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Spectrophotometric, atomic absorption spectrometric and conductometric methods for determination of naftidrofuryl oxalate and propafenone HCl

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ABSTRACT

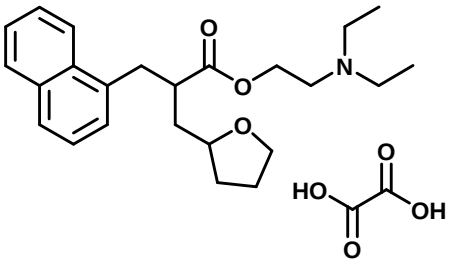
Four methods are described for the determination of naftidrofuryl oxalate and propafenone HCl based on the formation of their ion-associates with ammonium reineckate. Pink coloured complexes were determined spectrophotometrically at λ_{max} 525 in the range of 0.6-3.8 and 0.4 -3.2 mg ml^{-1} for naftidrofuryl oxalate and propafenone HCl respectively. The second and third methods involved direct atomic absorption spectrometric (AAS) and indirect (AAS) by measuring the excess metal ion present in supernatant solutions in the range of 80-320 and 40-280 μg ml^{-1} for naftidrofuryl oxalate and propafenone hydrochloride for both methods. The fourth method included conductometric titration using ammonium reineckate as titrant, the studied drugs were evaluated in double distilled water in the range 20-140 and 40-140 μg ml^{-1}. For naftidrofuryloxalate and propafenone. Various experimental conditions were established, results obtained showed good recoveries with relative standard deviation of (0.54, 0.52), (0.42, 0.65), (0.92, 0.39)and (0.48,0.31) for spectrophotometric, direct, indirect (ASS) and conductometric methods for naftidrofuryl oxalate and propafenone hydrochloride respectively. The proposed procedures were applied successfully to the analysis of these drugs in their pharmaceutical formulations. Results were favorably comparable to the official methods. The molar combining ratio reveal that (1:1) (drug: reagent) ion associates were formed.

KEYWORDS

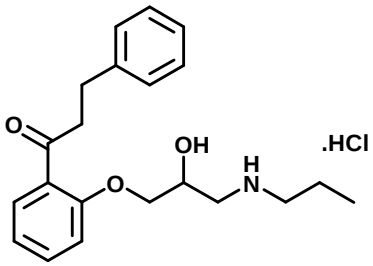
Atomic absorption spectrometry;
Spectrophotometric determination;
Conductometric titration;
Naftidrofuryl oxalate;
Propafenone HCl.

INTRODUCTION

Naftidrofuryl oxalate is known as nafronyl oxalate, (2-(diethylaminoethyl)-2-[(naphthalene-1-yl)methyl]-3-(tetrahydrofuran-2-yl)propanoate hydrogen oxalate)[1a]. It is used as a vasodilator in the treatment of peripheral and cerebral vascular disorders. It is claimed to enhance cellular oxidative capacity thereby protecting cells against the results of ischaemia[2a]. Few analytical methods were reported for the determination of naftidrofuryl in biological fluids and/or pharmaceutical preparations. Most of these studies focused on derivative spectrophotometry, spectrofluorimetry, differential-pulse voltammetry[3], HPLC-fluorimetric[4-7], HPLC-UV de-



Naftidrofuryl oxalate



Propafenone hydrochloride

tection methods[8,9] and phosphorimetric analysis[10-13]. Others include a potentiometric method with nafronyl ion-selective electrodes[14] and flow injection analysis with fluorescence optosensor[15].

Propafenone hydrochloride [2-(2-hydroxy-3-propylaminopropoxy)- 3-phenylpropiophenone hydrochloride][16]. It is used in the treatment of cardiac arrhythmias[2b]. A spectrofluorimetric method was reported for its determination[17]. Several methods including capillary electrophoresis[18-20], HPLC methods[21-24] were reported for propafenone enantioselective determination and its metabolites in human plasma. Other reported methods of analysis include LC-MS[25], adsorptive stripping voltammetry[26], and gas chromatography using chemical ionization mass spectrometry (CIMS)[27].

Reineckate salt is ammonium tetrathiocyanotodiamminochromate (III) monohydrate in which it can be used for quantitative determination of many pharmaceutical compounds applying spectrophotometric, conductometric and (AAS) techniques. It was used for many drugs such as fluoroquinolone antibacterials[28,29], clomiphene citrate[30], nefazodone HCl[30], antimalarial drugs[31],cephalosporins[32] and lignocaine[33].

EXPERIMENTAL

Apparatus

The absorption spectra for all measurements were carried out using Shimatzu 260 recording spectrophotometer equipped with 10mm quartz cells.

The conductometric measurements were carried out using Conductometer, Model (CM-1K), Tokyo TOA electronics Itd Japan. CV-161SC dip-type cell was used with a cell constant, K_{cell}, of 0.975.

The atomic absorption measurements for the determination of chromium ion were carried out using Buck Scientific 210VGP Atomic Absorption spectrophotometer. For AAS, the chromium was measured at λmax 357.87 nm, slit width, 0.2 nm, relative noise, 1.0, detection limit, 0.01 gml^{-1}, linear dynamic range, 0.01–100gm^{-1}, lamp current, 5.0mA and integration time, 10 s, the flame used was the acetylene–air.

Materials and reagents

All solvents and chemicals used are of analytical grade and double distilled water was used to prepare all solutions.

- Ammonium reineckate (Aldrich) was used
- Naftidrofuryl oxalate pure drug obtained from (Mina Pharm, under licence of Merck Santé France)
- Propafenone HCl pure drug obtained from (Kahira pharm, and chem. Ind. Co., under licence from Abott Laboratories).

Preparation of sample solution

For atomic absorption spectrometric and spectrophotometric procedures, Solution of 4 mg ml^{-1} was prepared in distilled water for Naftidrofuryl oxalate and Propafenone HCl.

For conductometric procedure, a stock standard solution of 1mg ml^{-1} naftidrofuryl oxalate and propafenone were prepared.

Preparation of reagent

1. 3×10^{-2} M ammonium reineckate (Aldrich) solution were prepared in 100 ml double distilled water for atomic absorption spectrometric and spectrophotometric measurements,
2. 5×10^{-3} M ammonium reineckate was used for conductometric measurement.

Pharmaceutical preparations

The following commercial formulations were subjected to the analytical procedures:

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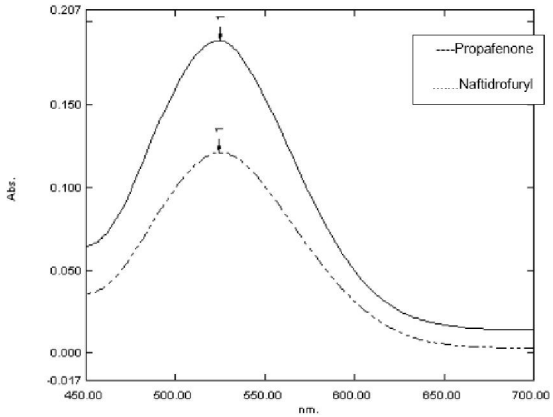

Figure 1 : Absorption spectra of the complex formed through reaction of 0.6 mg/ml, Naftidrofuryl and propafenone with 0.03M ammonium reineckate

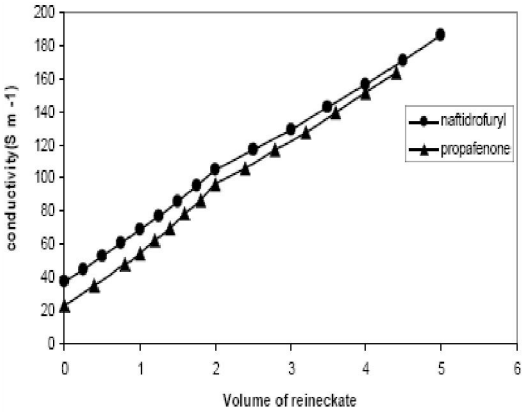

Figure 2 : conductometric titration curves of 100 µg ml^{-1}Naftidrofuryl and 80 µg ml^{-1}, Propafenone vs (5×10^{-3})M ammonium reineckate

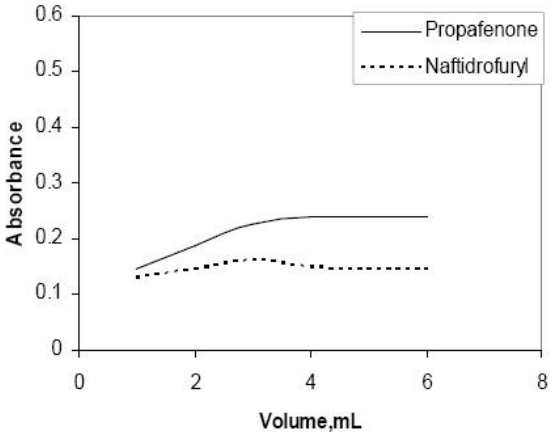

Figure 3 : Effect of reagent volume (0.03M) on the absorbance of the complex formed with 0.8 mg/ml, Naftidrofuryl oxalate And propafenone HCl

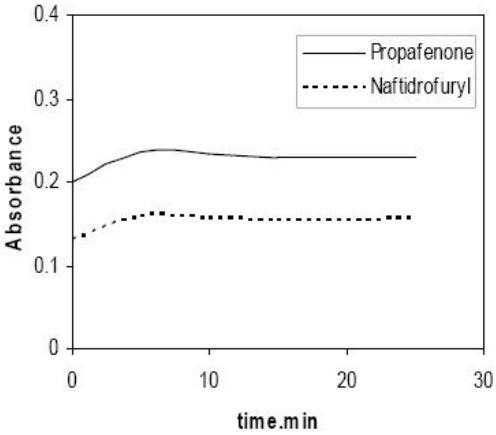

Figure 4 : Effect of precipitation time on the absorbance of the complex formed through reaction of 0.8 mg/ml, Naftidrofuryl and propafenone with0.03M ammonium reineckate

- Praxilene® tablets, each tablet contains 200 mg of naftidrofuryl oxalate per tablet. obtained from (Mina Pharm, under licence of Merck Santé France)
- Rytmonorm® tablets, each tablet contains 150 mg of propafenone HCl per tablet. (Kahira pharm, and chem. Ind. Co., under the licence from Abott Laboratories)

General procedures

Spectrophotometric procedure

Aliquots containing 6–38 and 4-32mg of naftidrofuryl and propafenone respectively were were transferred into 10ml calibrated flask, 3.0ml and 4.0 ml of 3×10^{-2} M of ammonium reineckate for naftidrofuryl and propafenone respectively were added. The mixture was left to stand for 5 min and then the precipitate was filtrated, washed with water, dissolved in least amount of acetone and then completed to the mark with the same solvent in 10 ml volumetric flask. The absorbances of solutions were measured at 524 nm (Figure 1), against a reagent blank solution prepared simultaneously. The calibration graph was obtained by applying the procedure, using standard drug solutions.

Direct atomic absorption spectrometric procedure

Aliquots containing 8–32 and 4-28mg of naftidrofuryl and propafenone respectively were proceeded as above in spectrophotometric procedure till (dissolved in least amount of aceton), completed to the mark in a 100 ml calibrated flask with water. This solution is then aspirated directly in the atomic absorption spectrometer then measured the chromium ion concentration. Calculate the concentration of the tested drug from the relevant calibration graph.

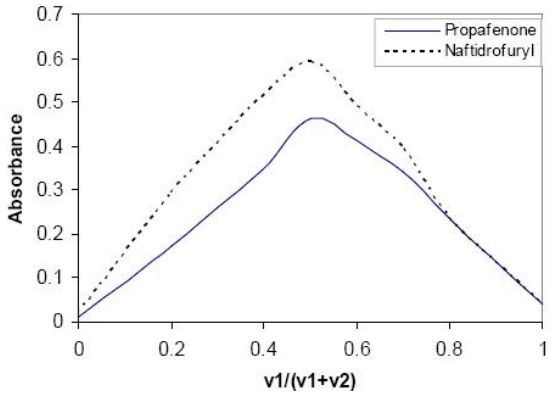

Figure 5 : Determination of the stiochiometry of the reaction of 0.03M Naftidrofuryl and Propafenone with 0.03M ammonium reineckate

Indirect atomic absorption spectrometric procedure

The filtrate and washings from the direct procedure were collected in100 ml volumetric flask and completed to volume with water then aspirated to determine the residual chromium ion. A blank (omitting addition of drugs) was prepared and absorbance was measured.

Conductometric procedure

Aliquots containing 1–7 and 2-7mg of Naftidrofuryl oxalate and propafenone HCl(1mg/ml) respectively were transferred to a 50 ml calibrated flask and made up to the mark with distilled water.The contents of the calibrated flask were transferred to a beaker and the conductivity cell was immersed. 5×10^{-3}M ammonium reineckate solution was then added and the end point was detected conductometrically. The conductance reading was corrected for dilution[34] by means of the following equation, assuming that conductivity is a linear function of dilution,

$$\Omega^{-1}_{correct} = \Omega^{-1}_{obs}[v_1+v_2/v_1]$$

where Ω^{-1}_{obs} is the observed electrolytic conductivity, V_1 the initial volume and V_2 is the volume of reagent added.

Agraph of corrected conductivity versus the volume of added titrant was constructed and the end-point determined.

0.1 ml of 5×10^{-3}M ammonium reineckate is theoretically equivalent to 0.237and 0.169 mg of naftidrofuryl and propafenone respectively. The procedure takes 15–30 min in all.

The amount of drugs under study was calculated

TABLE 1 : Quantitative parameters for the spectrophotometric determination of Naftidrofuryl oxalate and propafenone HCl

Items	Naftidrofuryl oxalate	Propafenone HCl
Beer's law range, mg/mL	0.6-3.8	0.4-3.2
Apparent molar absorpitivity, $mol^{-1}Lcm^{-1}$*	8.95×10^4	9.02×10^4
Sandell's sensitivity mg/ml per 0001A	5×10^{-3}	3.7×10^{-3}
Regression equation		
intercept(a)	0.0251	0.0533
Slope(b)	0.1687	0.2215
Correlation Coefficient®	0.9992	0.9998
Variance	0.29	0.27
Detection limit	0.616	0.555

***Calculated on the basis of the molecular weight of the drug**

according to the following equation:

Amount of drug = VMR / N

where V is volume of titrant, M is molecular weight of drug, R is molar concentration of titrant and N is number of moles of titrant consumed by one mole of drug.

Assay of pharmaceutical preparations

The contents of 20 tablets of each of the studied drugs were thoroughly ground. A quantity equivalent to 400 mg drug for (AAS) and spectrophotometry 100 mg for conductometry were accurately weighed into a 100 ml volumetric flask, completed to volume with bidistilled water, filtered and the procedure was completed as under the previous methods.

RESULTS AND DISCUSSION

According to Babko[35], large number of analytically important complexes consists of metal ion-electronegative ligand-organic base were reported. Most of these complexes are extractable in the usual organic solvents such as hydrocarbons and hologenated derivatives. Naftidrofuryl oxalate and propafenone HCl were found to react with ammonium reineckate to form stable ion pair complexes. These complexes are sparingly soluble in aqueous solution, but are readily soluble in acetone.

propafenone HCl + ammonium reineckate → ammonium chloride + propafenone-reineckate

Propafenone HCL + $NH_4[Cr(NH_3)_2(SCN)_4]$———— ropafenone$[Cr(NH_3)_2(SCN)_4]$ + NH_4CL

Investigations were carried out to establish the most

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TABLE 2 : Determinationof Naftidrofuryl oxalate and Propafenone HCl through complexation with ammonium reineckate by spectrophotometric method

Statistic	Naftidrofuryl oxalate		Propafenone HCl	
	Taken, mg/ml	Recovery,%	Taken, mg/ml	Recovery,%
	0.6	100.67	0.4	100.11
	0.8	100.7	0.8	99.72
	1.2	100.72	1.2	99.59
	1.6	100.73	1.6	100.08
	2	99.26	2	99.93
	2.8	100.54	2.4	100.58
	3.8	100.13	2.8	100.89
			3.2	99.28
Mean*±SD		100.39±0.54		100.02±0.52
N		7		8
SD		0.543		0.523
RSD		0.541		0.523
V		0.29		0.27
SE		0.205		0.18

***Mean of three different experiments**

TABLE 3 : The intra-day and inter- day accuracy and precision data for Naftidrofuryl and propafenone obtained by spectrophotometric method

	Naftidrofuryl oxalate					Propafenone				
	Taken	Found	Recovery	RSD	Er	Taken	Found	Recovery	RSD	Er
	mg/ml	mg/ml	%	%	%	Mg/ml	mg/ml	%	%	%
Intra day	0.8	0.803	100.33	0.528	0.33	0.8	0.798	99.72	0.47	-0.28
	1.2	1.212	100.97	0.743	0.97	1.2	1.200	99.96	0.40	-0.04
	1.6	1.612	100.73	0.866	0.73	1.6	1.601	100.08	0.44	0.084
	2	1.988	99.41	0.625	-0.59	2	1.999	99.93	0.29	-0.068
Inter day	0.8	0.803	100.33	0.971	0.33	0.8	0.798	99.72	0.47	-0.28
	1.2	1.203	100.23	0.691	0.23	1.2	1.195	99.59	0.47	-0.41
	1.6	1.612	100.73	0.886	0.73	1.6	1.601	100.08	0.29	0.085
	2	1.991	99.56	0.996	-0.44	2	1.996	99.82	0.47	-0.18

favourable conditions for the ion pair complex formation of the two drugs with ammonium reineckate to achieve maximum colour and sharp end point (Figure 1-2).

The influence of some variables on the reaction were tested as follow:

Conditions for spectrophotometric and (AAS) methods

(1) Effect of reagent concentration and volume

Experiments was carried out in which the volume was kept constant while the concentration of the reagent was increased, 3ml and 4.0 ml of 3×10^{-2}M was found to be the optimum concentration for naftidrofuryl and propafenone respectively (Figure 3).

TABLE 4 : Application of the proposed spectrophotometric method for the analysis of Naftidrofuryl oxalate and Propafenone HCl in dosage forms

Commercial product	Praxilene® tablets(200mg/tablet)			Rytmonorm® tablets(150mg/tablet)		
	Claimed amount, mg/ml	Authentic added, mg/ml	Recovery, %	Claimed amount, mg/ml	Authentic added, mg/ml	Recovery, %
	0.8	---	101.44	0.8	---	99.15
	---	0.6	99.68	---	0.4	100.11
	---	0.8	99.21	---	0.8	100.28
	---	1.2	100.23	---	1.2	99.96
	---	1.6	99.99	---	1.6	99.52
	---	2	102.22	---	2	99.48
	---	2.4	101.73	---	2.4	100.4
Mean*±SD			100.51±1.19			99.96
SD			1.19			0.38
V			1.43			0.15
SE			0.49			0.16

***Mean of three different experiments**

TABLE 5 : Quantitative parameters for the atomic absorption spectrometric determination of Naftidrofuryl oxalate and propafenone HCl

Items	Direct AAS		Indirect AAS	
	Naftidrofuryl Oxalate	Propafenone HCl	Naftidrofuryl Oxalate	Propafenone HCl
Beer's law range, µg/mL	80-320	40-280	80-320	40-280
Apparent molar absorpitivity, $mol^{-1}L\ cm^{-1}$*	1.71×10^3	1.77×10^3	1.7×10^3	2.49×10^3
Sandell's sensitivity mg/ml per 0001A	0.277	0.191	0.279	0.19
Regression equation				
intercept(a)	0.1127	0.1151	0.1108	0.116
Slope(b)	0.0029	0.0042	0.0029	0.0042
Correlation Coefficient®	0.9999	0.9999	0.9999	1
Variance	0.175	0.428	0.851	0.153
Detection limit	0.474	0.694	1.046	0.444

***Calculated on the basis of the molecular weight of the drug**

(2) Effect of PH

The effect of PH on the precipitation of the drug-reineckate complexes was studied, different buffers with pH range (1-10) were tried. It was found that buffer had no effect on the reaction. The PH of reaction media was measured and it was 3.8 and 3.5 for Naftidrofuryl and Propafenone respectively.

TABLE 6 : Determination of Naftidrofuryl oxalate and Propafenone HCl through complexation with ammonium reineckate by atomic absorbtion spectrometry

Statistics	Naftidrofuryl oxalate			Propafenone HCl		
	Taken, µg/ml	Recovery,%		Taken, µg/ml	Recovery,%	
		DirectAAS	IndirectAAS		DirectAAS	IndirectAAS
	80	100.13	101.38	40	99.94	99.40
	120	99.80	98.33	80	100.57	100.30
	160	100.93	100.26	120	98.59	100.00
	200	100.74	100.21	160	98.94	99.26
	240	100.47	100.46	200	99.39	99.76
	280	100.65	100.52	240	99.79	100.20
	320	100.89	100.45	280	99.4	99.66
Mean±S.D		100.52±0.42	100.23±0.92		99.52±0.65	99.8±0.39
N		7	7		7	7
SD		0.418	0.922		0.654	0.391
RSD		0.416	0.920		0.658	0.392
V		0.175	0.851		0.428	0.153
SE		0.158	0.349		0.247	0.148

***Mean of three different experiments**

TABLE 7 : Application of the proposed atomic absorption spectrometric method for the analysis of Naftidrofuryl oxalate and Propafenone HCl in dosage forms

Commercial product	Praxilene® tablets (200mg/tablet)				Rytmonorm® tablets (150mg/tablet)			
	Claimed amount, µg/ml	Authentic added, µg/ml	Recovery,%		Claimed amount, µg/ml	Authentic added, µg/ml	Recovery,%	
			Direct AAS	Indirect AAS			Direct AAS	Indirect AAS
	80	---	100.56	100.09	40	---	101.13	100.60
	---	80	99.70	100.52	---	40	100.54	100.00
	---	120	100.95	100.34	---	80	101.16	100.89
	---	160	100.50	100.91	---	120	102.16	100.40
	---	200	99.53	99.34	---	160	99.54	99.70
	---	240	101.77	101.47	---	200	100.94	100.95
Mean±S.D			100.49± 0.92	100.52± 0.78			100.87± 0.95	100.39± 0.55
SD			0.92	0.78			0.95	0.55
V			0.85	0.61			0.91	0.30
SE			0.41	0.35			0.43	0.24

***Mean of three different experiments**

(3) Effect of solvent

Distilled water, Acetone, acetone: water (1:1), acetonitrile, ethanol, benzene and chloroform were tried. Acetone was found to be the best solvent for dissolving the precipitated ion-pair formed. On the other hand, acetonitrile and (acetone: water) were suitable but the results were lower, ethanol, benzene and chloroform were unsuitable owing to the limited solubility of ion-pair in these solvents.

For AAS measurements, it was not practical to aspirate the dissolved ion-pair in acetone to the atomic absorption spectrometer. It is better to dilute the formed ion-pair with water in a ratio 10% (v/v) acetone aqueous media, which can be aspired directly to the atomic absorption spectrophotometer.

(4) Effect of precipitating time

A series containing equal concentrations of drug was analyzed using the same procedure, but filtering the precipitate after various time intervals. 5 minutes was sufficient to give complete precipitation, increasing time than this has no effect on absorption (Figure 4).

(5) Effect of temperature

The effect of temperature on the formation of the coloured precipitate was investigated.It was found that increasing temperature decrease absorbance, so experiments were done at room temperature.

(6) Conditions for conductometric method

Conductometric analysis can be used in many titration procedures when ionic solutions are involved. As the conductance of a solution is related to the total ionic content, it can be applied to follow reaction that results in a change in this quantity.

Conductance measurements are used successfully in quantitative titration of systems in which the conductance of solution varies before and after the equivalence point. In these cases, the titration curve can be represented by two lines intersecting at the end point.

Representative titration curves are shown in (Figure 2). Two straight lines are obtained, intersecting at the end-point. The increase of conductance may be attributed to the formation of ion-pair in solution as a result of the complexation reaction. After the end-point, the titration curves indicate a slight increase of conductance due to the excess of the reagent.

The shape of the titration curve depends on all the species present during the titration process and other factors such as viscosity, dielectric constant, solvation, ion pair association and proton transfer.

The optimum conditions for performing the titration in quantitative manner were elucidated as following:

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TABLE 8 : Determination of Naftidrofuryl oxalate and Propafenone HCl through complexation with ammonium reineckate by conductometric method

Statistics	Naftidrofuryl oxalate			Propafenone HCl		
	Taken, μg ml^{-1}	Found, μg ml^{-1}	Recovery, %	Taken, μg ml^{-1}	Found, μg ml^{-1}	Recovery, %
	20	19.89	99.45	40	40.06	100.14
	40	39.78	99.46	60	59.71	99.51
	60	60.38	100.64	80	79.74	99.67
	100	99.92	99.93	100	100.14	100.14
	120	119.35	99.46	120	120.36	100.30
	140	139.24	99.46	140	139.82	99.87
Mean*±S.D.			99.45±0.48			100.01±0.31
N			6			6
SD			0.483			0.307
V			0.234			0.094
SE			0.197			0.125

***Mean of three different experiments**

TABLE 9 : Application of the proposed conductometric method for the analysis of Naftidrofuryl oxalate and Propafenone HCl in dosage forms

Statistics	Naftidrofuryl oxalate			Propafenone HCl		
	Taken, μg ml^{-1}	Found, μg ml^{-1}	Recovery, %	Taken, μg ml^{-1}	Found, μg ml^{-1}	Recovery, %
	20	19.89	99.46	40	39.68	99.19
	40	40.26	100.64	60	59.52	99.2
	60	59.20	98.67	80	79.36	99.2
	100	98.27	98.27	100	100.14	100.14
	120	120.77	100.64	120	119.98	99.98
	140	139.71	99.79			
Mean*±S.D			99.63±0.985			99.19±0.478
N			6			5
SD			0.985			0.478
V			0.971			0.228
SE			0.402			0.195

***Mean of three different experiments**

Titration in different media

Different media were attempted to obtain the best results. Preliminary experiments in:

1. Aqueous drug solution with aqueous reagent solution,
2. Ethanol drug solution with Ethanol reagent solution,
3. Drug solution with reagent solution, both in ethanol – water (50%, v/v) mixture
4. Acetone drug solution with acetone reagent solution
5. Drug solution with reagent solution, both in acetone – water (50%, v/v) mixture
6. Preliminary experiments showed that procedure in water media was the most suitable for successful results (higher conductance and most sharp end point.)

The reagent concentration

The reagent concentration in each titration must be not less than 10 times that of the drug solution in order to minimize the dilution effect on the conductivity through the titration. The optimum concentration of ammonium reineckate was 5×10^{-3}Mto achieve a constant and highly stable conductance reading after 2.0 min mixing. Concentrations less than these led to unstable readings and more time was needed to obtain constant conductance values.

Effect of temperature

On raising the temperature to 40°C, no change in the conductance reading was observed, so experiment was done at room temperature.

Stoichiometric relationships

The stoichiometric ratio of the studied drugs to reineckate in the complex were determined by applying Job's method of continuous variation[36], the results indicated a molar ratio of 1:1 drug to reineckate (Figure5).

Validation method

Calibration graphs with good linearity were obtained. The linear regression equations were calculated. Correlation coefficient, intercept and slope values for calibaration data were calculated, detection limit and quantification limit were evaluated and reported in TABLE (1, 2, 5, 6, 8).

The validity of proposed methods was assessed by its application to the determination of the two drugs in their pharmaceutical preparations, TABLE (4, 7, 9).

Student's t-test and F-test(at 95% confidence level) were applied to the results obtained compared with that obtained when applying the official methods for Naftidrofuryl oxalate and Propafenone HCl, the results showed that it didn't differ significantly and there are no systematic differences between the proposed and official methods. The results of different statistical treatment of the data are shown in TABLE 10.

Accuracy and precision were carried out by six

TABLE 10 : Statistical analysis of the results obtained by the proposed methods and the official methods of Naftidrofuryl oxalate and Propafenone HCl

Naftidrofuryl oxalate	Official methods	Spcctro-photometry	Direct AAS	Indirect AAS	Conducto-metry
Mean*(p=0.05)	100.05 0.42	100.39 ±0.54	100.52 ±0.42	100.23 ±0.92	99.46 ±0.48
t-value	--	0.96 (2.306)**	1.63 (2.306)**	0.31 (2.306)**	1.695 (2.365)**
F-value	--	1.66 (5.14)**	1.0 (5.14)**	4.86 (5.14)**	1.34 (5.79)**
Propafenone HCl					
Mean*(p=0.05)	100.29± 0.39	100.02± 0.52	99.52± 0.65	99.8± 0.39	100.01± 0.31
t-value	--	0.73 (2.262)**	1.72 (2.306)**	1.54(2.306)**	0.93(2.365)**
F-value	--	1.46 (4.74)**	1.08 (5.14)**	2.58(5.14)**	4.20(5.79)**

***Mean ±SD(mean of three different experiments), **Theoretical values for t and F at p=0.05**

determinations at four different concentrations of the two drugs in the same day (intra-day), and in six different days (inter-day) using spectrophotometric method. Percentage relative standard deviation (RSD %) as precision and percentage relative error (Er%) as accuracy of the suggested method were calculated. The percentage relative error calculated using the following equation:

Er% = [(founded - added) / added] × 100

The results of accuracy and precision (TABLE 3) show that the proposed methods have good repeatability and reproducibility.

CONCLUSION

The proposed methods have the advantages of being simple, rapid, accurate, highly reproducible and time saving, in addition to stability indicating method especially AAS method so they can be applied in quality control of these drugs in pure form and pharmaceutical preparations. The conductometric method is found to be more sensitive than AAS and spectrophotometric methods.

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