Synthesis of a Novel MIP Thin Layer and Monodisperse MIP-Nanoparticles for Detection of Creatinine

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Abstract

Herein we report molecularly imprinted polymers (MIP) to design a novel biomimetic assay for the detection of creatinine, which is evaluation bioindicator of renal function and muscle damage. Creatinine MIPs both as thin films and nanoparticles (NPs) were synthesized by precipitation polymerization and characterized with quartz crystal microbalance (QCM) and dynamic light scattering (DLS). Selectivity was verified against creatine. The experimental results show the limit of detection nearly 41 ppm for MIP NPs and 121 ppm for MIP thin film. Selectivity factor recorded four-time higher amount for MIP NPs in comparison with MIP thin film.

Key words: QCM, molecularly imprinted polymer, creatinine, nanoparticles.

Introduction

Creatinine is the end product of creatine catabolism. The measurement of creatinine levels in human blood and urine is clinically essential, because it partially reflects renal, muscular and thyroid functions [1].

Molecularly imprinted polymers (MIPs) are artificially synthesized polymeric materials with specific molecular recognition abilities that have proven highly interesting biomimetic receptors. They are synthesized from monomer and cross-linker around a template molecule. Advantages of MIPs include selectivity, physicochemical, stability, ruggedness and sensitivity combined with comparably low cost [2]. Herein we report synthesis and application of creatinine MIP, both as thin film and nanoparticles for sensing purposes.

Preparing creatinine MIP

To synthesize creatinine MIP thin films, creatinine was dissolved in Tetrahydrofuran (THF); Methacrylic acid (MAA) and 2-vinylpyridine were employed as the monomers, Divinyl-benzene (DVB) as the cross-linker, and AIBN as the initiator. The non-imprinted (NIP) sample was prepared in the same manner without template. After thermal polymerization until reaching the gel-point, the oligomer was spin-coated onto the quartz electrode and hardened overnight. Imprinted polymer NPs are based on the same polymer recipe, as MIP thin films with the exception of switching the solvent from THF to acetonitrile, which leads to precipitation. Then resulting particles were rinsed with distilled water and acetonitrile six times and centrifuged. Collected particles were placed in the oven with 100°C for 24h to dry. NIP NPs were synthesized in the same way without template for using as a reference. For spin coating, MAA was added to stabilize the MIP NPs on the QCM electrodes.

Results and Discussion

Polymer recipes published by [3] Miura et al. were modified to prepare MIP thin films on QCM electrodes. For that purpose 2-vinylpyridine was selected as the co-monomer in addition to MAA to enhancing the efficiency of polymer chains to mimic creatinine shape with increased precision during the polymerization process.

In a first step, the polymer was optimized by varying the ratio between two monomers in six different volume steps. During screening by QCM measurements, a ratio of 1:1 turned out optimal. The results of sensor characteristic measurements for that material are shown in Figure 2a. It clearly reveals concentration dependent sensor signals of the system. Furthermore, the MIP reaches about five times the frequency shifts of the NIP thus clearly proving feasibility of imprinting.
Moreover, selectivity of the MIP layer was verified with creatine as shown in Figure 2b. Evidently, the MIP prefers its own template over the competing compound by almost half an order of magnitude.

Compared to MIP thin films, the corresponding NP layers revealed substantially higher signal in Figure 4a. Evidently, the particle layers give rise to more than three times higher signals on both MIP and NIP. Hence, overall sensitivity is also three times higher. Additionally MIP NPs presented more recognition selectivity of creatinine (Figure 4b) which may be very interesting to be used of MIP NPs matrix as a reliable sensing strategy for creatinine.

**Conclusion**

MIP offer appreciably binding affinity and high selectivity for creatinine on QCM. By switching to NP films this could further be improved by around a factor of three.

**References**

