

A Novel Potentiometric Sensor for the Determination of Nimesulide

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Abstract

A novel electrochemical sensor has been developed for the determination of nimesulide. The sensor is based on the NIM- molybdophosphoric acid (MPA) as the electroactive material in PVC matrix in presence of bis(2-ethyl hexyl) phthalate (BEP) as a plasticizer. The sensor showed a fast, stable, near Nernstian response for 1×10^{-2} – 1×10^{-6} M NIM over the pH range 5 – 8 with a slope 55.6 ± 0.5 m V/decade and the response time is < 45 s. Selectivity coefficient data for some common ions show negligible interferences. The sensor was successfully applied for the determination of NIM in tablet and the results obtained are in good agreement with those obtained by the official method.

Keywords: Nimesulide, PVC membrane sensors, molybdophosphoric acid, potentiometric determination, pharmaceutical analysis.

Introduction

Nimesulide (NIM), chemically, 4-nitro-2-phen-oxymethanesulfonamide, is a non-steroidal anti-inflammatory drug (NSAID), which acts as a cyclooxygenase-2 inhibitor but also has other novel pharmacological features, which account for its effect in the control of pain and inflammation.

There has been continuing increase in the number of PVC membrane sensors that have been prepared for a variety of substances. These sensors can be prepared by incorporating the ion exchanger within the plasticized membrane and used as very useful tool for clinical, chemical and environmental analysis. Ion selective electrodes have found useful applications [1-9] that are simple, economical, applicable over a wide range of concentration and offer sufficient selectivity to the drug in presence of pharmaceutical excipients.

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Several analytical methods have been reported for the quantitative determination of NIM. Among these, second order UV spectrophotometry [10], high performance liquid chromatography (HPLC) [11-13], spectrophotometry [14] and differential pulse polarography [15] are the most important ones. Most of these methods involve several time consuming manipulation steps and require sophisticated instruments. Hence it is worthwhile to develop a simple and sensitive method for the analysis of this drug.

In continuation to our work on drug analysis [16-18], an attempt has been made to develop an electrochemical sensor for the quantitative determination of NIM.

This paper describes the preparation, electrochemical evaluation and possible applications of a novel PVC sensor based on the use of nimesulide – molybdophosphoric acid ion pair complex (NIM-MPA) as the electroactive material and bis(2-ethyl hexyl) phthalate as the plasticizer. The sensor shows a sensitive response with good performance characteristics.

Experimental

Reagents and materials

Di-butyl sebacate (DBS), Bis(2-ethyl hexyl) phthalate (BEP), Bis(2-ethyl hexyl) adipate (BEA), Bis(2-ethyl hexyl) sebacate (BES), Di-n- butyl phthalate (DBP) and molybdophosphoric acid (MPA) were purchased from Lancaster and used as received. Tetrahydrofuran (THF) was obtained from s.d. fine chemicals. High molecular weight polyvinyl chloride powder (PVC), methanol and all the metal salts used (all from Merck) were of the highest purity available. Aqueous solutions of the metal salts were prepared by dissolving the appropriate salt or diluting standard solutions as specified in doubly distilled water. Aqueous solutions of the drug (10^{-2} – 10^{-6} M) were freshly prepared by accurate dilutions of a standard 10^{-1} M stock drug solution using the appropriate solvent. Pure-grade NIM was obtained as a gift sample. Pharmaceutical formulations containing NIM were obtained from local drug stores.

Apparatus

All potentiometric measurements were carried out at 25 ± 1 °C using a Systronics 335 digital ion meter. Saturated calomel electrode (SCE) was used as the external as well as the internal reference electrode. The electrochemical cell assembly may be represented as: saturated calomel electrode / internal filling solution (1×10^{-1} M NaCl solution + 1×10^{-3} M drug solution) / PVC membrane / test solution / KCl salt bridge // saturated calomel electrode.

Preparation of NIM - MPA ion association

NIM – MPA ion association was prepared by mixing an aliquot of 45 mL of 10^{-2} M nimesulide with 15 mL of 10^{-2} M MPA. The mixture was continuously stirred for 30 min. The dull white precipitate of the ion association so obtained was filtered, washed thoroughly, dried at room temperature for 24 h and stored in a desiccator.

Preparation of the membrane electrode

The electrode was constructed according to the Craggs' procedure [19]. Four different membrane compositions were studied by varying the percentages of ion association, PVC and the plasticizer. The ion association, plasticizer and PVC was mixed in 5-7 mL of THF and poured into a petri dish. The petri dish was covered with a filter paper and left to stand overnight to allow slow evaporation of the solvent. The membrane thus obtained was cut to small discs and glued to one end of a hollow Pyrex glass tube using Araldite. The membrane was conditioned by dipping it in a 1.0×10^{-3} M NIM solution for 2 days. The electrode was washed with distilled water before measurement.

Procedure

Standard solutions of 1×10^{-2} – 1×10^{-6} M were prepared by serial dilution of a 1×10^{-1} M NIM solution. The electrodes were placed into well-stirred 20 mL standard solutions in the order 1×10^{-6} – 1×10^{-2} M and stable potentials were recorded. The resulting calibration graph was used for subsequent determination of unknown NIM.

Application of the proposed sensor in pharmaceutical formulation

Ten NIM tablets (Nimulase and Nimegesic) were weighed accurately, crushed, mixed in a mortar and dissolved in methanol. The solution was filtered into a volumetric flask and was quantitatively diluted to a known volume. The presently developed sensor was directly immersed into 10 mL of sample solution six times and the potential was measured each time. The mean potential was used to evaluate the content of the drug in the tablet from the calibration graph (potential vs. log concentration).

Results and discussion

Performance characteristics of the sensor

Five different plasticizers viz. BEP, BES, DBS, BEA, DBP were employed to study their effect on the electrochemical behaviour of the membrane (Fig. 1). Generally, the use of plasticizers improve certain characteristics of the membranes, and in some cases, the slopes get affected adversely. Here, the slopes in the case of the BES, DBS and DBP are super-Nernstian and BEA is sub-Nernstian. It was found that BEP gave a near Nernstian slope (Table 1). The potentiometric response characteristics of the NIM sensor based on the use NIM – MPA ion pair as the electroactive material and BEP as a plasticizer in a PVC matrix were examined. Several different membrane compositions that contained 1%, 1.2%, 1.8% and 2% of ion-pair were investigated. The results revealed that the best composition of the membrane for ion association: PVC: plasticizer is 2: 40.8: 57.2 (Table 2). The sensor exhibited a slope of 55.6 mV/decade over the concentration range 1.0×10^{-6} – 1.0×10^{-2} M NIM (Fig. 2). The lower limit of detection was 3.2×10^{-7} M and the prepared membrane could be used for 4 weeks without any considerable divergence in the potential (Table 3). The average

response time is the time required for the sensor to reach a stable potential within ± 1 mV of the final equilibrium value. The response time for the NIM membrane sensor was found to be < 45 s.

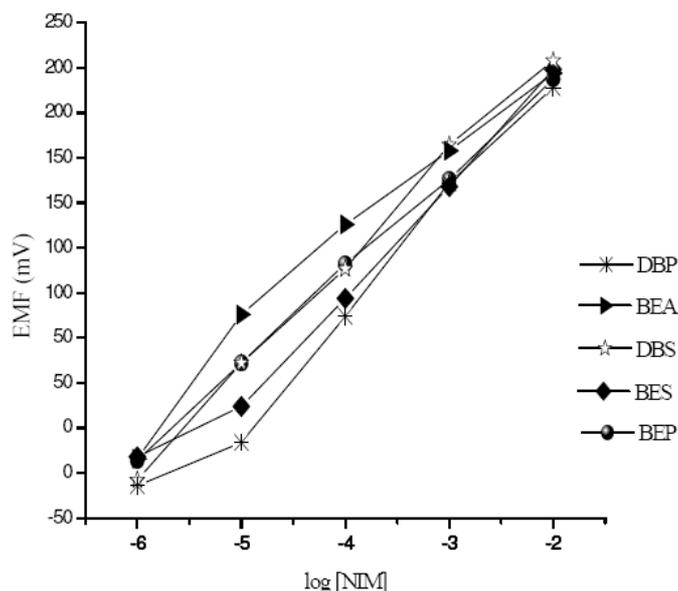


Figure 1. Effect of plasticisers on the performance of the sensors.

Table 1. Effect of plasticisers on the performance of the sensors.

Plasticizer used	Slope (mV/decade)
BEP	55.6
BES	64.8
DBS	66.5
BEA	45.9
DBP	70.7

Table 2. Effect of membrane composition of the sensor.

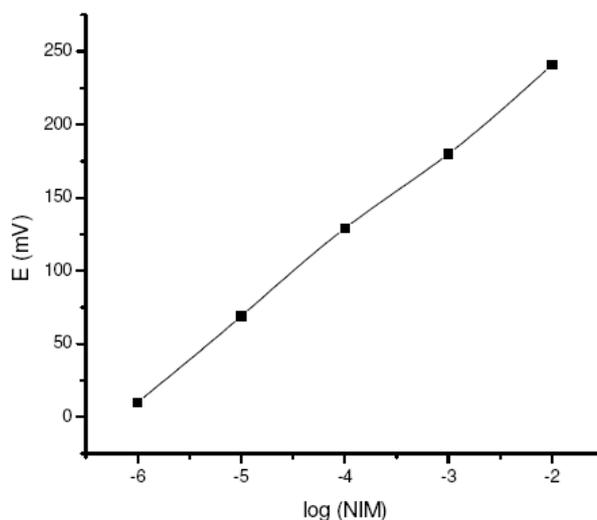
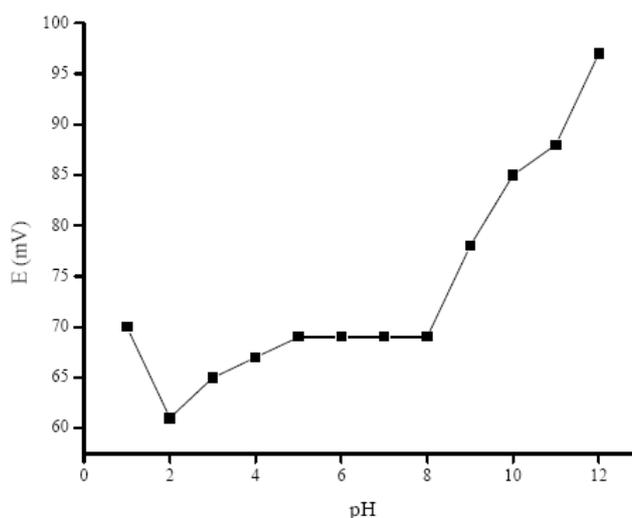
Membrane	Ion association	Composition % (w/w)		Slope mV/decade
		PVC	BEP	
I	1.0	49.5	49.5	37.2
II	1.2	46.0	52.8	62.5
III	1.8	63.5	34.7	73.6
IV	2.0	40.8	57.2	55.6

Effect of pH

The potential stabilities of the sensor over a wide pH range were examined using 1.0×10^{-4} M NIM. The pH was adjusted using different buffer solutions. The results revealed a stable potential over the pH range 5-8 (Fig. 3). Hence this was chosen as the working pH range.

Table 3. Response characteristics of NIM PVC matrix membrane sensor.

Parameter	Response
Slope (mV/decade)	55.6±0.5
Intercept	332.1±0.2
Concentration range (M)	$1.0 \times 10^{-6} - 1.0 \times 10^{-2}$
Detection limit (M)	3.2×10^{-7}
Response time (s)	<45
Life span (weeks)	4

**Figure 2.** Calibration graph for NIM- selective membrane sensor at 25 °C.**Figure 3.** Effect of pH of the test solution on the potential response of NIM membrane sensor.

Interference studies

The essential quality of a sensor is that it has to be selective to the particular ion over all the other ions. This is particularly important for the applicability of the

developed sensor. The selectivity of the developed NIM sensor was determined using the Fixed Interference Method (FIM) [20]. The selectivity coefficient values are shown in Table 4. None of the examined ions were found to interfere as shown by the small values of K^{pot} . The values indicate that the developed NIM - PVC membrane sensor is highly selective to NIM.

Table 4. Selectivity coefficient values of various interfering ions, K^{pot}

Interferent	K^{pot}
Na^+	5.0×10^{-2}
K^+	7.3×10^{-4}
NH_4^+	1.9×10^{-3}
Cl^-	6.7×10^{-3}
Ca^{2+}	8.9×10^{-3}
Pb^{2+}	4.6×10^{-3}
Co^{2+}	3.2×10^{-3}
Ni^{2+}	1.4×10^{-3}
Mg^{2+}	5.6×10^{-2}
NO_3^-	3.1×10^{-3}
Glycine	1.7×10^{-4}

3.4 Analytical Applications

The developed sensor was successfully applied for the determination of NIM in pharmaceutical formulations (Nimulase and Nimegesic). The results (Table 5) obtained were comparable with those of the standard method (potentiometric titration) [21]. The results reveal that the sensor can be used for the determination of the drug with high accuracy and precision.

Table 5. Determination of NIM in pharmaceutical formulations.

Sample	Declared amount (mg)	Found*					
		Proposed sensor			Official method		
		Recovery	SD	CV(%)	Recovery	SD	CV(%)
Nimulase	100	98.64	0.90	0.92	97.85	0.85	0.87
Nimegesic	100	98.71	0.91	0.92	98.16	0.87	0.89

* Average of six replicates.

Conclusion

The membrane sensor incorporating NIM – MPA ion pair as the electroactive material has been used for the preparation of the NIM sensor. The developed sensor is found to have good characteristics in terms of slope, concentration range, detection limit, response time, pH range and shelf life. It is also found to be highly selective over a number of ions. Further, the developed sensor can be used in the determination of NIM in pharmaceutical formulations.

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