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RESEARCH PAPER

A New Screen-printed Ion Selective Electrode for Determination of Citalopram Hydrobromide in Pharmaceutical Formulation

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Abstract: Novel citalopram screen-printed ion selective electrodes were fabricated, characterized and used for the determination of citalopram in pharmaceutical formulations. The proposed sensors incorporated potassium tetrakis(*p*-chlorophenyl) borate (KTpClPB) ionophore (electrode V) and citalopram-phosphotungstate (CP-PT) ion pair complex (electrode X) as electroactive materials in screen-printed electrodes and tricresylphosphate (TCP) as solvent mediator. The fabricated electrodes demonstrated near Nernstain response over wide linear range of 4.9×10^{-7}–1.0×10^{-2} M and 1.0×10^{-6}–1.0×10^{-2} M citalopram with lower limit of detection of 4.9×10^{-7} M and 1.0×10^{-6} M and slope of (60.47 ± 0.80) mV decade^{-1} and (59.93 ± 1.45) mV decade^{-1} for electrode (V) and (X), respectively. The results showed that the proposed sensors had the characteristics such as fast and stable response, good reproducibility, long term stability (5 and 4 months) and applicability over a wide pH range of 2–9 and 2–8 for electrodes (V) and (X). The sensors displayed good selectivity for citalopram with respect to number of common foreign inorganic, organic species, excipients and the fillers added to the pharmaceutical preparation. The sensors were successfully applied for the determination of citalopram in tablet, urine and serum.

Key Words: Citalopram ion-selective electrode; Screen-printed electrode; Pharmaceutical preparation; Potentiometric determination

1 Introduction

Citalopram (Fig.1), 1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-5-phthalan carbonitrile, is an antidepressant drug used to treat depression associated with mood disorders. It is also used on occasion for the treatment of body dysmorphic disorder and anxiety. Citalopram belongs to a class of drugs known as selective serotonin reuptake inhibitors (SSRIs). It is primarily used to treat the symptoms of depression and can also be prescribed for social anxiety disorder, panic disorder, obsessive-compulsive disorder, the Huntington's disease, and premenstrual dysphoric disorder[1–4]. Citalopram affects neurotransmitters, the chemical transmitters within the brain. Neurotransmitters manufactured and released by nerves attached to adjacent nerves and alter their activities. Thus, neurotransmitters are considered the communication system of the brain. Many experts believe that an imbalance among neurotransmitters is the cause of depression. Citalopram works by preventing the uptake of serotonin by nerve cells after it has been released. Such uptake is an important mechanism for removing released neurotransmitters and terminating their actions on adjacent nerves. The reduced uptake caused by citalopram results in stimulation of the nerve cells by the free serotonin in the brain[5–7].

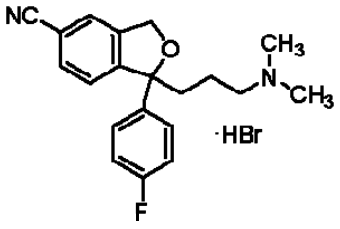

Fig.1 Chemical structure of citalopram hydrobromide (CPB)

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An ion-selective electrode (ISE) is capable of measuring selectivity and activity of a given ion regardless of other ions present in the solution[8]. It was used for determination of many drugs[9–12]. Compared with other analytical techniques, ISE has an impressive list of advantages such as being portable, suitable for either direct determination or using as a sensor in titrations besides, these membrane electrode don't affect the studied solutions[13–16].

In this work, the construction of plasticized screen-printed type citalopram ion selective electrodes and their application in pharmaceutical analysis were described. It was based on using ion-associate species, formed by drug cation and phosphotungstic acid (PTA) as counter ion or incorporating KTpClPB ionophore in the electrode matrix. The fabricated potentiometric sensors were applied for the determination of CPB in pure and in tablets, urine and serum.

2 Experimental

2.1 Apparatus and reagents

Laboratory potential measurements were performed using HANNA 211 pH meter. An Ag/AgCl double-junction reference electrode (Metrohm 6.0726.100) was used in conjugation with different ion selective electrodes. Digital burette was used for the field measurement of drugs under investigation.

Elemental analysis for carbon, hydrogen, nitrogen, and sulphur were carried out at the Microanalytical centers, Cairo University, using a Perkin-Elmer CHN 2400 Elemental Analyzer.

All chemicals used were of analytical reagent grade unless otherwise stated, and doubly distilled water was used. Citalopram hydrobromide (CPB) was purchased from Western pharmaceutical industries, Egypt. Depaway 40 (sample 1), cipram® 20 (sample 2) were purchased from Memphis, Egypt and multi pharma/lundbeek, Denmark. Sodium tetraphenylborate (NaTPB) and phosphotungstic acid (PTA) were commercially available from Sigma-Aldrich and Fluka, respectively. Tricresylphosphate (TCP) from Alfa Aesar was used for the preparation of the sensors. Other types of plasticizers, namely dioctylphthalate (DOP), dibutylphthalate (DBP) and dioctylsebacate (DOS) were purchased from Sigma, Merck and Merck, respectively. Relative high molecular weight polyvinyl-chloride (PVC) (Aldrich), potassium tetrakis (*p*-chlorophenyl) borate (KTpClPB) (Aldrich) and graphite powder (synthetic 1–2 μm, Aldrich) were used for the fabrication of different electrodes.

2.2 Procedures

2.2.1 Preparation of citalopram-modified screen-printed electrodes

Modified SPEs were printed in arrays of six couples consisting of the working and the reference electrodes (each 5 mm × 35 mm) following the procedures previously described[17–20]. A polyvinyl chloride flexible sheet (0.2 mm) was used as a substrate which was not affected by the curing temperature or the ink solvent and easily cutted by scissors. A pseudo Ag/AgCl electrode was firstly printed using a home-made polyvinyl chloride ink containing silver-silver chloride (65:35, *V/V*) which was cured at 60 ºC for 30 min. The working electrodes were prepared depending on the method of fabrication. The working electrode was printed using homemade carbon ink which was prepared by mixing 2.5–15 mg potassium tetrakis (*p*-chlorophenyl) borate (KTpClPB) ionophore or CP-PT ion pair, 450 mg TCP, 1.25 g of polyvinyl chloride (8%, *w/V*) and 0.75 g carbon powder. They were printed using homemade carbon ink and cured at 50 ºC for 30 min. A layer of an insulator was then placed onto the printed electrodes, leaving a defined rectangular shaped (5 mm × 5 mm) working area and a similar area (for the electrical contact) on the other side. Fabricated electrodes were stored at 4 ºC and used directly in the potentiometric measurements[17–21].

2.2.2 Sensor calibration

SPE sensors in conjunction with Ag/AgCl reference electrode was immersed in standard CPB solutions with concentration of 5.0×10^{-7}–1.0×10^{-2} M in a 50-mL beaker. The solutions were stirred and the potential was recorded after stabilization and plotted as a function of CPB concentration, and the graph was used for the subsequent determination of unknown concentration of CPB.

The potential readings were recorded after stabilization and the emf were plotted as a function of logarithm citalopram concentration. The lower detection limit was taken at the point of intersection of the extrapolated linear segments of the citalopram calibration curve.

2.2.3 Preparation of ion-pair compound

Ion-pair of citalopram-phosphotungstate (CP-PT): About 20 mL of 0.01 M CPB solution was mixed with 65 mL of 0.01 M phosphotungstate under stirring. The resulting precipitates were filtered off, washed with water, dried at 60 °C, washed with petroleum ether to remove any residual moisture, then ground to fine powder and kept dry in desiccator. Small sample portions were sent for elemental analysis.

2.3 Interference effects

The response of the electrodes was also examined in the presence of a number of organic and inorganic ions. The potentiometric selectivity coefficients $K^{pot}_{drug,\ j}$ were used to evaluate the degree of interference[17,22,23].