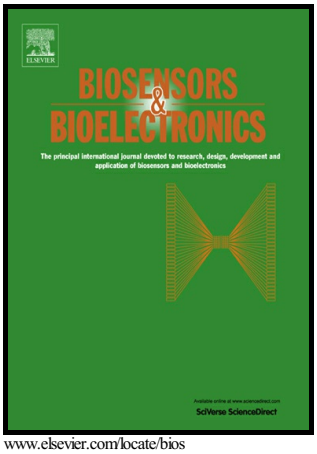

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Molecularly imprinted polymer based micromechanical cantilever sensor system for the selective determination of ciprofloxacin

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A B S T R A C T

The main objective of this study is to develop molecularly imprinted polymer (MIP) based micromechanical cantilever sensor system that has high specificity, fast response time and is easily applicable by user for the detection of ciprofloxacin (CPX) molecule in water resources. Highly specific CPX imprinted nanoparticles were synthesized by miniemulsion polymerization technique. The average size of the synthesized nanoparticles was measured about 160 nm with high monodispersivity. Covalent and monolayer binding of the MIP nanoparticles on cantilevers was provided by EDC/NHS activation. Validation of the developed cantilever nanosensor was performed in air with dip-and-dry technique by employing the dynamic sensing mode. According to the results obtained, micromechanical cantilever sensor system worked linearly for the concentration range of 1.5–150.9 μM. This concentration range resulted with 18.4-48.9 pg mass load on the MIP modified cantilever. The sensitivity of the developed sensor was calculated as 2.6 Hz/pg. To control the specificity of MIPs, a different antibiotic enrofloxacin (ENF), with a similar physical and chemical structure with CPX, was used, which showed 7 folds low binding affinity. The developed highly specific microcantilever sensor has a response time of approximately 2 minutes and is reusable up to 4 times. The results indicate that the MIP based AFM nanosensor has high sensitivity for the CPX molecule. This combination of MIP nanoparticles with micromechanical sensors is one of the pioneer studies in the mass sensing applications. This fast, low cost and highly sensitive CPX specific MIP nanoparticle based nanosensor developed in this research have the potential to pave the way for further studies.

Keywords: Micromechanical biosensor; Microcantilever; Ciprofloxacin; MIP; Nanoparticle

1. Introduction

Recently, there has been a growing interest in the presence of Pharmaceutical Emerging Contaminants (PECs) in aquatic environment, since they treat drinking water and create serious adverse effect on human health and wildlife. There is a noticeable rising in antibiotic resistance in bacteria that obstructs the treatments of infections. Hence, a great number of hospital-acquired infections are caused by multidrug-resistant bacteria (Acar and Rostel, 2001) (Miranda and Zemelman, 2002). Several pharmaceuticals are now added to the latest contaminant candidate lists of the United State Environmental Protection Agency (US-EPA). Ciprofloxacin (CPX), as a class of antibiotic, is suggested as one of the priority drinking water contaminants at latest European Union Water Framework Directive (EU-WFD). Ciprofloxacin [1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolone carboxylic acid] (CPX) is a third generation fluoroquinolone that show a broad-spectrum of antibacterial activity. CPX is low cost antibiotic with a distinct curative effect (Li et al., 2008) (Wang et al., 2014). Due to this fact its prevalent use made it become one of the most commonly used antibiotics (Wang et al., 2014). Nevertheless, CPX residues were found to imperil people's health by affecting mammalian cell replication as well as adverse drug reactions (Wang et al., 2014) (Gao et al., 2014) (Qiao and Sun, 2010) (Torriero et al., 2006b). Like in the case of many antibiotics, CPX is also not completely metabolized in the body and therefore there is high possibility that it enters the environment through urine samples of patients and wastewater.

It is crucial to detect the presence of broad spectrum antibiotics with high efficiency. So far, number of methods have been applied for the detection of CPX including spectrophotometry (C. L. Cazedey et al., 2013), mass spectrophotometry (Caro et al., 2006), liquid chromatography (Urraca et al., 2014) (Desai et al., 2013), solid phase extraction (SPE) (Sun et al., 2014) (Yan et al., 2008), capillary electrophoresis (Barrón et al., 2001) (Zhou et al., 2008) and electrochemical techniques (Torriero et al., 2006a) (Torriero et al., 2006b)(Ionescu et al., 2007). The major drawback of these methods is that they all are time consuming, expensive, rather complicated and requires sophisticated automation and help of experienced users. Throughout the last decade new detection methods in the concept of biosensors have been developed. These new biosensors allow faster and more sensitive real-time measurements. Moreover, the usage of biological molecules, such as antibodies, with these sensors may increase the cost dramatically. Conversely, the Molecularly Imprinted Polymers (MIPs), which are synthetic materials designed to mimic recognition sites, are being studied quite a lot during the last decade for its