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Potentiometric determination of ketoprofen and piroxicam at a new PVC electrode based on ion associates of Rhodamine 6G

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ABSTRACT

The characteristics, performance and application of ion-selective electrodes for ketoprofen and piroxicam ions based on Rhodamine 6G as electrode-active substances are described. These electrodes respond with sensitivities of (58.0 ± 1.0) and (57.0 ± 2.0) mV/decade over the range 1.0×10^{-4}–1.0×10^{-1} and 1.0×10^{-4}–5.0×10^{-2} mol/l at pH 5–9 and 6–10 and a detection limit of 6.3×10^{-5} and 3.2×10^{-5} mol/l for ketoprofen and piroxicam, respectively. The electrodes are easily constructed at a relatively low cost, have a fast response time and can be used for a period of 5 months without any considerable divergence in potential. The proposed sensor displayed good selectivity for ketoprofen and piroxicam in the presence of several substances and inorganic anions. It was used for the direct assay of ketoprofen and piroxicam in commercial pharmaceutical preparations.

1. Introduction

A rapid increase in the development and production of sensors during the last three decades signifies a fundamental change in chemical analysis tools. The most numerous group of these chemical sensors is composed of potentiometric sensors that include ion-selective electrodes (ISEs) [1–3]. Active development of ionometry began with the studies of new chemical sensors and their promising use in pharmaceutical analysis [4]. Currently a wide assortment of commercially available ISEs is being enriched with new developments and improvements in the known types of sensors.

Interest in the development of ISEs for the determination of non-steroid anti-inflammatory drugs (NSAIDs), particularly ketoprofen (Ket) and piroxicam (Pir), derives from the manifest advantages of the potentiometric technique and by the role of various non-steroid anti-inflammatory drugs in modern pharmacy. They simultaneously anaesthetize the pain and stop the inflammatory process in the human organism; thus they are widely used in the treatment of rheumatoid arthritis and osteoarthrosis.

The structure and chemical properties of ketoprofen (2-(3-benzoylphenyl)propionic acid) and piroxicam (4-hydroxy-2-methyl-N-(2-pyridinyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide) (Fig. 1 (a,b)) are favourable for the formation of the compounds of the ion associate (IA) type with the basic dyes (BD), particularly with Rhodamine 6G. Such compounds, according to fragmentary data from the literature, can be efficient analytical forms for the potentiometric determination of some NSAIDs, namely diclofenac [5] and indomethacine [6]. These were the grounds for the assumption that ion associates of ketoprofen and piroxicam with a cation dye Rhodamine 6G (Fig. 1(c)) may be suitable electrode-active substances (EAS) for the development of new sensors for ketoprofen and piroxicam anions. One can see that the possibilities of the potentiometric analysis technique using ion associates of basic dyes as electrode-active substances lack practical implications. The literature reports only episodic data on the use of BDs as analytical forms for the spectrophotometric determination of certain NSAIDs [7–9].

Several types of analytical procedures have been proposed for the analysis of ketoprofen in pharmaceutical formulations. These procedures include chromatography [10–14], spectrophotometry [15,16] and use of partial least squares regression method [17–19]. The ion associate of methyltrioctylammonium-3-benzoyl-α-methylbenseneacetate is used as an EAS for the ISEs for ketoprofen determination [20].

The data on reported techniques for the determination of piroxicam in various objects from 1990–2008 were reviewed by Małgorzata Starek and Jan Krzek [21]. They are mainly based on chromatographic techniques, though voltamperometric and spectrophotometric methods were also encountered. Only a PVC sensor using tricaprylmethyl ammonium chloride and piroxicam [22] was reported in the literature for the potentiometric determination of the latter.

Therefore, the development of new potentiometric sensors using ion associates of basic dyes is of current interest. The simultaneous

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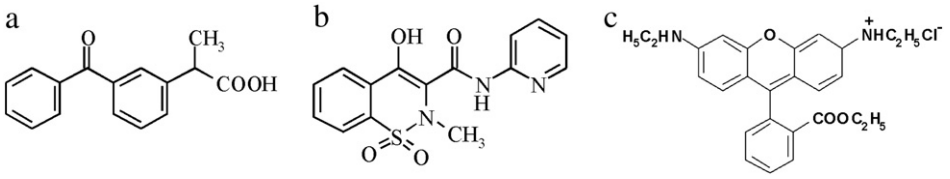

Fig. 1. Chemical structure of ketoprofen (a) and piroxicam (b), and Rhodamine 6G (c).

study of chemical–analytical characteristics of isolated solid ion associates, the effect of the EAS used, pH of the analyzed solution, properties of the membrane plasticizer, etc. are also of importance. The combination of those factors which define the electrochemical properties of ISEs and the determination and consideration of the relations between certain parameters would permit, in our opinion, the improvement of the electrochemical characteristics of electrodes and would predict the properties of other ISEs in their development for new classes of substances.

2. Experimental

2.1. Apparatus

All EMF measurements were carried out with the following cell assembly. An I-160 M model pH/mV meter with a Ag–AgCl saturated reference electrode was used for the measurements of potential difference at 25.0 ± 1.0 °C.

The homogeneity of the membranes was evaluated by the microstructure photographs obtained by a LEICA VMHT Auto microhardness tester.

2.2. Reagents and materials

All chemicals were of analytical-reagent grade. Distilled water was used to prepare all solution and in all experiments.

The modeling of the membrane composition of the ion-selective sensors utilised high molecular weight polyvinylchloride (PVC), dibutyl phtalate (DBP), dibutyl sebacate (DBS), dioctyl phtalate (DOP), dinonyl phtalate (DNP), tricresyl phosphate (TCP) and tetrahydrofurane (THF). All were obtained from Sigma-Aldrich.

The 0.04 mol/l buffer solutions of pH 3.0–11.0 were freshly prepared. Buffer solutions (pH 3.0–11.0) were prepared by mixing corresponding amounts of 0.04 mol/l H_3BO_3, 0.04 mol/l CH_3COOH, 0.04 mol/l H_3PO_4 and 0.2 mol/l NaOH. The ionic strength was adjusted with 0.1 mol/l NaCl.

The stock solution of ketoprofen of concentration 1×10^{-1} mol/l was prepared by neutralizing the appropriate weighed amount of 3-benzoyl-α-methylbenzeneacetic acid with aqueous sodium hydroxide solution to a glass electrode until a clear solution and pH = 8 were achieved. Working solutions (1×10^{-2}–1×10^{-7} mol/l) were prepared by diluting the stock solution with distilled water of pH = 8 (alkalized with NaOH).

The stock solution of piroxicam of concentration 5×10^{-2} mol/l was prepared by dissolving a weighed amount of 4-hydroxy-2-methyl-N-(2-pyridinyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide in 0.02 mol/l aqueous sodium hydroxide solution. Working standard solutions (1×10^{-3}–1×10^{-7} mol/l) were prepared by appropriate dilution of the stock solution with 0.02 M NaOH.

2.2.1. Gel

1 g of "Fastum gel" emulgel contains 0.025 g of ketoprofen and other simple excipients. 5 g of emulgel was dissolved in 0.02 mol/l NaOH; the excipients were then separated by filtration and the filter paper was washed three times and diluted in a 50 ml volumetric flask with water to the mark.

2.2.2. Injections

The contents of 10 ampoules were mixed. Accurately measured portions of the injection solution equivalent to 50 mg/2 ml of the ketoprofen were analyzed by the proposed electrode.

2.2.3. Tablets and capsules

The contents of 10 capsules or finely ground tablets were weighed and mixed. An accurately weighed portion of the tablet powder, or capsule powder equivalent to 10 and 20 mg of the piroxicam under investigation was weighed and dissolved in about 50 ml of 0.02 mol/l NaOH. The solution was filtered (if necessary) and the clear solution was diluted to 100 ml with 0.02 mol/l NaOH in a 100 ml calibrated flask.

2.3. Electrode-active material and construction of the electrode

The formation and precipitation of IA are equilibrium processes that depend on numerous factors such as the salt content of the solution, exposure time, temperature, etc. Ion associates of ketoprofen and piroxicam with Rhodamine 6G (Rh 6G) were prepared by mixing equal quantities of $1 \cdot 10^{-2}$ mol/l ketoprofen (piroxicam) and $1 \cdot 10^{-2}$ mol/l basic dye (Rhodamine 6G) solutions. The resulting solution was settled for 2 h and the sediment of ion associate was filtered out (quantitative rapid filter paper). This residue was treated with 50 ml of cold distilled water. The filter paper containing the precipitate was then dried for 24 h at room temperature. These ion associates of ketoprofen and piroxicam with Rhodamine 6G were used as an electrode-active material for preparing membranes of ion-selective electrodes for ketoprofen and piroxicam determination. Ion associates of ketoprofen and piroxicam with Rhodamine 6G suit the requirements for electrode-active materials, namely low solubility in water and good solubility in membrane plasticizers, along with ion-exchange properties.

Plasticized PVC membranes were prepared according to the recommendations of [23]. The generally accepted technique of plasticized membrane production by Moody, Oke, Thomas [24–26], consists of thorough mixing of the electrode-active substance with PVC dissolved in cyclohexane or tetrahydrofuran followed by the evaporation of the solvent in a glass ring. We weighed 0.1 g PVC and the respective amount of isolated IA (such that its concentration in the membrane was 5–25 mass%), then mixed the materials thoroughly for homogenizing. The degree of materials homogeneity was estimated from photomicrographs obtained with a LEICA VMHT Auto microhardness tester. Afterwards, 0.1 ml of a plasticizer (DBP, DBS, DOP, DNP, and TCP) and 0.5 ml of plasticizer solvent (cyclohexanone or tetrahydrofuran) were added. The resulting solution was transferred into a previously polished glass form 1.7 cm in diameter, glued to the glass substrate, and dried in air for 1–2 days.

The films obtained after evaporation of the solvent were cut using a rubber cork cutter into disks of 0.5–1.0 cm diameter. These were then glued to the end of the PVC tube with 10% PVC solution in cyclohexanone. The tube was filled with the concentrated standard solution of ketoprofen or piroxicam (10^{-2} mol/l), and a copper wire was immersed into it. The electrode was then used for the investigation.