SONOCHEMICAL FORMATION OF BIOACTIVE NANOPARTICLES AND THEIR EMBEDMENT IN POLYURETHANE SURFACES

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Introduction

Nanotechnology represents a dynamically developing section of the research and techno-economic sector with various application areas. Nanometric materials (especially nanoparticles) often exhibit properties dissimilar to their bulk equivalents because of the increase in the surface area, unsaturated sites, quantum effects, etc. As a result, fundamental studies for the generation, processing, characterization, and modelling of nanoparticles are carried out extensively. Nanoparticles and nanostructured materials are considered as a potential for revolutionizing medicine and create new classes of drugs and medical devices. One of the promising and efficient techniques for the synthesis of both inorganic and organic nanoparticles is sonochemistry. This approach is particularly interesting in terms of using it for nanoparticles of bioactive substances fabrication. Moreover, 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) [1-3].
The detailed understanding of the mechanism of nanoparticles formation via the sonochemical method is challenging. To investigate the impact of ultrasounds on the first steps of nanoparticles formation we coupled the experimental approach with the Molecular Dynamics simulations (MD).

Materials and Methods

Polyurethane (aromatic polyether polyurethane, American Polyfilm, Inc.) films were modified using oxygen plasma (FEMTO system, Diener Electronics). Fluorouracil and carbenicillin nanoparticles were formed and deposited on the oxygen plasma modified and unmodified polyurethane surfaces using a homogenizer (Sonics Vibracell CV18). The size of the sonochemically formed NPs was determined using the LM10 Nanosight instrument (Malvern Instruments Ltd) equipped with a sCMOS camera (Hamamatsu Photonics, Hamamatsu, Japan) and a 450 nm blue laser. Data were processed with NTA software version 3.1 Build 3.1.45. The developed system was thoroughly characterized in terms of particle size (NTA, TEM) and surface (ATR-IR).
The atomistic MD simulations were carried out in an NVT ensemble using GROMACS 5.1.x software and the parameters for bioactive molecule were taken from the Amber03 and for water form TIP3P force field.

Results and Discussion

The developed system, as well as nanoparticles, were thoroughly characterized by spectroscopic and microscopic methods. The sonochemical synthesis parameters were optimized to obtain nanoparticles of desired size, with the use of NTA set up. The adjusted parameters of the ultrasound generator resulted in nanoparticles up to 100 nm for fluorouracil and carbenicillin. As this method includes the hydrodynamic diameter, to directly measure nanoparticles size, TEM observations were conducted. The obtained nanoparticles were amorphous with a spherical shape (FIG. 1).

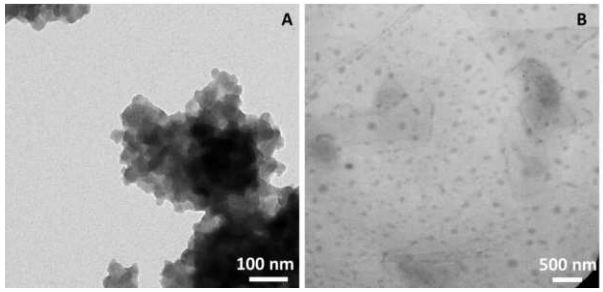

FIG. 1. TEM image of sonochemically created fluorouracil (A) and carbenicillin nanoparticles (B).

The impact of ultrasounds on the molecular structure of bioactive substances was also investigated with the use of ATR-IR spectroscopy. The therapeutic function of the polyurethane surfaces was obtained in one-step sonochemical process with the use of optimized parameters for fluorouracil and carbenicillin nanoparticles formation. The embedment of nanoparticles in polyurethane structure was then confirmed using IR spectroscopy. An apparent increase in the absorbance for a characteristic band (1640-1720 cm^{-1} and 1750-1800 cm^{-1}, for fluorouracil and carbenicillin, respectively) was observed for drug–containing samples when compared to the parent polyurethane, indicating the presence of the drug.
In parallel, MD simulations illustrated the relevant mechanistic step of nanoparticles formation. The aggregation of drug molecules at the bubble interface was observed and considered as an early stage of NPs nucleation.

Conclusions

In the study, the sonochemical method was applied for the production of therapeutic polyurethane material. This method was proposed as an alternative, more effective for preparing hybrid systems with the function of controlled in-site drug release. The principal benefits of the proposed method are: short preparation time, increased drug availability for the targeted tissue, lack of chemical waste and toxic solvents. For the investigated bioactive molecules no changes in chemical structure, activity and bioavailability upon sonochemical synthesis were observed. The obtained results open the door for the rational development of hybrid NPS/polymer implantable materials.

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