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Microfabricated disposable nanosensor based on CdSe quantum dot/ionic liquid-mediated hollow fiber-pencil graphite electrode for simultaneous electrochemical quantification of uric acid and creatinine in human samples

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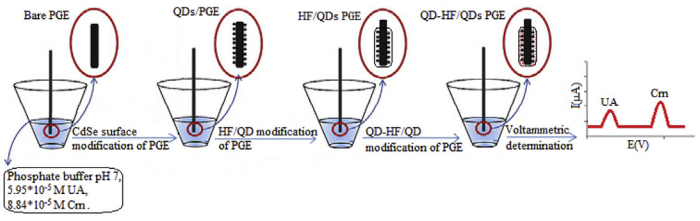
HIGHLIGHTS

- Sensor based on modified CdSe quantum dot/ionic liquid mediated hollow fiber graphite electrode.
- One-step simultaneous purification, pre-concentration, extraction, back-extraction and determination of electroactive analytes.
- Target analyte uric acid (UA) and creatinine (Crn) in urine and serum samples.
- Disposable nature of sensor reduced risk of carry-over.

GRAPHICAL ABSTRACT



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ABSTRACT

In this research, a novel sensitive electrochemical nanosensor based on the cadmium selenide quantum dots (QDs)/ionic liquid mediated hollow fiber-pencil graphite electrode (HF-PGE) was prepared and applied for simultaneous determination of uric acid (UA) and creatinine (Crn) in urine and serum samples. The electrocatalytic oxidation of the analytes was investigated via differential pulse (DPV) and cyclic voltammetry (CV). The experiments were designed, in two different steps, according to Taguchi's method; OA9 L9 (3^3) and OA9 L9 (3^4) orthogonal array to optimize experimental runs. The results revealed that the electrode response was initially influenced by the types of sensor and types of ionic liquids and their ratios. The amount of QD, buffer pH, equilibration time and scan rate also influenced electrode response efficiency. According to the results of Taguchi analysis, the amount of tetra phenyl phosphonium chloride (TPPC) and QD were the most influencing parameters on the yield response of the modified electrodes. Linear ranges were obtained between 0.297–2.970 $\times$ 10^3 and 0.442 –8.840 $\times$ 10^3 μM, with the detection limits of 0.083 and 0.229 μM and relative standard deviations (RSD) of 2.4% and 1.8%, for UA and Crn, respectively. Finally, the proposed method was successfully examined for simultaneous determination of UA and Crn in human urine and serum samples.

1. Introduction

Uric acid (UA) and creatinine (Crn) (Fig. 1) have been reported as crucial small biomolecules for physiological processes in human

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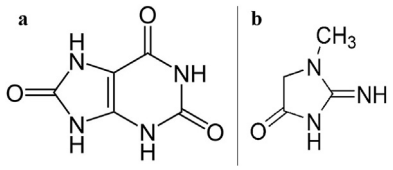

Fig. 1. Chemical structures of (a) uric acid and (b) creatinine.

metabolism. It is well known that UA and Crn usually coexist in biological matrices. Abnormal levels of these species may cause various diseases and disorders [1]. Abnormal concentration levels of uric acid in biological liquids are related to various diseases, such as gout, renal disease and hyperuricemia [2,3]. In addition, creatinine (Crn) is a fairly reliable indicator of kidney function and has been proved as a potential biomarker for kidney impairment. In fact, variation in creatinine level reveals different kidney conditions in a patient. Elevated Crn level signifies impaired kidney functions or kidney diseases [4,5].

Hence, the feasibility study of simultaneous determination of UA and Crn has been of great importance. Traditionally, UA is often quantified calorimetrically [6]. Generally accepted method of Crn determination is the Jaffe reaction including the use of picric acid [7]. However, these methods are tedious, time-consuming, include instable reactants and suffer from the severe interferences of organic compounds which exist in human biological fluids. Lots of different techniques have been developed to identify these biologically active compounds involving high performance liquid chromatography (HPLC) [8–10], capillary electrophoresis (CE) [11–13] and electrochemical methods [14,15]. Determinations via HPLC and CE methods are associated with the demand of sample preparation. Uses of expensive solvents and equipment, highly skilled specialists, etc. are some of the limitations of HPLC method. To solve these problems electrochemical methods were developed with a number of advantages: low cost of equipment, high sensitivity, low detection limit and fast response. In recent decades, voltammetry with chemically surface-modified electrodes have become reliable electrochemical methods extensively used for determination of biologically active compounds in pharmaceuticals and human samples [16]. However, the reported methods of simultaneous determination of UA and Crn using chemically modified electrodes are finite [17,18]. On the other hand, use of sample preparation techniques is of great importance for preconcentration and separation of trace biological species in aqueous systems prior to their analysis. Among the useful available techniques, solid phase microextraction (SPME) is one of the most practical methods [19–22]. But then, SPME fibers are expensive and should be handled very carefully because of their fragile coatings. To overcome these technical problems, Es'haghi and coworkers introduced hollow fiber solid-phase microextraction (HF-SPME) technique [23,24]. This approach has improved sample preparation techniques. Because it combined several stages of the procedures such as: sampling, pre-concentration, purification and integrates multiple sample pretreatment steps into a single step. It also has other benefits such as simplicity, selectivity, high enrichment, use of many kinds of nanosorbents and a variety of interesting coating materials. The HF-SPME technique is based on the establishment of equilibrium between the target analyte in the feed sample and nano-adsorbent stabilized in the fiber [25–27]. Thus, this study is intended to improve the SPME technique by inserting CdSe semiconductor QDs into the pores of polypropylene hollow fibers using an organic solvent as a solid/liquid sorbent. The idea was to have an activated nanoparticle-membrane based support as the analyte trap that eventuates in higher selectivity and enrichment, due to the role of QDs as semiconductor solid nanosorbents in SPME fibers. The attachment of the analyte can be achieved through two different chemical models; non-covalent and covalent linkage. QDs have been revealed a significant new class of materials because of their amazing physical and chemical properties such as electronic, magnetic, optical and catalytic effects for applications in the fields of bioindustry [28–35]. In the research, CdSe QDs were deposited directly on the pencil graphite electrode (PGE) in order to make a novel electrochemical sensor. Then, the electrode was placed inside a piece of hollow fiber and the HF-SPME device was coupled with an electrochemical system. So, in the new application, we decided to make an electrochemical sensor with the assistance of this extraction device. The role of the background solvent is really important in this sensor because the solvent would allow the analytes to interpenetrate into the membrane. Many solvents were tested and finally the mixture of three different ionic liquids was selected. Moreover, an electrical conductor interface was indispensable. The electrical contact was established via a graphite pencil that was put inside the fiber and then connected to a copper wire. The used device for this study was provided in the authors' lab. Although this fiber can be reused multiple times, disposable nature of the fiber eliminates the risk of carry over. Owing to the simple preparation process, high sensitivity, stability, small loading of QDs and low background current, using this combination can form new potentials and applications for creating robust sensors for the desired analytes and many other important species. According to the mentioned conditions, the present study aimed to couple this novel nano QD-assisted hollow fiber pencil graphite sensor with an electrochemical analyzer in a way that the fiber plays the role of a solid/liquid phase microextraction device and simultaneously, acts as the working electrode for simultaneous determination of UA and Crn. The effect of some important electrochemical parameters on the method efficiency and optimum experimental conditions for determination of the two analytes, was investigated via Taguchi experimental designs [36]. Also, the chemical structure of the synthesized QDs was characterized by TEM, XRD, EDAX and FT-IR techniques. To the best of our knowledge, until today there is no report on the fabrication of hollow fiber based CdSe QDs/PGE via electrochemical route. The superiority of this work compared with the similar reported works [37–40], would be coupling this advanced innovative nanoparticle assisted hollow fiber graphite sensor with an electrochemical system. So that the fiber would play the role of a solid/liquid microextraction device and simultaneously, serve as the working electrode or a pseudo electrochemical sensor for UA and Crn. Considering the advantages of electrochemical method, electrode surface modification and experimental design, the key purpose of the present study is to construct an electrochemical sensor with acceptable selectivity and high sensitivity for simultaneous detection of UA and Crn in biological real sample matrices.

2. Experimental

2.1. Chemicals

All the used analytical grade chemicals were purchased from Merck (Darmstadt, Germany) and used without further purification. Deionized double distilled water (ddH_2O) was used throughout all the experiments. The electrical conductivity of ultrapure water is 5.5×10^{-6} S/m (18 MΩ·cm in the reciprocal terms of electrical resistivity) [41]. Stock solutions of UA, Crn and buffer solutions were prepared in ddH_2O. The Accurel Q 3/2 polypropylene hollow fiber membranes used to make the electrodes were obtained from Membrana (Wuppertal, Germany). The wall thickness of the fiber was 200 μm, with the inner diameter of