A Novel Membrane Sensor for Histamine H1-Receptor Antagonist "Fexofenadine"

M. N. ABBAS,*† A. A. ABDEL FATTAH,** and E. ZAHRAN*

*Microanal. Lab., Appl. Org. Chem. Dept., National Research Centre, Dokki, Cairo, Egypt

**Chem. Dept. Fac. Sci., Benha Branch, Zagazig University, Benha, Egypt

The construction and general performance of thirteen new polymeric membrane sensors for the determination of fexofenadine hydrochloride based on its ion exchange with reineckate, tetraphenylborate and tetraiodomercurate have been studied. The effects of membrane composition, type of plasticizer, pH value of sample solution and concentration of the analyte in the sensor internal solution have been thoroughly investigated. The novel sensor based on reineckate exchanger shows a stable, potentiometric response for fexofenadine in the concentration range of 1×10^{-2} – 2.5×10^{-6} M at 25°C that is independent of pH in the range of 2.0 – 4.5. The sensor possesses a Nernstian cationic slope of 62.3 ± 0.7 mV/concentration decade and a lower detection limit of 1.3×10^{-6} M with a fast response time of 20 – 40 s. Selectivity coefficients for a number of interfering ions and excipients relative to fexofenadine were investigated. There is negligible interference from almost all studied cations, anions, and pharmaceutical excipients, however, citrizine that has a structure homologous to that of fexofenadine was found to interfere. The determination of fexofenadine in aqueous solution shows an average recovery of 99.83% with a mean relative standard deviation (RSD) of 0.5%. Direct potentiometric determination of fexofenadine in tablets gave results that compare favorably with those obtained by standard spectrophotometric methods. Potentiometric titration of fexofenadine with phosphomolybdic acid as a titrant has been monitored with the proposed sensor as an end point indicator electrode.

(Received November 25, 2003; Accepted April 6, 2004)

Introduction

Antihistamines are H1-receptor antagonists widely used in human and veterinary medicine to provide symptomatic relief of allergic signs caused by histamine release, including pruritus and anaphylactic reactions. They are also commonly used as sedatives and antiemetics.¹ Antihistamines can be divided into first- and second-generation (also called non-sedating) agents. First-generation antihistamines are small lipophilic molecules, so they may cause adverse effects because of their cholinergic activity and their ability to cross the blood-brain barrier. Second-generation antihistamines are more lipophobic than first-generation antihistamines and are thought to lack central nervous system (CNS) and cholinergic effects when given at therapeutic doses.² Fexofenadine hydrochloride, the active ingredient of Allegra and Telfast, is a second-generation histamine H1-receptor antagonist with the chemical name (±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]- α,α -dimethylbenzeneacetic acid hydrochloride, and has the chemical structure shown in Fig. 1(a). It is the active metabolite of terfenadine, it does not cross the blood-brain barrier and appears to display some anti-inflammatory properties. The literature reports that no evidence of toxicosis was observed in dogs and cats receiving relatively high oral fexofenadine doses.³ For all mentioned properties, fexofenadine is widely and successfully used as anti-allergic agent in many parts of the world. The determination of fexofenadine has been

described using HPLC,⁴⁻⁶ spectrophotometry^{7,8} and fluorimetry.⁸ No electrochemical method has been yet reported in the literature for the determination of fexofenadine; therefore it is worth developing a simple potentiometric sensor for its fast determination. ISE's are known to offer an excellent low cost tool for the selective, sensitive and rapid determination of a vast variety of analytes in different fields of application,⁹⁻¹³ including pharmaceutical analysis.^{9,11,12} The present study aims to develop a potentiometric sensor for the selective, accurate and fast determination of fexofenadine in its pharmaceutical preparations.

Experimental

Reagent and materials

All chemicals used were of analytical reagent grade unless otherwise stated and doubly distilled water was used throughout. Fexofenadine was kindly supplied by Hockest, Marion, Roussel, Alexandria, Egypt and Telfast was kindly supplied by Avintes Pharma, Cairo, Egypt. A stock solution of 0.01 M was prepared by dissolving 0.53813 g of fexofenadine hydrochloride in 100 ml of phthalate buffer of pH 3.5. The working standards of 10^{-3} , 10^{-4} , and 10^{-5} M concentration were prepared by proper dilution of the stock solution. Phthalate buffer of pH 3.5 was prepared by adding 50 ml of 0.2 M potassium phthalate solution to 15.7 ml of 0.1 M HCl; the mixture was brought up to 200 ml with water. Dioctyl phthalate (DOP), dibutyl phthalate (DBP), dibutyl sebacate (DBS), *o*-nitrophenyl octyl ether (2-NPOE), and tetrahydrofuran (THF) were purchased from Aldrich, sodium tetraphenyl borate and

† To whom correspondence should be addressed.
E-mail: mnabbas@menanet.net

ammonium reineckate were purchased from Reidel de Haen. Polyvinyl chloride (PVC) (high molecular weight) fine powder was purchased from Fluka, Switzerland.

Apparatus

All potentiometric measurements were made at $25 \pm 1^\circ\text{C}$ unless otherwise stated using a Metrohm pH/ion meter (Model 692). A combined glass pH electrode (Metrohm 6.0202.100) was used for all pH measurements and a Metrohm double junction Ag/AgCl reference electrode (Model 6.0726.100) containing 3 M potassium chloride in outer and inner tubes was used.

Preparation of ion-pairs

The fexofenadine-reineckate ion-pair (Fexo-R) was prepared by mixing 100 ml of 10^{-2} M fexofenadine hydrochloride solution with 100 ml of 10^{-2} M ammonium reineckate. The formed precipitate was filtered off, thoroughly washed with distilled water and allowed to air dry. The fexofenadine-tetraphenylborate (Fexo-TPB) and fexofenadine-tetraiodomercurate (Fexo-TIM) ion-pairs were similarly prepared using proper concentrations.

Preparation of the membrane

PVC membranes containing 1.8%, 2.7%, and 3.7% concentrations (w/w) of Fexo-R, Fexo-TPB, and Fexo-TIM ion-pairs were prepared⁹ by dissolving 10 mg, 15 mg, and 20 mg respectively of the named ion-pairs in 350 μl of DOP as a plasticizer. The ion-pair solution was then well mixed with 190 mg of PVC in a 5-cm Petri dish. The mixture was then completely dissolved in 5 ml THF, and allowed to evaporate over night while the sensing membrane slowly formed. Three other electrodes of fexofenadine-reineckate ion-pair with 2.7% concentration were prepared using DBP, DBS, and NPOE plasticizers.

Construction of the electrode

A disc of 0.8 cm diameter was cut out from the master membrane by a cork borer, and stacked onto one end of a polyethylene tube using a solution of PVC in THF;^{14,15} then the tube was fitted onto a locally-made glass shaped electrode. The electrode was always filed with a mixture of equal volumes of 10^{-2} M fexofenadine hydrochloride and 10^{-2} M KCl solutions, except for sensor (G), where 10^{-3} M fexofenadine hydrochloride was used.

Calibration of the sensor

The sensor was calibrated by immersion in conjugation with the reference electrode in a 50 ml tall beaker containing 10 ml of fexofenadine solution of concentration ranging from 10^{-4} to 10^{-2} M in phthalate buffer of pH 3.5 with continuous stirring. The potential was recorded after stabilization to ± 0.2 mV. A calibration graph was then constructed by plotting the recorded potential versus $-\log[\text{fexofenadine}]$. The sensor was soaked in 10^{-2} M fexofenadine solution for 2 h before its first use and stored in the same solution.

Determination of fexofenadine hydrochloride in "Telfast" tablets

Ten tablets of Telfast, 60, 120 or 180 mg were pulverized and carefully homogenized. Then a weight that is equivalent to the average weight of one tablet was dissolved in water by shaking for 5 min with a mechanical shaker. Filtration, the filtrate was made up to 100 ml and 1 ml of that solution was delivered into a measuring beaker containing 9 ml of phthalate buffer solution of pH 3.5. The potential was then measured using the proposed

Fig. 1 The molecular structural formula of (a) fexofenadine hydrochloride, (b) fexofenadine-reineckate, (c) fexofenadine-tetraphenylborate and (d) fexofenadine-tetraiodomercurate.

electrode for three replicates. The concentration of fexofenadine was obtained by applying the following electrode equation:

$$E = 331.2 + 62.3 \times \log[\text{fexofenadine}]$$

Eosin spectrophotometric method for determination of fexofenadine

A 100- μl volume of the sample solution was transferred using a micropipette into a 10 ml volumetric flask, then 0.5 ml of (0.5 g w/v %) methylcellulose solution in water was added followed by 1.5 ml of eosin solution and 1 ml of Melivaine's citric acid phosphate buffer of pH 3.0. After standing for 10 min at room temperature the mixture was diluted to volume with water. The absorbance was measured at 541 nm.⁷

Results and Discussion

Fexofenadine hydrochloride is a white to off-white crystalline powder that is freely soluble in methanol and ethanol, slightly soluble in chloroform and water, and insoluble in hexane. It exists as a zwitterion in aqueous media at physiological pH, and was found to give insoluble precipitates with sodium reineckate, sodium tetraphenylborate and potassium tetraiodomercurate. The composition of the resulting ion-pairs show molar

Table 1 Percentage composition of the different membranes of fexofenadine sensors

Membrane	PVC, %	Ion-pair, %	Plasticizer, %
A	35.0	Fexo-R, 1.8	DOP, 63.0
B	34.6	Fexo-R, 2.7	DOP, 62.5
C	34.3	Fexo-R, 3.7	DOP, 62.0
D	34.6	Fexo-R, 2.7	DBP, 62.5
E	34.6	Fexo-R, 2.7	DBS, 62.5
F	34.6	Fexo-R, 2.7	2-NPOE, 62.5
G ^a	34.6	Fexo-R, 2.7	DOP, 62.5
H	35.0	Fexo-TPB, 1.8	DOP, 63.0
I	34.6	Fexo-TPB, 2.7	DOP, 62.5
J	34.3	Fexo-TPB, 3.7	DOP, 62.0
K	35.0	Fexo-TIM, 1.8	DOP, 63.0
L	34.6	Fexo-TIM, 2.7	DOP, 62.5
M	34.3	Fexo-TIM, 3.7	DOP, 62.0

a. Internal solution = 10^{-3} M.

Table 2 Characteristic performance of the different fexofenadine sensors

Membrane	Slope, mV/decade	Intercept/ mV	Linear range/ M	LDL/ M
A	50.6	241.2	$1 \times 10^{-4} - 1 \times 10^{-2}$	2.6×10^{-5}
B	58.1	264.3	$5 \times 10^{-6} - 1 \times 10^{-2}$	3.0×10^{-6}
C	43.2	178.8	$3 \times 10^{-4} - 1 \times 10^{-2}$	1.3×10^{-4}
D	45.5	205.1	$5 \times 10^{-5} - 1 \times 10^{-2}$	6.0×10^{-6}
E	53.9	255.0	$5.610^{-6} - 1 \times 10^{-2}$	2.8×10^{-6}
F	30.0	161.2	$1 \times 10^{-4} - 1 \times 10^{-2}$	8.1×10^{-5}
G	62.3	331.2	$2.5 \times 10^{-6} - 1 \times 10^{-2}$	1.3×10^{-6}
H	49.5	243.2	$5 \times 10^{-5} - 1 \times 10^{-2}$	1.4×10^{-5}
I	51.0	224.4	$1 \times 10^{-4} - 1 \times 10^{-2}$	6.8×10^{-5}
J	53.0	249.4	$1 \times 10^{-4} - 1 \times 10^{-2}$	1.0×10^{-5}
K	28.6	127.9	$5 \times 10^{-5} - 1 \times 10^{-2}$	4.1×10^{-5}
L	44.4	220.6	$1 \times 10^{-4} - 1 \times 10^{-2}$	1.2×10^{-5}
M	45.4	210.8	$1 \times 10^{-5} - 1 \times 10^{-2}$	3.6×10^{-5}

LDL: lower detection limit.

compositions of 1:1, 1:1, and 2:1 for Fexo-R, Fexo-TPB and Fexo-TIM, respectively, which was supported by elemental analysis; their structural forms are shown in Fig. 1.

Potentiometric performance of the fexofenadine sensor

Twelve plasticized PVC-based membrane ion-selective sensors incorporating Fexo-R, Fexo-TPB and Fexo-TIM ion-pairs as the electro-active material in three different concentrations and four different plasticizers were prepared and their performance characteristics were evaluated according to IUPAC recommendations.¹⁶ In addition, a thirteenth sensor that has a back-fill solution with 10^{-3} M fexofenadine has been also evaluated. Table 1 shows the percentage composition of the different fexofenadine electrodes prepared.

Influence of the membrane composition

The potentiometric sensitivity and selectivity for a given ion-pair is known to depend significantly on the membrane composition.¹⁷⁻²⁰ Therefore, study was performed to optimize the membrane composition using membranes containing 1.8%, 2.7% and 3.7% w/w concentration of each of the three prepared ion-pairs (Fexo-R, Fexo-TPB and Fexo-TIM). The study was performed at 10^{-6} M to 10^{-2} M fexofenadine in a phthalate buffer solution of pH 3.5. The potentiometric characteristic

Fig. 2 The effect of ion-pair concentration on the sensors response. (a) Fexo-R sensors (A, B, C), (b) Fexo-TPB sensors (H, I, J), (c) Fexo-TIM sensors (K, L, M).

performance of thirteen newly constructed fexofenadine-polymeric sensors is given in Table 2. The data in the table show that the performance of electrodes (H, I, J, K, L and M) has improved with increasing the percentage of ion-pair in the membrane. A membrane that contains 1.8% of the Fexo-R ion-pair (electrode A) showed a sub-Nernstian slope of 50.6 mV/decade with a linear concentration range of 1×10^{-4} M to 1×10^{-2} M and a lower detection limit LDL of 2.6×10^{-5} M of the fexofenadine. However, increasing the content of ion-pair in the membrane to 2.7% (electrode B) resulted in a Nernstian slope of 58.1 mV/decade with a linear concentration range of 5×10^{-6} M to 1×10^{-2} M and a LDL of 3×10^{-6} M of the fexofenadine. Further increase in the percentage of the ion pair to 3.7% (electrode C) resulted in a decrease of the slope to 43.2 mV/decade with a linear concentration range of 5×10^{-6} M to 1×10^{-2} M and a LDL of 1.3×10^{-4} M of the fexofenadine. The results are shown in Fig. 2. These data can be compared with those reported in the literature; the membrane sensitivity improved by increasing the ionophore in the membrane composition up to a critical value, above which the sensitivity starts to diminish. The reason for that inflection may be attributed to saturation of the membrane or its inhomogeneity.^{21,22}

Fig. 3 The effect of different plasticizer (62.5%) on sensor response: ●, sensor (B); ▲, sensor (D); ■, sensor (E); ◆, sensor (F).

Fig. 5 The effect of concentration of fexofenadine in the internal solution on sensors (B and G).

Fig. 4 The effect of pH on different fexofenadine sensors: (a) sensor B, (b) sensor I, and (c) sensor L.

Effect of plasticizer type on the sensor response

The plasticizer plays a vital role in the sensor performance, as it is responsible for the ion-pair solvation and distribution in the membrane, thus controlling the detection limit,^{23,24} affecting the selectivity and sensitivity^{25–27} and giving the plastic membrane the proper elasticity and strength. Also, there are many results indicating its responsibility on the mobility of the ion through the membrane.²⁸ Therefore, the effects of four different plasticizers (DOP, DBP, DBS and 2-NPOE) on the performance

of the fexofenadine membranes (B, D, E and F) have been investigated. The effect of different plasticizers is shown in Fig. 3, where it is clear that DOP resulted in the best sensor performance. As is clear from Table 2, sensor B with the membrane composed of 2.7% Fexo-R and plasticized with DOP showed a linear response over a concentration range from 5×10^{-6} to 1×10^{-2} M with a close Nernstian slope 58.1 mV/decade with a lower detection limit of 3×10^{-6} M.

Effect of pH on the response of fexofenadine sensor

The effect of pH on the fexofenadine sensors (B, I and L) containing the Fexo-R, Fexo-TPB and Fexo-TIM ion-pair respectively, was investigated by measuring the sensor response to 1×10^{-4} , 1×10^{-3} and 1×10^{-2} M fexofenadine solutions at pH 1 – 10, the pH being adjusted using HCl and/or NaOH. From Fig. 4, it is clear that the three sensors showed a stable response over the pH range of 2.0 – 4.5, above which the sensors response started to decrease. Above pH 10 the response became unstable. Therefore, a phthalate buffer of pH 3.5 has been used in all further measurements.

Effect of the concentration of the back-fill solution

It is anticipated that the linear range and limit of detection could be considerably improved by varying the composition of the reference solution, as described in the literature recently.^{29,30} The response of the membrane electrode in relation to the variation of internal solution was investigated using the optimum membrane composition (membrane B). Three different concentrations of the analyte in back-fill solution were investigated using equal volumes of 10^{-2} M potassium chloride with 10^{-2} M (sensor B), 10^{-3} M (sensor G) and 10^{-4} M fexofenadine solution. The sensor containing 10^{-2} M fexofenadine gave a linear response with a Nernstian slope of 58.1 mV/decade and a linear concentration range from 5×10^{-6} to 1×10^{-2} M and with a lower detection limit of 3×10^{-6} M. That with 10^{-3} M fexofenadine gave a linear response over the concentration range from 2.5×10^{-6} to 1×10^{-2} M with a super Nernstian slope of 62.3 mV/decade and has a lower detection limit 1.3×10^{-6} M. The results are shown in Fig. 5. This result favorably agrees with that recently reported.^{13,31} The sensor with 10^{-4} M fexofenadine internal solution showed unstable response.

Effect of diverse ions on the fexofenadine sensor

Potentiometric selectivity coefficients k_{ij}^{pot} of the ion selective electrodes are in common use as a quantitative expression of the ability of the electrode to respond primarily to the analyte ion in the presence of interfering ion that has the same charge sign.³² The effect of divers ions on the proposed fexofenadine electrode

Fig. 6 The dynamic response of the fexofenadine sensor G.

was evaluated according to the recommended IUPAC 1976 separate solution method (SSM)³³ in which the potential response of 10^{-2} M fexofenadine solution was measured in the first time. Then, the potential of 10^{-2} M of the divers ion was measured in the second time and the equation:

$$\log k_{IJ}^{\text{pot}} = \frac{E_j - E_i}{62.3} - \left(\frac{1}{z-1} \right) \log[\text{fexofenadine}]$$

was applied where: k_{IJ}^{pot} , the selectivity coefficient; E_i , the potential measured of 10^{-2} M fexofenadine solution; E_j , the potential measured of 10^{-2} M of the divers ion; S , the slope (62.3 mV) of the fexofenadine electrode; Z , the charge number of the divers ion.

Table 3 shows the selectivity coefficients of 27 different cations. Most of the studied ions possess negligible interference to fexofenadine. Cetirizine that has a chemical structure similar to that of fexofenadine was found to interfere as expected; however, it is not likely to be present with fexofenadine in any drug formulation since they are not prescribed to patients at the same time, so they can not be present in one sample. The selectivity coefficients for glycine, loratadine, cetirizine, caffeine, and potassium ions were also evaluated using the mixed solution method (MSM);³⁴ the potentiometric selectivity coefficient k_{IJ}^{pot} was calculated using the following equation:

$$k_{IJ}^{\text{pot}} = \frac{\exp[(E_1 - E_2)/62.3](a_i - a_j)}{a_j}$$

E_1 is the potential measured of the activity of the pure 10^{-3} M fexofenadine solution. E_2 is the potential measured in the mixture of 10^{-3} M fexofenadine and 5×10^{-2} M of the diverse ion. It is clear from the data shown in Table 4 that the selectivity coefficient for some monovalent ions determined using the MSM are comparable to those determined using SSM, while citriline still possesses the highest interference measured.

Response time

The average dynamic response time of the fexofenadine sensor as determined by immersion of the electrode in 10^{-5} , 10^{-4} , 10^{-3} , and 10^{-2} M solutions of fexofenadine and measuring the steady state potential within ± 0.5 mV was less than 30 s. 95% of the final response being reached within about 15 s (Fig. 6). In general, the response time is more rapid when proceeding from dilute to concentrated solutions. A 20-s response time was normal for solutions of fexofenadine concentration of more than 10^{-4} M.

Table 3 Selectivity coefficient of some cations with respect to fexofenadine measured using SSM

Ion	k_{IJ}^{pot}	Ion	k_{IJ}^{pot}	Ion	k_{IJ}^{pot}
DL-Methionine	6.07×10^{-4}	NH_4^+	6.8×10^{-4}	Mn^{2+}	7.3×10^{-3}
DL-Alanine	6.07×10^{-4}	K^+	7.35×10^{-4}	Sr^{2+}	6.5×10^{-3}
Tryptofane	6.8×10^{-4}	Na^+	6.3×10^{-4}	Ba^{2+}	7.07×10^{-3}
Glycine	7.6×10^{-4}	Cu^{2+}	7.3×10^{-3}	Hg^{2+}	6.3×10^{-3}
Caffeine	1×10^{-3}	Co^{2+}	6.8×10^{-3}	In^{3+}	1.72×10^{-2}
Atropine	2.8×10^{-3}	Cd^{2+}	6.3×10^{-3}	As^{3+}	1.47×10^{-2}
Loratadine	7.07×10^{-3}	Pb^{2+}	6.8×10^{-3}	Fe^{3+}	1.86×10^{-2}
Cetirizine	0.46	Ni^{2+}	7.07×10^{-3}	Cr^{3+}	1.47×10^{-2}
Ag^+	7.35×10^{-4}	Sn^{2+}	7.9×10^{-3}	Ce^{3+}	1.59×10^{-2}

Table 4 The selectivity coefficient of some cations measured using MSM

Ion	Caffeine	Glycine	Cetirizine	Loratadine	K^+
k_{IJ}^{pot} (MSM)	3.3×10^{-3}	2.03×10^{-4}	0.12	2.1×10^{-3}	3.4×10^{-4}
k_{IJ}^{pot} (SSM)	1.0×10^{-3}	7.6×10^{-4}	0.46	7.07×10^{-3}	7.35×10^{-4}

Table 5 Determination of fexofenadine in pure solution using the proposed sensor

Added/ mg ml ⁻¹	Found	
	Potentiometry R% $\pm$ S.D.%	Spectrophotometry R% $\pm$ S.D.%
1.6	99.97 $\pm$ 0.11, $F = 0.76$, $t = 0.6$	100.01 $\pm$ 0.13
0.16	99.78 $\pm$ 0.37, $F = 0.76$, $t = 0.88$	99.81 $\pm$ 0.32
0.016	99.75 $\pm$ 0.28, $F = 0.033$, $t = 0.32$	99.89 $\pm$ 0.08

Repeatability and reproducibility

No change in the response of the sensor was observed for up to 20 min. After 1 h the potential was changed only by about 3 mV for concentrations less than 10^{-4} M and by 5 mV for concentrations more than 10^{-4} M to 10^{-2} M. The membrane sensor is useable for at least 45 days without any important change in potential. The master membrane can be used after 3 months with the same response, when stored below 4°C.

Determination of fexofenadine hydrochloride in pure solution and in Telfast tablets

The determination of fexofenadine in its pure solution was carried out using the proposed sensor. The results were compared to those obtained using the Eison spectrophotometric method.⁷ Table 5 shows that the average recovery of fexofenadine from its pure solution is $99.83 \pm 0.76\%$. The determination of fexofenadine in its pharmaceutical formulations Telfast tablets and capsules gave an average recovery of $99.23 \pm 0.76\%$ as shown in Table 6. The data reveal that results compare favorably with those obtained by spectrophotometry, as predicted from the F and t values of F -test and Student's t -test compared to their theoretical values of $F = 6.39$ and $t = 2.31$.

Determination of fexofenadine by potentiometric titration

In addition, the developed electrode in conjunction with an Ag/AgCl reference electrode has been used as an end point indicator electrode for some potentiometric reactions. Titration of fexofenadine solution with a standard solution of phosphomolybdic acid as titrants, has been performed. From

Table 6 Determination of fexofenadine in its pharmaceutical preparations using the proposed sensor

Sample	Nominal value/mg	Found	
		Potentiometry R% $\pm$ S.D.%	Spectrophotometry R% $\pm$ S.D.%
Tablet 180	180	99.7 $\pm$ 0.5, $F = 0.74$, $t = 0.89$	99.8 $\pm$ 0.4
Tablet 120	120	99.7 $\pm$ 0.8, $F = 0.60$, $t = 0.35$	98.9 $\pm$ 1.4
Capsule 60	60	98.3 $\pm$ 1.0, $F = 0.76$, $t = 0.39$	98.9 $\pm$ 1.5

Fig. 7, it is clear that fexofenadine reacts with phosphomolybdic acid in the molar ratio 3:1. The titration curve was symmetrical with a very well defined potential jump of about 220 mV indicating the high sensitivity of the sensor.

Conclusion

The three ion pairs fexofenadine-tetraphenylborate, fexofenadine-reineckate and fexofenadine-tetraiodomercurate, were prepared and used to construct thirteen polymeric membrane sensors containing three different concentrations (1.8%, 2.7% and 3.7%) of each ion-pair in the membrane and plasticized with different plasticizers. It was found that the sensor containing 2.7% of fexofenadine-reineckate, plasticized with DOP, and containing a 10^{-3} M fexofenadine concentration in the internal solution has a stable super-Nernstian slope of 62.3 mV over the pH range of 2.0 – 4.5, with a fast response time of 25 s and a lower detection limit of 1.3×10^{-6} M of fexofenadine. The sensor was used for the determination of fexofenadine in its pure solution and in drug formulation Telfast with 99.83 ± 0.76 and $99.23 \pm 0.76\%$ recovery, respectively. The sensor was also used as an end point indicator for the potentiometric titration of fexofenadine.

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Fig. 7 Potentiometric titration of 10 ml of 10^{-2} M fexofenadine solution with 10 ml of 10^{-2} M phosphomolybdic acid using fexofenadine sensor G.