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Characterization of a new ionophore-based ion-selective electrode for the potentiometric determination of creatinine in urine

Tomàs Guinovart [a], Daniel Hernández-Alonso [b], Louis Adriaenssens [b,c], Pascal Blondeau [a], F. Xavier Rius [a], Pablo Ballester [b,d], Francisco J. Andrade [a,*]

[a] Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili (URV), C/ Marcel·lí Domingo 1, 43007 Tarragona, Spain
[b] Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, Av. Països Catalans, 16, 43007 Tarragona, Spain
[c] School of Chemistry, University of Lincoln, Brayford Pool, Lincoln, LN6 7TS, UK
[d] Catalan Institution for Research and Advanced Studies (ICREA) Pg. Lluís Companys 23, 08010 Barcelona, Spain

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ABSTRACT

The optimization, analytical characterization and validation of a novel ion-selective electrode for the highly sensitive and selective determination of creatinine in urine is presented. A newly synthesized calix[4]pyrrole-based molecule is used as an ionophore for the enhanced recognition of creatininium cations. The calculation of the complex formation constants in the polymeric membrane with creatininium, potassium and sodium confirms the strong selective interactions between the ionophore and the target. The optimization of the potentiometric sensor presented here yields an outstanding analytical performance, with a linear range that spans from 1 μM to 10 mM and limit of detection of $10^{-6.2}$ M. The calculation of the selectivity coefficients against most commonly found interferences also show significant improvements when compared to other sensors already reported. The performance of this novel sensor is tested by measuring creatinine in real urine samples (N=50) and comparing the values against the standard colorimetric approach (Jaffé's reaction). The results show that this sensor allows the fast and accurate determination of creatinine in real samples with minimal sample manipulation.

1. Introduction

Creatinine is a normal metabolic byproduct generated by the body during energy production (Burtis et al., 2012). Since its accumulation is toxic for the cells, a fine-tuned mechanism of excretion to avoid harmful levels of this substance is essential to sustain life. For this reason, creatinine is transported by bloodstream mostly to the kidneys, where it is filtered out and excreted via urination. Therefore, monitoring the levels of creatinine in both blood and urine is of outmost importance. As a key indicator of the kidney function (Israni and Kasiske, 2012), the levels of creatinine are an essential parameter to diagnose and monitor both chronic and acute kidney diseases such as infections, chronic failures, drug effects, etc. It is widely known that the concentration of creatinine in blood beyond certain threshold is a life threatening condition (Davila and Gardner, 1987). In chronic kidney disease (a condition that affects almost 10% of the world population (Eknoyan et al., 2013)) the evolution of the patient is monitored through the blood levels of creatinine. Urinary levels (in particular 24 h urinary excretion) are also important to evaluate the creatinine clearance. Last but not least, from an analytical standpoint the concentration of creatinine in urine is used as a normalization factor to minimize variability due to volume dilution (Viau et al., 2004; Wagner et al., 2010). For all these reasons, the determination of creatinine is among the most common routines of the clinical laboratory.

It may then come as something of a surprise that, despite of this relevance, current methods used for the determination of creatinine show so many drawbacks (Jacobs et al., 1991) that have raised serious concerns among the medical community (Delanghe et al., 2008). Today, the most widely used approach to determine creatinine is based on its reaction with picric acid (Jaffé reaction (Pizzolante, 1989)), a method that has been reported more than a century ago. Alternative enzyme-based colorimetric approaches are also used. However, most of these colorimetric methods are subject to errors deriving from sample color and common interferences like acetone and glucose that can perturb the color formation (Jacobs et al., 1991).

Potentiometry is a very attractive option for the clinical lab, mostly due to its robustness and simplicity of operation and instrumentation. Nowadays, potentiometric methods using ion-selective electrodes (ISEs) are part of the routine toolkit for the determination of pH and ions in biological fluids (Bakker and

* Corresponding author.
E-mail address: franciscojavier.andrade@urv.cat (F.J. Andrade).

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