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Characteristics of new composite- and classical potentiometric sensors for the determination of pioglitazone in some pharmaceutical formulations

Gamal A.E. Mostafa*, A. Al-Majed

Pharmaceutical Chemistry Department, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

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ABSTRACT

The construction and electrochemical response characteristics of poly(vinyl chloride) membrane sensors for pioglitazone HCl (PG) are described. The sensing membranes incorporate ion association complexes of pioglitazone cation and sodium tetraphenylborate (NaTPB) (sensor 1) or phosphomolybdic acid (PMA) (sensor 2) or phosphotungstic acid (PTA) (sensor 3) as electroactive materials. The sensors display a fast, stable and near-Nernstian response over a relative wide pioglitazone concentration range (1×10^{-2} to 10^{-6} M), with cationic slopes of 55.0 ± 0.5, 58.0 ± 0.5 and 53.0 ± 0.5 mV per concentration decade over a pH range of 1.0–5.0. The sensors show good discrimination of pioglitazone from several inorganic and organic compounds. The direct determination of 2.5–3900.0 μg/ml of pioglitazone show an average recovery of 98.5, 99.0 and 98.4% and a mean relative standard deviation of 1.6, 1.5 and 1.7% at 100.0 μg/ml for sensors 1, 2 and 3, respectively. The proposed sensors have been applied for direct determination of pioglitazone in some pharmaceutical preparations. The results obtained by determination of pioglitazone in tablets using the proposed sensors are comparable favorably with those obtained using the HPLC method. The sensors have been used as indicator electrodes for potentiometric titration of pioglitazone.

1. Introduction

Pioglitazone hydrochloride [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl) ethoxy] phenyl] methyl]-2,4-]thiazolidinedione hydrochloride (Fig. 1). Pioglitazone HCl is an oral antidiabetic agent that acts primarily by decreasing insulin resistance. Pharmacological studied indicate that PG improve sensitivity to insulin in muscle and adipose tissue and inhibits hepatic gluconeogenesis. Pioglitazone HCl improves glycaemic control while reducing circulating insulin levels. Fasting and postprandial glycaemic controls are improved in patients with type 2 diabetes mellitus. The decreased insulin resistance produced by PG results in lower blood glucose concentrations, lower plasma insulin levels and lower HBA_{1c} values [1,2].

Various method cited in literature for its determinations involve, high performance liquid chromatography (HPLC) [3–9], HPLC/MS [10], HPLC/MS/MS [11], capillary electrophoresis (CE) [8] and second derivative spectrometry [9]. However, most of these methods involve time-consuming procedures, derivatization and/or sophisticated instruments.

Recent years have seen an upsurge of interest in the application of sensors in the field of medicinal analysis [12–15]. This can be explained by the good analytical performances in terms of selectivity and accuracy, low detection limit, wide concentration range and relatively limited financial investment. For our knowledge till now no potentiometric membrane sensors for PG have been published. The proposed sensors are based on the use of PVC membrane sensor of pioglitazone–tetraphenylborate or pioglitazone–phosphomolybdate or pioglitazone–phosphotungstate as electroactive materials. The present work describes the construction and evaluation of novel PVC electrochemical sensors for the sensitive and selective determination of pioglitazone in its pharmaceutical preparations. The proposed methods are successfully applied for the determination of PG in some pharmaceutical formulation.

2. Experimental

2.1. Apparatus

All potentiometric measurements were made at 25 ± 1 °C unless otherwise stated using an Orion pH/mV meter (model 330) using pioglitazone membrane sensors in conjunction with an Orion double junction Ag/AgCl reference electrode (model 90-02) containing 10% (w/v) potassium nitrate in the outer compartment. Adjustment of pH was made with a combined Ross glass pH electrode (Orion 81-02) for all pH measurements.

* Corresponding author.
E-mail address: gamal_most@yahoo.com (G.A.E. Mostafa).

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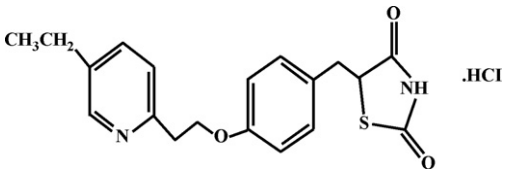

Fig. 1. Chemical structure of pioglitazone hydrochloride.

2.2. HPLC system

A Waters HPLC (Milford, MA, USA) system consisting of a binary solvent delivery pump (model 1525), an auto sampler (model 717), a dual wavelength absorbance detector (model 2487), and a computer having Empower software was used. A validation method for the determination of PG in pharmaceutical dosage form was used [8]. The analysis was performed using a reversed phase C18 (150 mm × 4 mm, 3 μm). The mobile phase consisted of a mixture of aqueous 10 mM potassium dihydrogen phosphate–acetonitrile (50:50, v/v) adjusted to a pH 6.0 with 0.1 M KOH at a flow rate of 1.0 ml/min. The UV detector was set at 225 nm. A calibration graph was constructed using standard PG solution. The data obtained with this method was utilized to compare the proposed potentiometric method using the developed sensors.

2.3. Reagents and materials

All chemicals used were of analytical reagent grade unless otherwise stated and doubly distilled water was used throughout. Polyvinyl chloride powder (PVC) high molecular weight, dibutyl sebacate (DBS), dioctyl phthalate (DOP), *o*-nitrophenyl octylether (NPOE), tetrahydrofurane (THF) of purity >99% were obtained from Aldrich Chemical Company and pioglitazone HCl was obtained from Tekeda Chemical Industrial Ltd., Oska, Japan. NaTPB, PMA and PTA were obtained from BDH. Actos tablets containing 15 and 30 mg of PG were obtained from local Pharmacy. The stock solution of 1×10^{-2} M pioglitazone–HCl was prepared by dissolving the appropriate amount of PG in 100 ml of aqueous acidic solution (0.5 M). The standard PG solution were prepared 1×10^{-3} to 1×10^{-6} by diluting the appreciate amount in double distilled water. Phosphate buffer solution of pH 3.0 was prepared by mixing appropriate amount of 0.1 M NaH_2PO_4 with 0.1 M H_3PO_4.

2.4. Preparation of the PG-PVC membrane sensors

Upon the addition of 25 ml of 1×10^{-2} M of pioglitazone HCl solution to equal amount of 1×10^{-2} M NaTPB or 75 ml of 1×10^{-2} M of PG to 25 ml each of phosphomolybdic or phosphotungstic acid, a whit or green or whitish precipitate of PG-TPB or PG-PM or PG-PT were formed, respectively. The precipitate was filtered off through a Whatman filter paper No. 42, washed with cold deionized water until no chloride ion was detected into the washing solution. The precipitate was dried under vacuum for 48 h, then grinded to a fine powder in mortar, forming ion-pairs complex. Elemental analysis confirmed the formation of 1:1 or 3:1 or 3:1 complexes of PG-TPB or PG-PM or PG-PT, respectively. 10 mg portions of the prepared ion associate complexes were thoroughly mixed with 190 mg PVC powder, 350 mg of DBS or DOP or NPOE and 5 ml THF in glass Petri dishes (5 cm diameter). After the constituents being well mixed, the solvent has been allowed to evaporate overnight while the sensing membranes have been formed. The PVC master membranes were sectioned with a cork borer (10 mm diameter) and glued to a polyethylene tube (3 cm length, 8 mm I.D.) using THF [16,17]. Laboratory made electrode bodies were used, which consisted of a glass tube, to which the polyethylene tube is attached at one end and filled with internal reference solution (equal volumes of 1×10^{-2} M aqueous solution of PG and KCl). Ag/AgCl internal reference electrode (1.0 mm diameters) was used. The indicator electrode was conditioned by soaking in a 1×10^{-2} M aqueous PG solution for 1 h and stored in the same solution when not in use.

2.5. Procedure

The pioglitazone PVC membrane sensors were calibrated by immersion in conjunction with the reference electrode in a 50 ml beaker containing 9.0 ml of phosphate buffer of pH 3.0. Then 1.0 ml aliquot of PG solution was added with continuous stirring, to give final PG concentration ranging from 1×10^{-2} to 1×10^{-6} M and the potential was recorded after stabilization to ±0.5 mV. A calibration graphs were then constructed by plotting the recorded potentials as a function of -log[PG]. The resulting graphs were used for subsequent determination of unknown pioglitazone concentration.

2.6. Determination of pioglitazone in the pharmaceutical dosage forms

Ten tablets of Actos (15 or 30 mg of pioglitazone) were accurately weighed and crushed and mixed in a mortar. An appropriate amount (30 mg of pioglitazone powder, from each) was weighed, transferred to a 100 ml beaker and dissolved in acidic water solution (0.5 M), sonication for about 15 min and completed to the mark with the same acidic solution. A 5.0 ml aliquot of this solution was transferred to 50 ml standard flask, the pH was adjusted to 3.0 using phosphate buffer and completed to the mark with water. The potential of the solution was measured using PG-sensors in conjunction with an Orion Ag/AgCl double junction reference electrode. The potential of the stirred solution was recorded after the signal stabilization (±1 mV/min) and the concentration was calculated from the previous calibration graph under identical experimental conditions from standard solutions of PG.

Alternatively, the potentials displayed by pioglitazone test solution before and after the addition of a 1.0 ml aliquot of 1×10^{-3} M pioglitazone were measured. The change in the potential readings was recorded and used to calculate the unknown pioglitazone concentration in the test solution using the standard addition technique [18].

Reconstituted powder: one mixture was prepared with a known amount of pioglitazone powdered and other components such as starch, lactose and magnesium stearate. The accuracy of the potentiometric determination of PG in this powdered was checked by evaluation the recovery.

3. Results and discussion

Sodium tetraphenylborate, phosphomolybdic acid, phosphotungstic acid were tested as ion-pairing agent for the preparation of an electroactive ion association complexes for PG. Sparingly soluble complexes of PG-TPB or PG-PM or PG-PT have been instantaneously formed upon the addition of PG solution to solutions of NaTPB or PMA or PTA, respectively. The dry powder of the formed ion-pairs is used for the construction of new pioglitazone ion selective electrodes. The elemental analysis showed that the composition of the complex is 1:1 or 3:1 or 3:1 for PG-TPB or PG-PM or PG-PT, respectively. Plastic membranes were prepared by using a casting solution of (1.82:34.45:63.64) ion-pair, PVC and DBS or DOP or NPOE as plasticizer, respectively.

Table 1
Response characteristics of pioglitazone-PVC matrix membrane sensors

Parameter	PG-TPB	PG-PM	PG-PT
Slope (mV/decade)	55.0 ± 0.5	58.0 ± 0.5	53.0 ± 0.5
Intercept (mV)	5.0 ± 0.5	34.0 ± 0.5	6.0 ± 0.5
Correlation coefficient, *r*	0.998	0.998	0.998
Lower limit of linear range (M)	6×10^{-6}	4×10^{-6}	6×10^{-6}
Lower detection limit (M)	4×10^{-6}	3×10^{-6}	5×10^{-6}
Response time for 1×10^{-3} M solution (s)	30 ± 0.5	25 ± 0.5	35 ± 0.5
Working pH range	1–5	1–5	1–5

3.1. Sensors characteristics

The potentiometric response characteristics of the pioglitazone sensors based on the use of PG-TPB or PG-PM or PG-PT as ion-pair complexes as an electroactive materials and DBS or DOP or NPOE as a plasticizer in a PVC matrixes were evaluated according to IUPAC recommendations [19]. Results in Table 1 show the characteristics performance of the PVC membrane sensors. The least squares equations obtained from the calibration data as follows:

$$E\,(\mathrm{mV}) = S\ \log[\mathrm{PG}] + \mathrm{Intercept} \quad (1)$$

where E is the potential of the electrode, S equal slope of the electrodes (55.0 ± 0.5, 58.0 ± 0.5 and 53.0 ± 0.5 mV for PG-TPB, PG-PM and PG-PT, respectively) and intercept (5.0 ± 0.5, 34.0 ± 0.5 and 6.0 ± 0.5 for PG-TPB, PG-PM and PG-PT, respectively).

3.2. Effect of plasticizer type on the characteristic performance of the sensors

Pioglitazone ion-selective membrane sensors with different electroactive materials were investigated in order to compare their performance. Three used reagents were investigated as possible counter ion for the preparation of the electroactive complex of PG, namely NaTPB, PMA and PTA. The obtained ion-pairs combined with three plasticizer, DOP, DBS and NPOE to give different combinations. It is well known that the construction of PVC based ISEs required the use of a plasticizer which acts as a fluidizer allowing homogenous dissolution and diffusion mobility of the ion-pair inside the membrane. PVC membrane sensor of PG-TPB with different plasticizer of different (DBS or DOP or NPOE) was found to be all suitable and optimum available mediators for PG-TPB membrane sensor. It plasticizes the membrane, dissolve the ion associate complex and adjusts both of the membrane permittivity and ion-exchanger sites mobility to give the highest possible selectivity and sensitivity. In this case all incoming study we use PG-TPB membrane sensor with the middle polarity (DOP).

Table 2
Potentiometric selectivity coefficients of some interfering ions, using PG sensors

Interferent, J	$K^{pot}_{A,B}$ PG-TPB	$K^{pot}_{A,B}$ PG-PM	$K^{pot}_{A,B}$ PG-PT
Na^+	1.9×10^{-3}	2.5×10^{-3}	1.5×10^{-3}
K^+	1.9×10^{-3}	2.0×10^{-3}	1.2×10^{-4}
Ca^{2+}	1.8×10^{-3}	2.6×10^{-3}	1.5×10^{-3}
Fe^{2+}	1.2×10^{-4}	1.0×10^{-4}	1.2×10^{-4}
PO_4^{3-}	1.2×10^{-4}	1.6×10^{-4}	1.4×10^{-4}
Magnesium stearate	1.8×10^{-3}	2.6×10^{-3}	1.8×10^{-3}
Acetate	1.9×10^{-3}	1.0×10^{-4}	1.2×10^{-4}
Citrate	1.1×10^{-3}	1.6×10^{-3}	1.0×10^{-4}
L-Tryptophan	2.0×10^{-4}	1.3×10^{-4}	1.0×10^{-4}
DL-Alanine	1.3×10^{-4}	1.5×10^{-4}	1.2×10^{-4}
Glycine	2.0×10^{-4}	2.0×10^{-4}	1.5×10^{-4}
Glucose	1.9×10^{-4}	2.9×10^{-3}	1.0×10^{-4}
Lactose monohydrate	1.5×10^{-4}	1.3×10^{-4}	1.5×10^{-4}
Starch	1.9×10^{-3}	2.7×10^{-3}	1.3×10^{-4}
Microcrystalline cellulose	1.8×10^{-3}	2.4×10^{-3}	1.2×10^{-4}

On anther hand, NPOE was found to be the optimum available mediator for PG-PM or PG-PT membrane sensors (ion-associates). The use of non-polar mediators such as DBS, DOP gave less response with little discrimination for concentration change (slope about 46 mV per concentration decade for both DBS and DOP, respectively). It seems that NPOE improves the membrane selectivity due to its high dialectical constant ($\varepsilon = 24$), affects considerable dissolution of ion-association within the membrane; consequently enhances its partition coefficient in the membrane and also provided suitable mechanical property of the membrane compared with less permittivity plasticizers DBS ($\varepsilon = 4$) or DOP ($\varepsilon = 7$) and the solubility of electroactive materials are relatively small compared with NPOE. NPOE was used in case of PG-PM or PG-PT for carrying out other experiments in this investigation.

3.3. Effect of pH and the response time

The electrode response for different pioglitazone concentrations was tested at different pH values, the pH being adjusted using hydrochloric acid or sodium hydroxide. The PG-PVC electrode dipped into PG solution of 1×10^{-3} and 1×10^{-4} M the potential of the electrode was plotted against the pH of solution. The potentials show that the slope per concentration decade is constant ~55.0 ± 0.5 or 58.0 ± 0.5 or 53.0 ± 0.5 mV for PG-TPB or PG-PM or PG-PT, respectively, in the pH range of 1–5. At higher pH values (>5.0), the potential decreased due to the gradual increase in the concentration of the unprotonated PG resulting in the precipitation of PG base. The effect of ionic strength at which the membrane sensors exhibit the best response was also studied. The potential values of the membrane sensor at different electrolyte concentrations (0.01–1 M NaCl) have been determined at pH 3.0. It was found that the electrodes followed a Nernstian response for NaCl concentration from 0.01–0.6 M NaCl.

The average response time is defined [19] as the time required for the electrode to reach a stable potential within ±1 mV of the final equilibrium value, after successive immersion of the electrode in different pioglitazone solutions each having a 10-fold difference in concentration or after rapid 10-fold increase in concentration by addition of PG. This time was found to be 25s for concentration of ≥1×10^{-3} M and ≤30 s for concentration 1×10^{-4} M. Day-to-day reproducibility of the sensor is about ±0.5 mV for the same solution and the useful lifetime of the sensor is 4 weeks, during which the potential slope is reproducible to within ±1 mV/decade. Also after more than one month a new section from the master membrane was found to function very properly.

3.4. Effect of diverse ions

The influences of different organic and inorganic ions on the response of PG sensors were investigated. The selectivity coefficients $K^{pot}_{A,B}$ were evaluated according to IUPAC guidelines using the separate solution method (SSM) and mixed solution method [19,20] in phosphate buffer solution of pH 3.0. The selectivity coefficient $K^{pot}_{A,B}$ measured by separate solution method was calculated from the following equation:

$$\log K^{pot}_{A,B} = \frac{E_B - E_A}{S} + \left[\frac{1 - Z_A}{Z_B}\right] \log a_A \quad (2)$$

where E_A and E_B are the potential reading observed after 1 min of exposing the sensor to the same concentration of PG and interfering species (1×10^{-3} each) alternatively. a_A the activity of PG and Z_A and Z_B are the charge of pioglitazone and interfering species and S is slope of calibration graph (mV/concentration). The selectivity coefficient by mixed solution method was defined as the activity

Table 3
Day to day reproducibility of the proposed membrane sensors

Parameter	Pioglitazone (100 μg/ml)[a], between-days			Pioglitazone (100 μg/ml)[a], within-days		
	PG-TPB	PG-PM	PG-PT	PG-TPB	PG-PM	PG-PT
R (%)	98.5	99.0	98.5	97.7	98.0	98.0
R.S.D. (%)	1.7	1.5	1.8	1.8	1.6	1.8
Slope	55.0 ± 1.7	58.0 ± 1.5	53.0 ± 1.8	54.5 ± 1.8	57.5 ± 1.6	52.5 ± 1.8
Correlation coefficient	0.998	0.999	0.998	0.997	0.998	0.997

R%, recovery percentage; R.S.D., relative standard deviation.
[a] Average of 5 measurements ± R.S.D.

ratio of primary and interfering ions that give the same potential change under identical conditions as given in Eq. (3).

$$K^{pot}_{A,B} = \frac{a'_A - a_A}{a_B} \quad (3)$$

where a'_A known activity of primary ion is added into a reference solution that contains a fixed activity (a_A) of primary ions, and the corresponding potential change (ΔE) is recorded. Next, a solution of an interfering ion (a_B) is added to the reference solution until the same potential change (ΔE) is recorded. The change in potential produced at the constant background of the primary ion must be the same in both cases. The results are given in Table 2. The results reveal reasonable selectivity for PG in presence of many related substances.

3.5. Validity of the proposed method

3.5.1. Limit of quantification and limit of detection

Each of different concentration of standard solution was tested five times. The potentials obtained for the five analyses were averaged at each concentration. The average potential was plotted versus concentration. The relation between potential and concentration is logarithmic (Eq. (1)) $X = S \log[PG] + Y$, where X is equal the potential, S is the slope, and Y is the intercept and r is the correlation coefficient. The sensors display a linear response over the concentration range of 1×10^{-2} to 5×10^{-6} or 1×10^{-2} to 4×10^{-6} or 1×10^{-2} to 5×10^{-6} M pioglitazone with a Nernstian cationic slope of 55 ± 0.5 or 58.0 ± 0.5 or 53.0 ± 0.5 mV/concentration decade (Fig. 2). The limits of detection (LOD) and limits of quantification (LOQ) were determined using the formula: LOD or LOQ = k S.D.a/b, where k = 3 for LOD and 10 for LOQ, S.D.a is the standard deviation of the intercept, and b is the slope. Also lower limit of detection (LOD) defined as the concentration of PG corresponding to the intersection of the extrapolated linear segment of the calibration graph which are 4×10^{-6} or 2×10^{-6} or 4×10^{-6} M for PG-TPB or PG-PM or PG-PT, respectively.

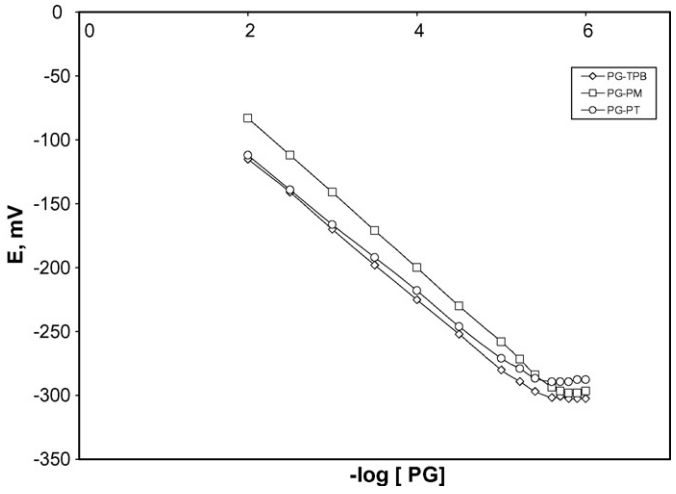

Fig. 2. Calibration graph of pioglitazone membrane sensors.

3.5.2. Precision and accuracy of the method

The precision and the accuracy of the method were investigated by inter-day (repeatability) by the analysis of PG, five replicate at the limit of qualification range. The precision and the accuracy of the method are expressed as R.S.D. and % of deviation of the measured concentration. Also reproducibility (day to day or intra-day) was investigated. The results obtained (Table 3) are within the acceptance range of less than 1.8% (precision) and 2.3 (accuracy).

3.5.3. Ruggedness

The ruggedness of the potentiometric method was evaluated by carrying out the analysis using two different analyst (operator) and different instruments on different days. The R.S.D. of less than 2.0% were observed for repetitive measurements in three different day time periods using two different instruments and operators. The results indicate that the method is capable of producing results with high precision.

3.5.4. Robustness

The robustness of the method is demonstrated by the versatility of the experimental factors that affecting the potential response. Preliminary inspection of the results under these various conditions suggested that the method is fairly robust, but the pH of the measuring solution should be in the range of pH range 1.0–5.0.

3.6. Determination of pioglitazone

The applicability of the PG membrane sensors for determination of the drug in the dosage forms was firstly cheeked by the studying the recovery of an accurate amount of pure PG in solutions.

The direct determinations of pioglitazone were carried out using the developed membrane sensors (PG-TPB or PG-PM or PG-PT). The analysis of 2.5–3900 μg/ml pioglitazone solutions (in five repli-

Table 4
Direct determinations of pioglitazone using PVC membrane sensors

Added (μg/ml)	Recovery (% ± R.S.D.)*		
	PG-TPB	PG-PM	PG-PT
2.5	97.5 ± 1.8	98.0 ± 1.7	97.5 ± 1.8
5.0	97.5 ± 1.8	98.0 ± 1.7	97.5 ± 1.8
10.0	98.1 ± 1.7	98.4 ± 1.7	98.0 ± 1.7
20.0	98.5 ± 1.7	98.5 ± 1.6	98.3 ± 1.7
50.0	98.5 ± 1.7	98.6 ± 1.6	98.4 ± 1.7
100.0	98.5 ± 1.6	99.0 ± 1.5	98.4 ± 1.7
200.0	99.0 ± 1.6	99.0 ± 1.5	99.0 ± 1.6
500.0	99.5 ± 1.5	99.5 ± 1.4	99.0 ± 1.5
1000.0	100.0 ± 1.5	100.0 ± 1.3	100.0 ± 1.5
3900.0	100.0 ± 1.4	100.0 ± 1.3	100.0 ± 1.4

* Average of 5 measurements ± R.S.D.

Table 5
Determination of pioglitazone in some pharmaceutical preparations using the proposed membrane sensors

Preparation	Pioglitazone (nominal value)	Proposed method[a], *R* (%) (R.S.D., %)			HPLC, *R* (%) (R.S.D., %)[a]
		PG-TPB	PG-PM	PG-PT	
Reconstituted powder	50 mg	99.5 (1.6)	99.3 (1.5)	99.0 (1.6)	99.4 (1.6)
Actos tablets 15 mg	15 mg/ml	98.5 (1.7)	99.0 (1.5)	98.3 (1.8)	98.5 (1.8)
Actos tablets 30 mg	30 mg	99.0 (1.6)	99.0 (1.5)	98.5 (1.6)	99.0 (1.6)

[a] Average of five determinations.

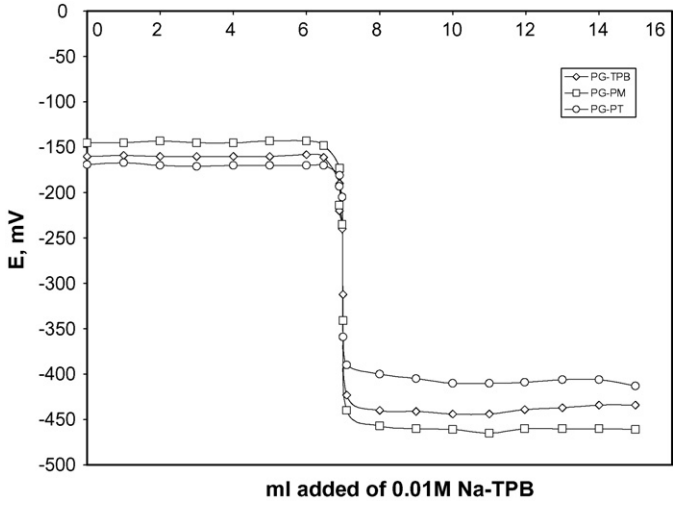

Fig. 3. Typical potentiometric titration curves of 7.0 ml of 1×10^{-2} M PG with 1×10^{-2} M sodium tetraphenylborate using pioglitazone membrane sensors.

cate) by direct potentiometry gave an average recovery of 98.6 ± 1.6, 99.0 ± 1.5 and 98.5 ± 1.7 for use sensor1, 2 and 3, respectively, at 100 μg/ml, results are shown in Table 4.

The applicability of the PG-membrane sensors to the determination of the drug in the dosage forms was firstly checked by studying the recovery of an accurate amount of pure pioglitazone in a reconstituted powder samples. The recovery obtained from five measurements was found to be 99.0, 99.0 and 98.5 with a relative standard deviation of 1.6, 1.5 and 1.6%, respectively, for PG-TPB, PG-PM and PG-PT sensors.

Results obtained for the analysis of PG in each formulations by direct measurements using the proposed sensors and the standard HPLC method [8] are given in Table 5. These data suggests the proposed method can be carried out on real products with equal confidence and accuracy. Moreover, comparison between the experimental means for the two method was carried out using the null hypothesis of $|t|_2$ for $P = 0.05$ and $n = 5$. It was found that $|t|_2 = 1.7$, 1.4 and 1.8 for PG-TPB, PG-PT and PG-PM, respectively, which is less than the tabulated value ($|t|_2 = 3.36$) [21], which indicated that the absence of systematic errors.

3.7. Application of PG-PVC electrodes as indicator electrode

The developed electrodes in conjunction with an Ag/AgCl reference electrode have been examined as an end point indicator electrode for potentiometric titrations of the drug. Titration PG with sodium tetraphenylborate using PG-TPB or PG-PM or PG-PT sensors has been performed (Fig. 3). From the results it is clear that PG reacts with NaTPB in the molar ratio of 1:1. The titration curves were symmetrical with a very well defined potential jump of about 250, 250 and 300 mV for PG-TPB, PG-PT and PG-PM, respectively, indicating the high sensitivity of the electrodes.

4. Conclusion

Experimental comparison of three ion-pair complexes of PG for use as electroactive material and different plasticizer in potentiometric membrane sensors revealed that in most cases, the PG membrane sensor displayed good analytical performance characteristics. The sensitivity, linear range and slope are independent over the pH range 1.0–5.0. The application of the proposed sensors to the determination of pioglitazone in its pure solutions and pharmaceutical preparations is characterized by a high degree of precision and accuracy compared to the validated HPLC method. The developed sensors are used as indicator electrodes for potentiometric titration of pioglitazone hydrochloride.

References

[1] R.F. Kletzien, L.A. Foellmi, P.K.W. Harris, B.M. Wyse, D. Clarke, Mol. Pharmacol. 42 (1992) 558–562.
[2] T. Sohda, K. Mizuno, Y. Momose, H. Ikeda, T. Fujita, K. Meguro, J. Med. Chem. 35 (1992) 2617–2626.
[3] P. Sripalakit, P. Neamhom, A. Saraphanchotiwitthaya, J. Chromatogr. B 843 (2006) 164–169.
[4] B.L. Kolte, B.B. Raut, A.A. Deo, M.A. Bagool, D.B. Shinde, J. Chromatogr. B 788 (2003) 37–44.
[5] K. Yamashita, H. Murakami, O. Teruaki, M. Motohashi, J. Chromatogr. B 677 (1996) 141–146.
[6] W.Z. Zhong, M.G. Williams, J. Pharm. Biomed. Anal. 14 (1996) 465–473.
[7] W.Z. Zhong, D.B. Lakings, J. Chromatogr. B 490 (1989) 377–385.
[8] T. Radhakrishna, D. Sreenivas Rao, G. Om Reddy, J. Pharm. Biomed. Anal. 29 (2002) 593–607.
[9] M.B. Shankar, V.D. Modi, D.A. Shah, K.K. Bhatt, R.S. Mehta, M. Geetha, B.J. Patel, J. AOAC Int. 88 (2005) 1167–1172.
[10] Y.-J. Xue, K.C. Turner, J.B. Meeker, J. Pursley, M. Arnold, S. Unger, J. Chromatogr. B 795 (2003) 215–226.
[11] Z. John Lin, W. Ji, D. Desai-Krieger, L. Shum, J. Pharm. Biomed. Anal. 33 (2003) 101–108.
[12] S. Riahi, M.F. Mousavi, S.Z. Bathaie, M. Shamsipur, Anal. Chim. Acta 58 (2005) 192–198.
[13] M. Shamsipur, F. Jalali, S. Ershad, J. Pharm. Biomed. Anal. 37 (2005) 943–947.
[14] J. Yuan, S. Yao, Talanta 58 (2002) 641–648.
[15] G.A.E. Mostafa, A.M. Homoda, Bull. Chem. Soc. Jpn. 81 (2008) 257–261.
[16] S.S.M. Hassan, S.A.M. Marzouk, Talanta 41 (1994) 891–899.
[17] A. Carggs, G.J. Moody, J.D.R. Tomas, J. Chem. Educ. 51 (1974) 541–544.
[18] T.S. Ma, S.S.M. Hassan, Organic Analysis Using Ion Selective Electrodes, vols. 1/2, Academic Press, London, 1982.
[19] IUPAC Analytical Chemistry Division, Pure Appl. Chem. 66 (1994) 2527–2536.
[20] IUPAC Analytical Chemistry Division, Pure Appl. Chem. 72 (2000) 1483–1492.
[21] J.C. Miller, J.N. Miller, Statistics for Analytical Chemistry, 1st ed., Ellis Harwood Limited, England, 1986, p. 43, 53, 59, 189, 192.