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Designing A Molecular Imprinted Polymer Based QCM Biosensor for Simple Synthetic Cannabinoid Testing in Urine

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Background/Introduction: Synthetic cannabinoids (SCs), molecules that mimic the effects of the active ingredient of marijuana, have gained popularity over the last decade. The analysis of synthetic cannabinoids in human matrices is of particular importance in the fields of forensic and clinical toxicology. Although there are countless different structures of synthetic cannabinoids available and these numbers are rising, the two most well-known are aminoalkylindole synthetic cannabinoids (*JWH-018 and JWH-073*). The diversity of these structures presents a challenge in detection of SCs. Although typically mass spectrophotometry is used for chemical identification of the compounds Quartz Crystal Microbalance (QCM) biosensors, a member of mass-sensitive chemical sensors, have been getting researchers' attention because of their properties such as high selectivity, low cost, portability, easy-to-use, stability and simplicity. In order to create sensitive QCM biosensor surface, although several methods can be applied, the most promising approach is molecular imprinting technique. The methodology mainly depends on the molecular recognition, is a type of polymerization which occurs around the interested molecules called as a template and creates specific cavities in the highly cross-linked polymeric matrices.

Objective: The objective of the present study was to engineer a robust, stable, fieldable and selective molecularly imprinted QCM biosensors for the detection of common use SCs *JWH-018*, *JWH-073* and their major metabolites *JWH-018 pentanoic acid, JWH-073 butanoic acid* respectively in artificial urine in real time.

Methods: *JWH-018*, *JWH-073* and their major metabolites *JWH-018 pentanoic acid, JWH-073 butanoic acid* imprinted nanoparticles (NPs) were prepared and attached to the surface of QCM chip and prepared as a biosensor. Prepared molecularly imprinted (MIP) NPs were characterized by Fourier transform infrared spectroscopy (FTIR), scanning electron microcope (SEM), Zeta-size, and transmission electron microscope (TEM). The synthetic cannabinoids imprinted and non-imprinted. QCM chips were characterized with ellipsometry, atomic force microscopy (AFM) and contact angle measurement. Specificity and selectivity of imprinted and non-imprinted QCM biosensor chips were determined and kinetics and isotherm parameters were calculated by applying association kinetics analysis. Reproducibility of the imprinted QCM biosensors was tested in the final step. Real-time and fast measurement, high sensitivity and specificity, no need of labeled reagents are the unique properties of QCM biosensors.

Results: The prepared MIP based QCM biosensors, characterized with the procedures mentioned in the "methods" section, were sensitive enough to yield signals from SCs *JWH-018*, *JWH-073* and their major metabolites *JWH-018 pentanoic acid* and *JWH-073 butanoic acid* in spiked artificial urine in ppm and ppb levels (0.5 ppb-5 ppm). Further developments are in order to enhance the sensitivity of the biosensor to allow the detection of the above-mentioned compounds in the ppt range.

Conclusion/Discussions: MIP-based QCM nanosensors possess the potential to become precise, reliable and economic approaches for the detection of synthetic drugs in biological samples, due to their novel and innovative technique of detection. They innovatively combine identification and detection capabilities in one portable system. Given the remarkable advantages of a MIP-based QCM sensory system for detection of illicit drugs over conventional detection methods, further studies to improve the practicality and in-field usability of such nanotechnology-based biosensors are well warranted.

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