Spectrophotometric and Potentiometric Determination of Piroxicam and Tenoxicam in Pharmaceutical Preparations

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Two simple and accurate methods are described for the determination of piroxicam and tenoxicam in their pharmaceutical preparations. The spectrophotometric method involves the oxidation of these drugs with potassium iodate in acid medium with the liberation of iodine and subsequent extraction with cyclohexane followed by measuring the absorbance at λ=522 nm. Beer's law is obeyed in the concentrartion range of 0.05—1.1 and 0.05—0.6 mg ml^{-1} for piroxicam and tenoxicam, respectively. The apparent molar absorptivities of the resulting coloured products are found to be 2.7×10^3 and 2.5×10^3 l mol^{-1} cm^{-1}, whereas Sandell sensitivities are 0.012 and 0.013 g cm^{-2} for piroxicam and tenoxicam, respectively. The potentiometric method involves the direct titration of both drugs with *N*-bromosuccinimide in acid medium and the end point is determined potentiometrically using platinum indicator electrode. Piroxicam and tenoxicam can be determined quantitatively in the concentration range of 0.33—3.37 and 0.33—4.08 mg ml^{-1} for tenoxicam and piroxicam, respectively. The standard deviation and relative standard deviation velues are found to be ranged from 0.05—0.07 and 0.37—0.98% and 0.025—0.078 and 0.25—1.2% for tenoxicam and piroxicam, respectively. The two methods are accurate within ±1.0%. Optimum conditions affecting both methods are studied. The proposed methods are applied for the determination of the drugs in pure form and in commercial pharmaceutical preparations.

Key words tenoxicam; piroxicam; potassium iodate; *N*-bromo-succinimide; spectrophotometry; potentiometry

Piroxicam and tenoxicam were a nonsteroidal anti-inflammatory drugs and the adverse effects associated with them had been reported.[1,2] A flow injection spectrophotometric method was described for the determination of piroxicam and tenoxicam.[3,4] Various reagents and metal chelate were used for the spectrophotometric determination of piroxicam in pharmaceutical formulations.[5—7] Tenoxicam and piroxicam were determined in tablets, plasma or urine samples using normal and derivative spectrophotometric techniques.[8—10] Piroxicam and tenoxicam were determined in human plasma, urine, serum and preparations using HPLC.[11—14] Voltammetric, polarographic, and ion selective electrode techniques were used in the determination of piroxicam and tenoxicam in pharmaceutical preparations.[15—17]

The main objective of this study is to find a fast, accurate and sensitive spectrophotometric and potentiometric methods for the determination of piroxicam and tenoxicam in their pure and pharmaceutical preparations. The mechanism of oxidation of both drugs with iodate and *N*-bromosuccinimide is suggested in order to throw more light on the nature of the oxidation product formed.

Experimental

Apparatus Shimadzu Model 160A UV–Visible double beam spectrophotometer with a 1.0 cm quartz cells was used.

Reagents All solvents and reagents were of analytical reagent grade. Tenoxicam was provided by EIPICO where it labeled to contain 20 mg of tenoxicam per tablet or capsule. Piroxicam was provided by Pfizer where it labeled to contain 20 mg of piroxicam per tablet or capsule. Potassium iodate solution, 1% m/v; sulphuric acid for spectrophotometric assay, 30% v/v; sulphuric acid for potentiometric assay, 1 M; *N*-bromosuccinimide (NBS) solution, 2×10^{-3} M; dissolve 534 mg of NBS in 1 l of distilled water and standardized iodimetrically.[18]

Reference Drug Solution Weigh accurately 50 and 100 mg of tenoxicam and piroxicam, respectively, into a 100 ml calibrated flask and dissolve in methanol up to the mark.

Sample Preparation Solution Dissolve an accurately weighed amount of the tablet or capsule powder, equivalent to 50 and 100 mg of tenoxicam and piroxicam, respectively, in methanol in a 100 ml calibrated flask. Shake for 15 min, dilute to the volume and filter.

Spectrophotometric Procedure Transfer different portions (containing amounts in the range 0.05—0.6 and 0.05—1.1 mg tenoxicam and piroxicam, respectively) into 50 ml stoppered conical flasks. Add 5 ml of potassium iodate solution and 3 ml of 30% v/v sulphuric acid and mix well. Add to each flask, 5 ml of cyclohexane and heat at 55 °C in a water bath for 5 min for tenoxicam and piroxicam. Cool, add another 5 ml cyclohexane and transfer the cyclohexane layer quantitatively into 10 ml calibrated flasks. Measure the absorbance at 522 nm against a reagent blank.

Potentiometric Procedure Transfer different portions (containing amounts in the range 0.33—3.372 and 0.33—4.08 mg tenoxicam and piroxicam, respectively) into 50 ml conical flasks. Add 3 cm^3 of sulphuric acid and dilute with bidistilled water to 50 ml. Titrate potentiometrically, using Pt electrode with 2×10^{-3} M NBS solution by dropwise addition and constant stirring. Detrmine the equivalent point by the plots of *E versus V* and $\Delta E/\Delta V$ *versus V*, where *E* is the potential (e.m.f.) of the titrating solution, *V* is the volume of the titrant and ΔE is the change in potential resulting from the addition of ΔV, at difinite volume of the titrant.

Results and Discussion

Spectrophotometric Method The concentrations of tenoxicam and piroxicam are found to be proportional to the measured absorbance at 522 nm obtained by the formation of iodine from potassium iodate during its reactions with both drugs under study in acidic medium. Different experimental conditions affecting the developed colour produced are shown in Fig. 1.

In order to study the effect of time, samples are assayed and the absorbancies determined after varying the time intervals at the reaction temperature of 55 °C (Fig. 1a). The results indicate that, 15 and 5—15 min time intervals for tenoxicam and piroxicam, respectively, are required to obtain complete reaction.

Figure 1b shows the effect of temperature on the colour reaction. Higher absorbancies are obtained at a temperature of 55 °C and hence it is chosen as it gives better reproducibility. Higher temperatures are not preferred possibly owing to the loss of iodine at higher temperatures and consequently low results. An investigation of the effect of sulphuric acid solu-

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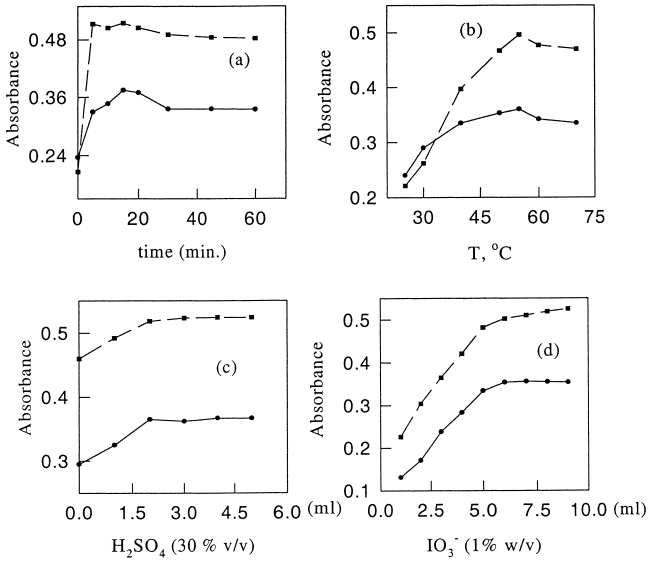

Fig. 1. Effect of Different Experimental Conditions on the Reaction between Piroxicam and Tenoxicam with IO_3^-

(a) Effect of time, (b) effect of temperature, (c) effect of H_2SO_4 (by volume) and (d) effect of IO_3^- (by volume). —●—, tenoxicam; —■—, piroxicam.

tion on the formation and extraction of iodine into cyclohexane is shown in Fig. 1c. It shows that, 3.0 ml of 30% v/v sulphuric acid solution in the presence of 0.5 and 0.6 mg of piroxicam and tenoxicam, respectively, is required to obtain the maximum absorbance. After this, the absorbance is nearly constant. A 5 ml volume of 1% m/v solution of potassium iodate is found to be optimum for the colour formation and stability (Fig. 1d).

It is observed that the end absorbance is different between the piroxicam and tenoxicam systems that may be due to the different reactivities of both drugs.

In order to prove the applicability of the proposed method and the reproducibility of the results obtained, four replicate experiments at different concentrations of piroxicam and tenoxicam are carried out. The within-day relative standard deviations are less than 4%. The values of the between-day relative standard deviation for different concentrations of the reported drugs, obtained from experiments carried out over a period of four days, are given in Table 1. The small values of the standard deviation, S.D., and relative standered deviation, R.S.D. indicate that, the proposed method is highly accurate, precise and reproducible.

Interference It should be noted here that, if any compounds, present as additives with tenoxicam and piroxicam preparations, are susceptible to oxidation by potassium iodate in acid medium (such as other sulphur containing compounds as well a 1,2-diols) they would interfere with the determination of piroxicam and tenoxicam using this procedure. Hence, suitable separation steps such as ion-exchange chromatography would be required. On the other hand, tablet filleres such as lactose, starch and stearic acid and preservatives and bacteriostatics used in parenteral preparations, which can represent a potential sourse of interference in other methods, do not interfere in the proposed method.

Applying the continuous variation (Fig. 2), and molar ratio (Fig. 3) methods under the selected optimum conditions, the ratio between tenoxicam or piroxicam and iodate is found to

Table 1. Between-Day Precision of the Determination of Tenoxicam and Piroxicam Using KIO_3

Drug	Conc. (mg ml^{-1})		% recovery	S.D.[a)]	R.S.D. (%)
	Taken	Found			
Tenoxicam	0.1	0.100	100.0	0.03	3.0
	0.25	0.255	102.0	0.087	3.40
	0.50	0.500	100.0	0.03	0.60
Piroxicam	0.10	0.0997	99.70	0.026	2.60
	0.60	0.600	100.0	0.05	0.83
	1.00	0.999	99.90	0.062	0.62

a) The number of replicates=5.

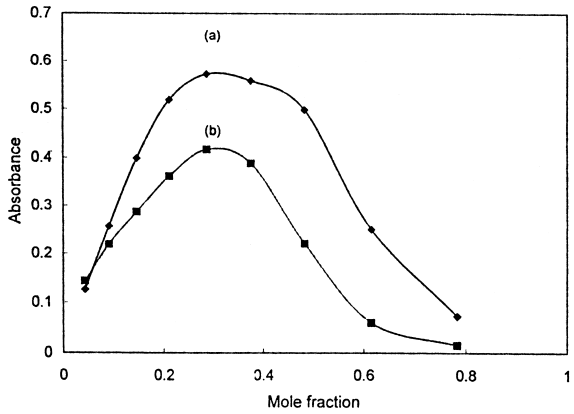

Fig. 2. Stoichiometric Ratio of the Redox Reaction between Iodate

(a) Piroxicam, (b) tenoxicam.

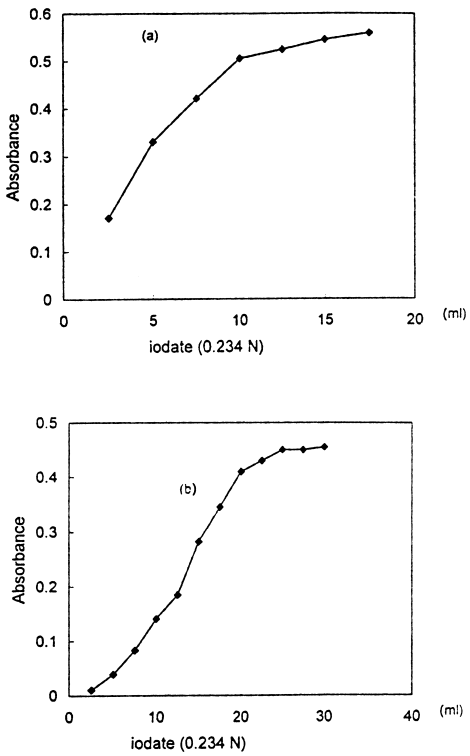

Fig. 3. Molar ratio of the Redox Reaction between Iodate

(a) Piroxicam, (b) tenoxicam.

Table 2. Analytical Parameters for the Determination of Piroxicam and Tenoxicam by the Proposed Method

Drug	λ_{max} (nm)	Conc. range ($\mu g\,ml^{-1}$)	ε ($l\,mol^{-1}\,cm^{-1}$)	Sandell sensitivity ($\mu g\,cm^2$)	$A=mc+z$		Range of error	R.S.D. (%)
					m	z		
Tenoxicam	522	0.05—0.6	0.25×10^3	0.013	1.02	−3.24	0.16—1.08	0.9—1.2
Piroxicam	522	0.05—1.1	0.27×10^3	0.012	1.07	−0.033	0.36—0.5	0.6—0.62

Table 3. Spectrophotometric Determination of Tenoxicam and Piroxicam in Pharmaceutical Preparations

Drug	Name of preparation	[Drug] $mg\,ml^{-1}$ taken	[Drug] $mg\,ml^{-1}$ Found±S.D. (%) ($n=5$)		t-test[f]	F-test[g]
			Proposed method	Official method		
Tenoxicam	Bulk	0.5	0.495±0.061	0.489±0.035	2.38	3.04
	Soral capsule[a]	0.5	0.491±0.025	0.494±0.06	2.14	5.75
	Epicotil tablet[b]	0.5	0.493±0.033	0.49±0.066	2.44	4.0
Piroxicam	Bulk	0.6	0.602±0.047	0.607±0.033	2.38	2.03
	Faldene capsule[c]	0.6	0.604±0.055	0.598±0.10	2.44	3.3
	Feldoral capsule[d]	0.6	0.60±0.04	0.597±0.04	1.62	5.06
	Piroxicam capsule[e]	0.6	0.602±0.043	0.598±0.10	2.13	5.41

a) Soral capsule, 20 mg/capsule (Global Napi, Pharmaceuticals, Egypt). *b*) Epicotil tablet, 20 mg/tablet (Eipico, Egypt). *c*) Faldene capsule, 20 mg/capsule (Pfizer, Egypt). *d*) Feldoral capsule, 20 mg/capsule (Sedico, Egypt). *e*) Piroxicam capsule, 20 mg/capsule (Adwic, Egypt). *f*) Standard t-test value at 95% confidence level=2.776. *g*) Standard F-test value at 95% confidence level=6.39.

be 1 : 2.5 [Drug] : [Iodate]. Let both drugs be represented as RH_2, so the mechanism of oxidation can be given as shown in Chart 1:

$$2IO_3^- + 12H^+ + 10e \rightleftharpoons I_2 + 6H_2O \quad (1)$$

$$5RH_2 \rightleftharpoons 5R^- + 10H^+ + 10e \quad (2)$$

$$2IO_3^- + 2H^+ + 5RH_2 \rightleftharpoons 5R^- + I_2 + 6H_2O \quad (3)$$

Chart 1. Mechanism of the Oxidation of Tenoxicam and Piroxicam with Iodate

Thus, it is clear from Eq. 3 that two moles of iodate can oxidize five moles of tenoxicam or piroxicam under the selected optimum conditions to give one mole of generated iodine.

Under these conditions, a linear correlation is obtained between absorbance (A) and the concentration (C) of piroxicam and tenoxicam over the range 0.05—1.1 and 0.05—0.6 $mg\,ml^{-1}$ of piroxicam and tenoxicam, respectively. The apparent molar absorptivities, Sandell sensitivities and the regression line equations for each drug are tabulated in Table 2. Moreover, the Ringbom[19] optimum concentration ranges can be calculated, which give more accurate results, *i.e.*, 0.08—1.0 and 0.07—0.55 $mg\,ml^{-1}$ for piroxicam and tenoxicam, respectively. The apparent molar absorptivities of the resulting coloured products (iodine) are found to be 2.7×10^3 and $2.5\times10^3\,l\,mol^{-1}\,cm^{-1}$, whereas Sandell sensitivities are 0.012 and 0.013 $g\,cm^{-2}$ for piroxicam and tenoxicam, respectively. The performance of the proposed method is assesed by comparison with the official method.[20] Mean values obtained in t- and F-tests[21] show the absence of any systematic error in the method (Table 3). On comparing the results obtained by the proposed method with those of the BP[20] using the t-test for the accuracy and F-test for the precision assessment,[21] the calculated values did not exceed the corresponding theoretical values, indicating insignificant differences between results, as shown in Fig. 4.

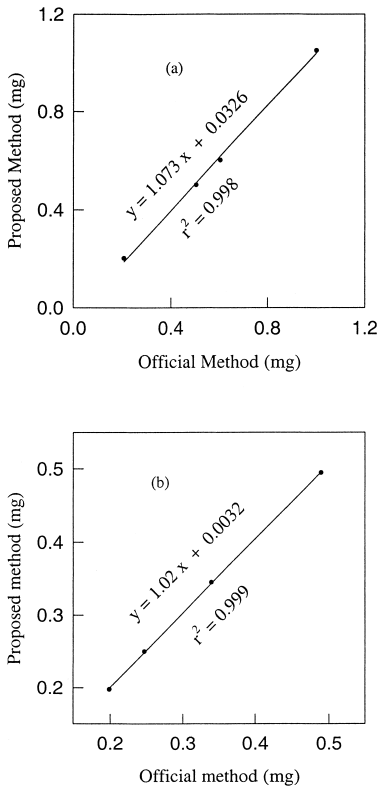

Fig. 4. Comparative Studies between the Official and Proposed Method in the Determination of (a) Piroxicam and (b) Tenoxicam Using Iodate

Potentiometric Method *N*-Bromosuccinimide is found to react quantitatively with piroxicam and tenoxicam in sulphuric acid medium. Tenoxicam and piroxicam are directly titrated potentiometrically in H_2SO_4 medium with 2×10^{-3} M NBS as a titrant. The titration curves of tenoxicam and piroxicam show one well-defined S-shaped stoichiometric end point. The determination of the end point Figs. 5, 6 from the potentiometric data will help in the calculation of the drug concentration. The potential (E_h) jump at the end point is amount in average to 140—260 and 160—180 mV/0.1 ml of

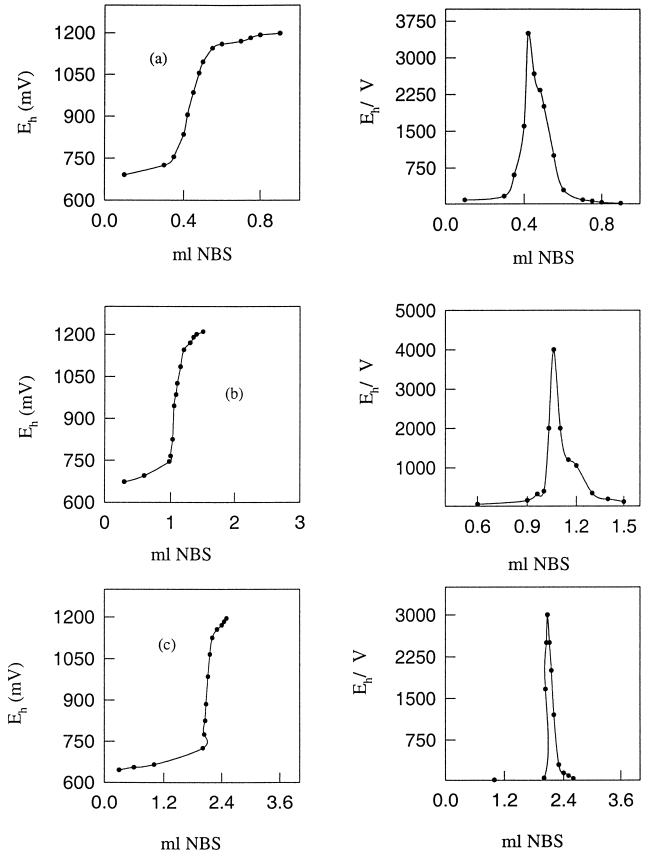

Fig. 5. Typical Titration Curves Used for Potentiometric Determination of End Point of the Reaction between NBS and Piroxicam Using Pt Electrode
(a) 0.2, (b) 0.5 and (c) 1.0 ml piroxicam (2×10^{-3} M).

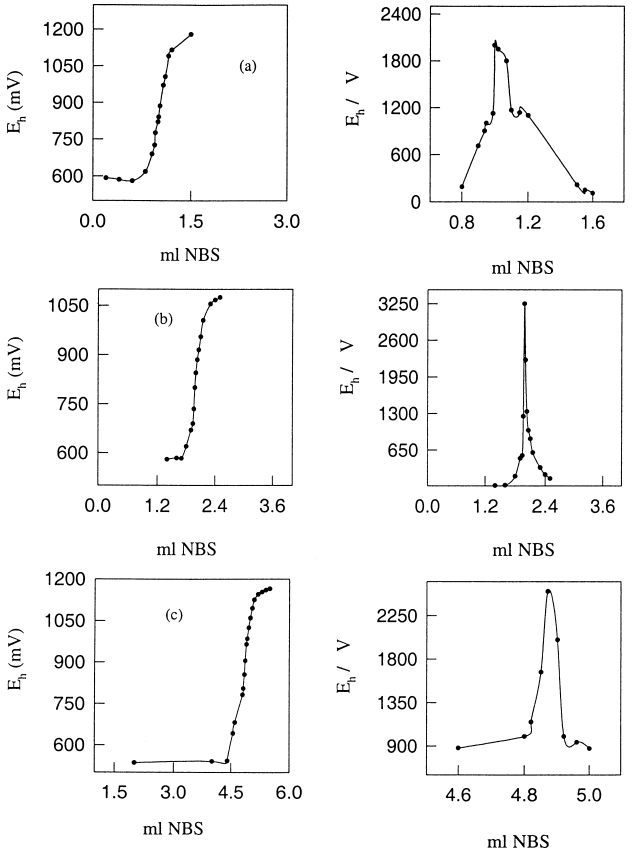

Fig. 6. Typical Titration Curves Used for Potentiometric Determination of End Point of the Reaction between NBS and Tenoxicam Using Pt Electrode
(a) 1.0, (b) 2.0 and (c) 5.0 ml of tenoxicam (10^{-3} M).

NBS titrant for piroxicam and tenoxicam, respectively, in 1 M H_2SO_4 medium (3 ml). It is found that, H_2SO_4 medium is chosen as the suitable medium for poteniometric determination of tenoxicam and piroxicam more than HCl and HNO_3 acids due to their oxidizing (HNO_3) and reducing (HCl) properties. A study of the stoichiometry of the reaction in different acids with different concentrations revealed that 3 ml of 1 M sulphuric acid give the best results.[21] Also, the jump in the potential at the end point per 0.1 ml NBS titrant is higher in H_2SO_4 medium than in HCl and HNO_3 mediums.

It is found that, two moles of NBS are required for complete oxidation of each mole of tenoxicam and piroxicam. The mechanism of the reaction between NBS and each of piroxicam and tenoxicam may take place *via* the respective NH, and OH groups of both drugs.[18] The first molecule of NBS may consumed in the bromination of the NH group while the second molecule may consumed in the bromination of OH group or *vice versa* to give dibromo derivative of tenoxicam or piroxicam. Let piroxicam and tenoxicam be represented by the general formula RH_2, so under the proposed experimental conditions, the mechanism of oxidation reaction between tenoxicam and piroxicam and NBS can be proposed as shown in Chart 2.

Piroxicam and tenoxicam can be determined quantitatively in the concentration range of 0.33—3.37 and 0.33—4.08 mg ml^{-1} for tenoxicam and piroxicam, respectively. The standard deviation and relative standard deviation values are found to be ranged from 0.05—0.07 and 0.37—0.98% and 0.025—0.078 and 0.25—1.2% for tenoxicam and piroxicam,

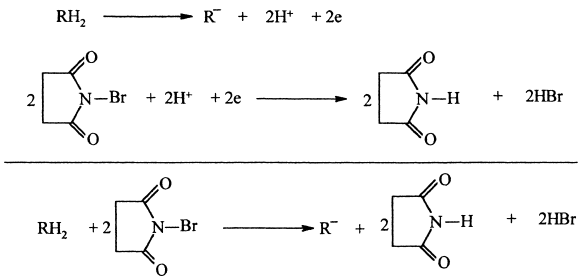

Chart 2. The Mechanism of the Redox Reaction between Piroxicam and Tenoxicam with NBS

respectively, which indicates that *N*-bromosuccinimide can be applied successfully in the determination of piroxicam or tenoxicam in pure and in pharmaceutical preparations.

In order to evaluate the applicability of the method to pharmaceutical preparations, piroxicam and tenoxicam are determined in different pharmaceuticals as given in Table 4. The fact that, the mV values before the end points in the titration curves of pure tenoxicam and piroxicam and their corresponding pharmaceuticals are almost identicals, provide evidence that, the other excipients that might be present in pharmaceuticals do not affect the titration curves. The excipients in the above mentioned pharmaceutical preparations do not include acidic substances.

Table 4 summarizes the results obtained for tenoxicam and piroxicam in their corresponding pharmaceuticals. The recoveries are in good agreement with the official method[19]

Table 4. Potentiometric Determination of Tenoxicam and Piroxicam in Pharmaceutical preparations

Drug	Name of preparation	[Drug] mg ml^{-1} taken	[Drug] mg ml^{-1} Found±S.D. (%) (n=5)		t-test[f]	F-test[g]
			Proposed method	Official method		
Tenoxicam	Bulk	1.685	1.649±0.01	1.657±0.02	1.789	4.0
	Soral capsule[a]	0.337	0.327±0.02	0.338±0.045	1.19	5.07
	Epicotil tablet[b]	0.337	0.326±0.015	0.338±0.035	1.79	5.44
Piroxicam	Bulk	0.663	0.676±0.015	0.665±0.03	1.65	4.0
	Faldene capsule[c]	0.663	0.657±0.02	0.638±0.04	2.16	4.0
	Feldoral capsule[d]	0.663	0.652±0.03	0.675±0.07	1.74	5.44
	Piroxicam capsule[e]	0.663	0.657±0.025	0.641±0.06	1.46	5.76

a) Soral capsule, 20 mg/capsule (Global Napi, Pharmaceuticals, Egypt). *b*) Epicotil tablet, 20 mg/tablet (Eipico, Egypt). *c*) Faldene capsule, 20 mg/capsule (Pfizer, Egypt). *d*) Feldoral capsule, 20 mg/capsule (Sedico, Egypt). *e*) Piroxicam capsule, 20 mg/capsule (Adwic, Egypt). *f*) Standard t-test value at 95% confidence level=2.776. *g*) Standard F-test value at 95% confidence level=6.39.

and the R.S.D. values are >2.0%. Thus, the reproducibility and accuracy is very satisfactory for the analysis of pharmaceutical preparations as well as bulk drugs. These results indicate that, the content of each drug in pharmaceuticals can be safely determined using this method without interference from other substances in the preparations.

Conclusion As general conclusion, the proposed potentiometric method could be utilized readily for routine analysis of pharmaceuticals since it offers a simple system and with short analytical time coupled with good reproducibility and accuracy.

On comparing the results obtained by the spectrophotometric method using IO_3^- and potentiometric method using NBS titarant, it is obvious that the iodate method is sensitive to low concentrarion while the NBS method is sensitive to high concentrations as given before.

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