ONE-STEP FABRICATION OF GENTAMICIN NANOPARTICLES EMBEDDED IN POLYMERIC BIOMATERIALS SURFACE: SONOCHEMICAL APPROACH

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Introduction

The most common postoperative complications after implantation are inflammation and infection. A solution to the problem can be controlled drug delivery from the surface of the implanted device which can bring several advantages for patients. Currently, such strategy is one of the most rapidly advancing areas of the biointerface development, offering numerous advantages: in–site treatment, effectiveness, reduced toxicity, and improved patient convenience. The most important benefits are the application of smaller doses of the drug and its delivery directly to the target tissue. Controlled site–specific drug delivery offers an attractive alternative to the typical administration. What is more, such delivery allows the achievement of necessary therapeutic doses at the desired location, while maintaining low or negligible systemic level.

Among several methods, which can be used to fabricate antibacterial surfaces, sonochemistry has proved to be a very effective technique, particularly for polymeric surfaces. The principles are based on the ultrasonic irradiation of water–soluble antibiotic which leads to the formation of nanoparticles (NPs). When the irradiation is performed in the presence of a polymeric surface, the antibiotic NPs are subsequently embedded into the exposed surface in a one–step process. This strategy allows obtaining a composite NPs/polymer with prolonged antibiotic release from the surface.

The aim of this study was to generate gentamicin nanoparticles under ultrasound irradiation, subsequently embed them into oxygen plasma modified parylene C films in a one–step reaction, evaluate the drug surface distribution and resultant elution kinetics.

Materials and Methods

Experiments were performed with chemical vapor deposition (CVD) prepared Parylene C (8 μm of thickness) films, provided by ParaTech Coating Scandinavia AB. To modify the parylene C surface, oxygen plasma treatment was carried out using a Diener electronic Femto plasma system (Diener Electronic GmbH, Nagold, Germany). Gentamicin sulphate nanoparticles were formed and deposited on the oxygen plasma modified parylene C using homogenizer (Sonics Vibracell CV18) with the frequency of 20 kHz, amplitude 30%, and time 6 min. The size of the sonochemically formed GNPs was determined using 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.

FTIR imaging analyses of the polymeric films were performed in reflectance mode on a Spectrum Spotlight 400 FTIR microscope connected to a Spectrum 100 FTIR spectrometer (PerkinElmer, Inc.). The images were taken at a resolution of 8 cm^{-1} between 4000 and 700 cm^{-1} with 16 scans per pixel.

Drug release studies of the parylene C with sonochemically embedded GNPs were performed in phosphate buffered saline solution (PBS). The prepared samples were placed in 4 mL of PBS (Lonza) and transferred into an orbital shaker−incubator (Biosan, ES-20/60) set at 130 rpm and 37°C.

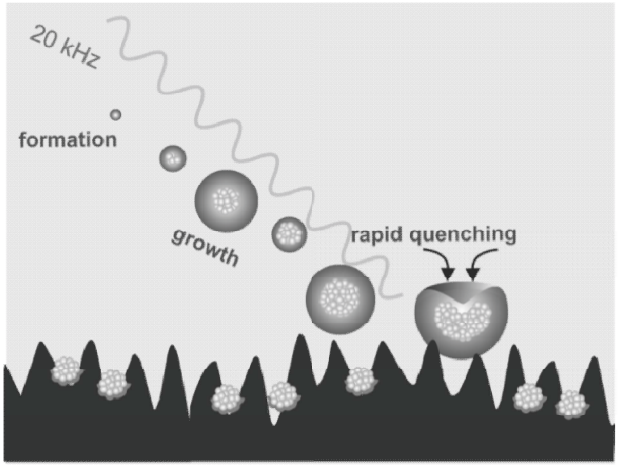

FIG. 1. Schematic representation of the sonochemical synthesis of genaminic nanoparticles and embedding to the nanopoares of parylene C surface.

Results and Discussion

It was found that using sonochemistry, gentamicin nanoparticles in the size range 35-70 nm can be obtained. The presence and homogenous distribution of the drug was confirmed using IR–image technique. The collected spectra revealed a characteristic band at 1037 cm^{-1} for gentamicin (group C–N, C–O). The corresponding absorbance maps (20 μm×20 μm) were collected at this characteristic selected wavelength.

Drug elution studies were performed to determine stability of the gentamicin NPs deposited on the parylene C. The average sample (2 cm^2) drug load was 3 μg. It was found that GNPs/parylene C system provided drug elution time up to 7 days. The obtained data were fitted into the first order kinetic and Korsmeyer–Peppas models. The experimental results were in good agreement only with Korsmeyer–Peppas (R^2 = 0.9796, n = 0.308, and k = 30.77) with the diffusion dominated mechanism. The drug elution is within the therapeutic window (MIC = 2 μg/ml), the GNPs/parylene C system can be successfully used as a coating with therapeutic function preventing contamination of the implant surface before surgery and actively lower the risk of post–operation infection.

Conclusions

It was concluded that sonochemical synthesis gives an effective alternative to biodegradable–based therapeutic layers providing prolonged elution of the active substance to the surrounding tissue which was proved for the GNPs/parylene C system as a representative example.

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