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Novel and selective potentiometric membrane sensor for amiloride determination in pharmaceutical compounds and urine

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ABSTRACT

A new PVC membrane sensor is described as a potentiometric sensor for amiloride. The sensor having amiloride–sodium tetraphenyl phthalate (ion-pair) as an electroactive material and dibutyl phthalate (DBP) as an anion excluder in PVC matrix in the percentage ratio of 4:66:30 (ion-pair: DBP:PVC) (w/w). The membrane sensor exhibits suitable response to amiloride in a concentration range of 1.0×10^{-2} to 1.0×10^{-6} mol L^{-1} with a limit of detection of 9.9×10^{-7} mol L^{-1}. The slope of the system was -54.3 ± 1.0 mV decade^{-1} over pH range of 2.0–7.0. Selectivity coefficients for amiloride relative to a numbers of potential interfering substances were investigated. The sensor was highly selective for amiloride over a large number of similar compounds. The sensor showing a fast response time of 6 s and was used over a period of 2 months with a good reproducibility. The sensor was successfully applied to determination of amiloride in pharmaceutical samples with satisfactory results.

1. Introduction

Amiloride hydrochloride, 3,5-diamino-*N*-(diaminomethylene)-6-chloropyrazine-carboxamide monohydrochloride (Fig. 1), is a potassium-conserving relatively weak natriuretic diuretic with anti-hypertensive activity [1]. It is a therapeutic drug and a pharmacological tool usually used in combination with thiazide diuretics or other kaliuretic–diuretic agents in congestive heart failure or hypertension [2]. Amiloride is used for its potassium-sparing effect in the treatment or prevention of hypokalemia induced by thiazide or other kaliuretics in patients with congestive heart failure or hypertension [1]. This natriuretic agent can be applied as a doping substance. In sports, diuretics are abused mainly for two reasons [3]. The first is to obtain a rapid diminution of corporal weight, which is important in sports that are divided into different weight categories. The second is to reduce the concentration of medical drugs in urine by diluting the latter by means of the rapid production of an elevated volume of urine, leading to a smaller possibility of detecting other doping substances. An advantage in the use of amiloride is that low doses lead to high-volume urine excretion, obstructing its determination and therefore highly sensitive methods are required.

Owing to the uncontrollable use of amiloride, the International Olympics Committee, since 1990 has included it in the list of forbidden substances [4]. Consequently there is a need for the development of selective and fast method for determining this doping substance. The therapeutic and doping dose of amiloride varies from 5 to 20 mg daily (one administration only). It is incompletely absorbed and it does not appear to be metabolized. The half-life in plasma varies from 6 to 10 h and about 50% of an oral dose is excreted in the unchanged form in urine [5]. Consequently, the determination of amiloride in urine demands highly selective methods. There have been only a few reports on the determination of amiloride in tablets [6–9] or in biological fluids [10,11]. Normally the determination of amiloride at therapeutic levels by liquid chromatography requires various tedious preliminary procedures, such as extraction and preconcentration in an organic solvent. This causes many disadvantages (such as low recoveries), since all these procedures are based on equilibrium reactions. Amiloride has been determined in pharmaceutical preparations and biological fluids using several methods including, spectrophotometry [2,12–14], fluorimetry [15–17], high performance liquid chromatography [18,19], differential pulse polarography [20,21], capillary isotachophoresis [22], and chemiluminescence oxidation [23]. Many of the above methods suffer from many interfering substances and/or suffer from time-consuming procedure.

Potentiometric detection based on ion-selective electrodes (ISEs), offers several advantages such as speed and ease of preparation and procedures, simple instrumentation, relatively fast response, wide dynamic range, reasonable selectivity, and low cost [24,25]. Based of our knowledge, there is not any report for the determination of amiloride based ISE. In this paper, we introduced a new potentiometric sensor for selective determination of amiloride in pharmaceutical compounds. The method is based on the ion-pair formation between amiloride and sodium tetraphenyl phthalate as

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