AN ANTIBIOTIC BIOSENSOR PLATFORM FOR PRECLINICAL EVALUATION OF DRUG RELEASE PROFILE OF NANOCAPSULES

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ABSTRACT
This paper presents an antibiotic biosensor platform for preclinical evaluation of drug release profile of nanocapsules. In this work, carbon nanotubes are used to modify the gold electrode surfaces to enhance the performance of the antibiotic biosensor platform. The results show that antibiotic nanocapsules significantly increase the drug release on the 4th day. And the release rate is 0.0258 µg/ml · hr. The drug release of antibiotic nanocapsules reached 24.98 µg/ml on the 7th day. The antibiotic biosensor platform for preclinical evaluation of drug release profile of nanocapsules presented in this work showed good performance in sensing of antibiotic Teoplanin drug samples.

KEYWORDS: Electrochemical Biosensor, Carbon Nanotube Electrode, Antibiotic Nanocapsule, Preclinical Evaluation

INTRODUCTION
Currently, there has been an increasing interest in the development of nanocapsules for drug delivery applications for localized treatments of diseases [1, 2]. It keeps away from traditional way of taking medicine which would be damaged before it is delivered to the affected tissues. It is to avoid the drug toxicity to damage the functional normal tissue and to increase therapeutic drug efficiency. In order to help the development of nanocapsules and understand drug release profile before the clinical experiments, it is important to set up an antibiotic biosensor platform which could monitor the real-time drug release profile of nanocapsules before planning the clinical experiment. In orthopedics, the osteomyelitis is one of the most troubled clinical diseases for the elders, which is infected by bacteria. Nowadays to apply partial antibiotic for localized treatment of the disease is one of the solutions [3]. However, it can only get partial of drug release information of nanocapsules. Nanocapsules have to refer to tissue consistency and long-term stable delivery. So, to use the biosensor platform in the clinics, the research design and accurately adjust the delivering speed and stability for nanocapsules. Fig. 1 shows a schematic drawing of the antibiotic biosensor platform for preclinical evaluation of drug release profile of nanocapsules. The antibiotic nanocapsules are injected into the biosensor platform to do real-time electrochemical detection of released Teoplanin concentrations.

PRINCIPLE AND DESIGN
Teoplanin is one of the most popular antibiotic drug for treatment of bacteria infection of bone tissues. Teoplanin binds with hydrophobic end of PLGA-PEG nanoparticles, and then would be packaged into nanocapsules, shown in Fig. 2(a). The characterization of drug release was done by HPLC, shown in Fig. 2(b). In order to evaluate drug release profile of antibiotic nanocapsules, an electrochemical biosensor platform using carbon nanotubes electrodes was designed. The antibiotic biosensor platform is composed of sensing electrodes and a plastic microfluidic chip. The antibiotic nanocapsules can be injected into the developed antibiotic biosensor platform for preclinical evaluation of drug release profiles of antibiotic nanocapsules.
Fig. 3 shows the fabrication process of the antibiotic biosensor and the photograph of fabricated device. The developed biosensor makes use of electrochemical sensing principles. The Au working electrode and counter electrode were fabricated by photolithography. The reference electrode was made by electroplating Ag/AgCl on the gold layer. The carbon nanotube solution with a concentration of 0.5 mg/ml was prepared by mixing carbon nanotubes in D.I. water. Then, drop-coating was applied to deposit carbon nanotubes on the Au electrode surfaces. Afterward a microfluidic chamber was integrated with the fabricated biosensor.

EXPERIMENTAL RESULTS
The detection of antibiotic samples was done by cyclic voltammetry scanning with a scanning rate of 0.05 V/s, which was controlled by a PC-based DAQ system, as shown in Fig. 4. The phosphate buffered saline (PBS) solution and drug sample were injected into the biosensor platform by a syringe pump. And the platform was heated over a hotplate at 37 °C. Fig. 5 shows that the comparison of the platform with/without electrode surface modification by carbon nanotubes. From the results, it’s found that the sensing signals are amplified up to 13.75 times for the biosensor platform using carbon nanotube-modified electrodes. In addition, the maximum affordable current has been improved from 0.0208 mA to 0.6680 mA by using the carbon nanotube electrodes. The linear range of the developed electrochemical biosensing platform using carbon nanotube electrodes is from 1 μg/ml to 10 μg/ml (R2=0.9837). The sensitivity of the developed system is 0.023 mA · ml/μg. The drug release profile of Teoplanin nanocapsules in PBS solution were measured using the developed antibiotic biosensor platform, shown in Fig. 6. According to the measurements using our developed electrochemical biosensing platform, it shows that antibiotic nanocapsules significantly increase the drug release on the 4th day. And the release rate is 0.0258 μg/ml · hr. The drug release of antibiotic nanocapsules reached 24.98 μg/ml on the 7th day.
CONCLUSIONS

The antibiotic biosensor platform for preclinical evaluation of drug release profile of nanocapsules presented in this work showed good performance in sensing of antibiotic Teoplanin drug samples. The antibiotic biosensor platform could be further integrated with a microfluidic platform for controlled synthesis of nanocapsules to feedback the drug release profile for optimization of the synthesis process.

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REFERENCES


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Figure 4. Experimental setup of the antibiotic biosensor platform.

Figure 5. Electrochemical measurement results of antibiotic drug samples with different concentrations.

Figure 6. Drug release profile of antibiotic nanocapsule samples at 37 °C: (a) photograph of the antibiotic nanocapsules on the 4th day and (b) the measurement results by the developed antibiotic biosensor platform.