provided prolonged drug elution time, reaching seven days.

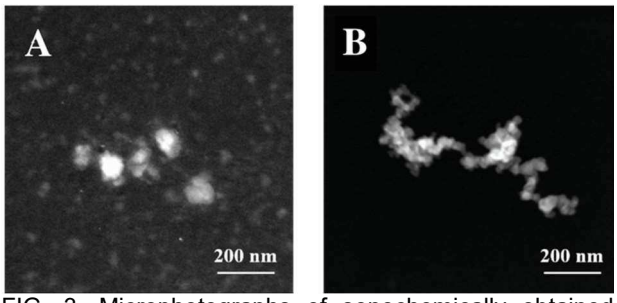

FIG. 3. Microphotographs of sonochemically obtained diclofenac (A) and fluorouracil (B) nanoparticles.

Conclusions

In this study, it was proved that sonochemical production of therapeutic coatings is an alternative, more effective method of producing hybrid systems for controlled in-site drug release. The most important advantages of the sonochemical synthesis are preparation time, increased drug availability for the targeted tissue, lack of chemical waste and toxic solvents.
The presented method is simple, efficient, environmentally friendly and non-destructive in relation to the parylene C surface and drug molecules. The applied sonochemical strategy can be successfully implemented for other drug–polymer coating couples. The sonochemical method is a promising technique in the context of designing novel implantable materials with the controlled drug release function.

References

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