Research Article

Drug Testing and Analysis

Received: 26 July 2009 Revised: 16 September 2009 Accepted: 4 October 2009 Published online in Wiley Interscience: 3 December 2009

(www.drugtestinganalysis.com) DOI 10.1002/dta.82

Spectrophotometric determination of peptic ulcer sulfur-containing drugs in bulk form and in tablets

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Two spectrophotometric procedures are suggested for the determination of three irreversible proton pump inhibitors, rabeprazole (RAB), omeprazole (OMP) and pantoprazole (PAN) in pure form and in different pharmaceutical formulations. The first method is based on the oxidation of RAB and PAN with potassium iodate in an acidic medium followed by extracting the liberated iodine with cyclohexane and measurement at $\lambda = 520$ nm. Beer's law is valid in the concentration ranges from 10–400 and 5–400 μg ml^{-1} for RAB and PAN, respectively. The apparent molar absorptivities of the resulting coloured product were found to be 1.34 × 10^3 and 1.64 × 10^3 l.mol^{-1}. cm^{-1} for RAB and PAN, respectively. The second method is based on the interaction of the basic drugs, OMP, RAB and PAN, in 1,2-dichloroethane with bromophenol blue (BPB), bromocresol green (BCG) and bromocresol purple (BCP) in the same solvent to produce stable coloured ion pairs with maximum absorbance at 385–405 nm. Regression analysis of Beer's plots showed good correlation in the concentration ranges 10–60, 10–60 and 5–40 μg ml^{-1} for OMP, 10–150, 10–150 and 10–60 μg ml^{-1} for RAB and 10–250, 10–150 and 10–100 μg ml^{-1} for PAN with BPB, BCG and BCP reagents, respectively. The limits of detection are 0.46–7.69 μg ml^{-1} and limits of quantitation range between 1.52–8.53 μg ml^{-1}. The optimum assay conditions were investigated and the recovery of the drugs from their dosage forms ranged from 99.33% to 100.5%. Intraday relative standard deviations (RSD) were 0.029–1.397% and the correlation coefficients ranged from 0.9992 to 1. The two methods can be applied successfully for the determination of these drugs in tablets. The results of analysis were validated statistically through recovery studies.

Keywords: dyestuffs; ion-pair; KIO_3; oxidation; peptic ulcer; spectrophotometry

Introduction

H^+/K^+ ATPase inhibitors omeprazole (OMZ) and pantoprazole sodium (PNZ) are effective in the treatment of gastric ulcers.[1–3] Both drugs decompose in acid media to yield two main products: sulfonamide and sulfenic acid.[4,5] Omeprazole was found to be unstable in neutral and weak alkaline media, where its maximum stability was at pH 11.[6,7] It is listed in the British Pharmacopoeia.[2] Methods used for the determination of the drugs under investigation in tablets, syrup, plasma and capsules have included high-performance liquid chromatography (HPLC),[5–11] high-performance thin-layer chromatography (HPTLC),[12,13] liquid chromatography with tandem mass spectrometry,[14,15] polarography,[4,16] electrophoresis,[17,18] and ulta-violet spectrophotometry.[19,20] Concerning visible spectrophotometry, very few studies have been reported for the determination of drugs.[21–26] The purpose of the current study was to develop spectrophotometric procedures for the determination of OMZ, PNZ and RAB in pure form and tablets. Different experimental conditions were optimized, then Beer's law was applied. The methods were successfully applied for the determination of these drugs in tablets, with high percentage recovery values. The data obtained using the proposed methods are compared well with those obtained by the official method.

Experimental

Apparatus

Shimadzu Model UV-1601, UV-Visible double-beam spectrophotometer with 1.0 cm quartz cells incorporated with a PC computer was used.

Small volumes were taken using automatic pipettes Socorex Swiss (50–200 μl).

Materials

Pure samples

Omeprazole was kindly supplied by Uni-pharma, Egypt. The purity of the sample was checked by thin-layer chromatography (TLC) and melting point.[3] Pantoprazole sodium sesquihydrate supplied from European Egyptian Pharmaceuticals; Egypt. Its purity was checked by TLC and melting point.[3] Rabeprazole was supplied by Sigma (USA).

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Market samples

Omepak capsules were supplied by Sedico Company, Egypt and each capsule was labelled as containing 40 mg OMZ. Pariet was supplied by Eisai Co., Ltd, Tokyo, Japan and tablets were labelled as containing 20 mg RAB. Pantopi (20 mg/tablet) was purchased from El-Obour Modern Pharm I.J.Co., Egypt. Each tablet was labelled as containing 20 mg PNZ (as PNZ sodium sesquihydrate).

Reagents

All reagents and chemicals used were of analytical grade and solvents were of spectroscopic grade. Potassium iodate solution (1% w/v) and sulphuric acid (30% v/v) were prepared. Stock solutions of OMP, RAB and PAN drugs containing 1 mg ml^{-1} in 10% ethanol were prepared. The dyestuffs were used as 0.02% solutions of bromocresol purple (BCP), bromophenol blue (BPB) and bromocresol green (BCG), all in ethanol. A series of buffer solutions in the pH range from 2–12 were prepared as recommended by Britton and Robinson.[27]

Application to dosage forms

The contents of 20 Omepak capsules were weighed, finely ground and mixed well. An amount of the fine powder equivalent to 50 mg OMZ was weighed and transferred to a 50 ml volumetric flask. It was dissolved in about 40 ml ethanol by shaking for 15 min and completed to volume with ethanol, then filtered. The clear filtrate purportedly containing 1 mg ml^{-1} OMZ was analysed.

Twenty Pantopi and 20 Pariet tablets were weighed and finely ground. An amount of the powder equivalent to 100 mg PNZ sodium and an amount equivalent to 100 mg RAB was weighed, dissolved in about 40 ml ethanol and shaken for 10 min. It was completed to volume then filtered. The clear aqueous filtrate labelled as containing 1 mg ml^{-1} of PNZ-sodium sesquihydrate and that containing RAB was analysed.

All solutions were protected from light by keeping them in dark-coloured quickfit bottles throughout the whole procedure.

General procedure using KIO_3 reagent

A portion of tablet powder equivalent to 100 mg of RAB or PAN was prepared in 100 ml of 10% (v/v) ethanol. Aliquots containing drug solutions of RAB or PAN of each drug (concentrations 50–200 μg ml^{-1}) were added separately, in a 100 ml separating funnel, to 1 ml of 30% (v/v) H_2SO_4, 1 ml of 1% (w/v) KIO_3 and 10 ml cyclohexane. The reaction mixture was shaken well for one minute, followed by separation of the cyclohexane layer and measurement of its absorbance at 520 nm against cyclohexane as a blank.

General procedure using ion-pair procedure:

Aliquots containing OMP, RAB or PAN in the working concentration range of (50–200 μg ml^{-1}) were prepared using 1–2 ml of 1 mg ml^{-1} of BPB, BCG or BCP reagents. This was followed by addition of 4 ml universal buffer of pH 4.6 and the solution was completed to 10 ml with bidistilled water. The reaction mixture was left for 20–40 minutes at 40 °C. The ion-pairs were collected in 10 ml measuring flasks using 1,2-dichloroethane. The absorbance of each was measured at its λ_{max} against 1,2-dichloroethane as a blank.

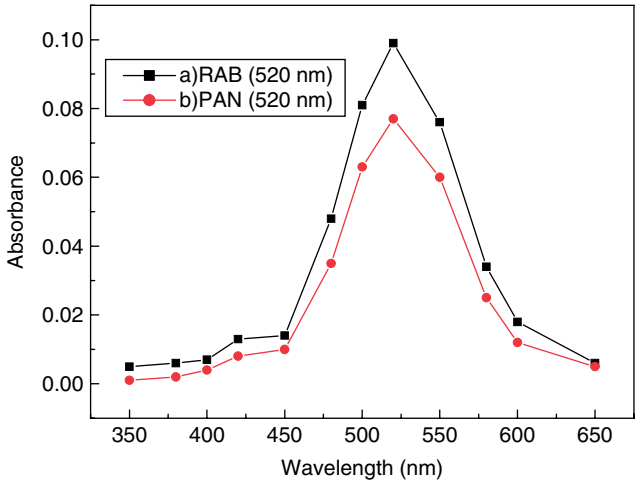


Figure 1. Absorption spectra of the reaction product of RAB and PAN drugs using KIO_3 in cycloexane.

Procedure for the assay of dosage forms

An amount of the tablet or capsule powder equivalent to 50 mg of the drug under investigation was weighed accurately and extracted into 50 ml chloroform with shaking. Filtration through a Whatman No. 42 filter paper was performed. The filtrate was evaporated to dryness under vacuum and the residue was taken up with ethanol and transferred to a 50 ml standard volumetric flask, diluting to volume. The assay was completed using the procedure described above.

Results and Discussion

Spectrophotometric determination of RAB and PAN drugs using KIO_3

The absorption spectra of the cyclohexane extract of the reaction of RAB and PAN drugs with KIO_3 in an acidic medium are represented graphically in Figure 1. The measured absorbance of the liberated iodine in cyclohexane has a maximum wavelength at 520 nm. Different experimental conditions affecting the development of the coloured product were taken into consideration and carefully controlled. An investigation of the effect of sulphuric acid solution on the formation and extraction of iodine in cyclohexane is shown in Figure 2A. It shows that 1 ml of 30% (v/v) sulphuric acid solution, in the presence of 1 mg ml^{-1} of either drugs, sufficient for complete oxidation of the drugs with KIO_3. The excess of H_2SO_4 concentration has no effect and the absorbance is nearly constant. In order to study the effect of time, samples are assayed and the absorbances are determined after varying the time intervals at room temperature as shown in Figure 2B. The results indicate that 25 minutes is the time required for completion of the oxidation process for both drugs. Figure 2C shows the effect of temperature on the colour reaction between RAB and PAN drugs with KIO_3 in acidic medium. The absorbance increased with the increase in temperature and became nearly constant at 25–30 °C. At higher temperatures the absorbance decreased, which may be attributed to loss of iodine at elevated temperatures. Figure 2D shows that 1 ml of 1% (w/v) KIO_3 is found to be the optimum reagent concentration.

In order to prove the validity and applicability of the proposed method and the reproducibility of the results obtained, five replicate experiments were carried out at four concentrations of

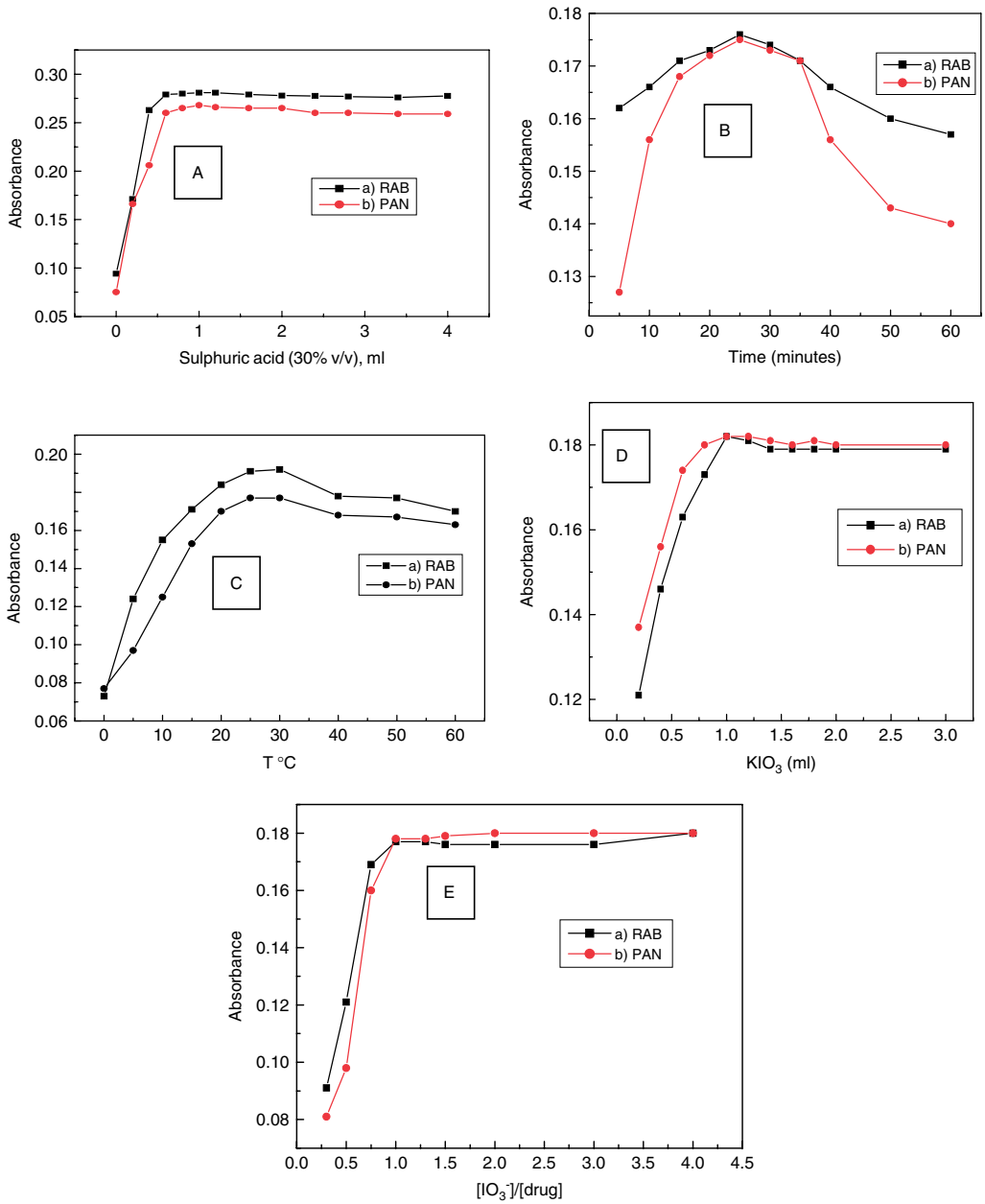


Figure 2. Effect of (A) sulphuric acid concentration (30%v/v); (B) time; (C) temperature; (D) KIO_3 concentration (1% w/v) and (E) stoichiometry using molar ratio method.

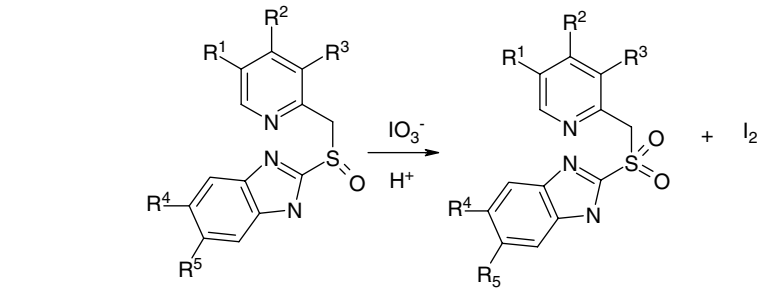
RAB and PAN. It was found that the between–day relative standard deviations for different concentrations of the drugs obtained from experiments carried out over a period of four days were less than 1% (Table 1), which indicates that the proposed method is highly reproducible and KIO_3 can be successfully applied to determine RAB and PAN drugs via the oxidative process. Applying the continuous variation and molar ratio methods at appropriate selected conditions, it was found that the ratio is equal to 1 : 1 (iodate : drug) as shown in Figure 2E. This stoichiometric ratio can be explained by the following redox reaction:[28]

$$2\,RSO + 2\,IO_3^- + 8\,H^+ \longrightarrow 2\,RSO_2 + 4\,H_2O + I_2$$

Hence, $1\,IO_3^- \equiv 1\,RSO \equiv 1/2I_2$

where RSO = RAB or PAN drugs, i.e. each mole of IO_3^- oxidizes one mole of either drug producing one mole of liberated iodine under selected optimal conditions (Scheme 1).

Under these conditions a linear correlation is obtained between absorbance (A) and concentration (C) of RAB and PAN over the concentration range from 10 to 400 ($r^2 = 0.9998$) and 5 to 400 $\mu g\,ml^{-1}$ ($r^2 = 0.9999$) for RAB and PAN, respectively. The apparent molar absorptivities, Sandell sensitivities and the regression line equations for each drug are tabulated in Table 2. The mean recovery values are ranged between 99.72–100.0% and 99.80–100% for RAB and PAN, respectively. The low values of the calculated standard deviation (SD = 0.017–0.446 and 0.019–0.129 for RAB and PAN, respectively) and relative standard deviation (RSD% = 0.006–0.559 and 0.007–0.501% for RAB and PAN drugs, respectively) indicate the high accuracy and precision



Scheme 1. Redox reaction of RAB and PAN drugs with KIO_3.

Table 1. Between– day precision for the determination of RAB and PAN drugs using KIO_3 reagent

Compound	[Drug] taken μg ml^{-1}	[Drug] found[a] μg ml^{-1}	% Recovery	SD	RSD(%)
RAB	50.00	49.98	99.96	0.089	0.178
	80.00	79.96	99.95	0.061	0.076
	130.0	130.0	100.0	0.098	0.075
	200.0	199.9	99.95	0.059	0.029
PAN	50.00	49.92	99.84	0.065	0.130
	80.00	79.96	99.95	0.089	0.111
	130.0	129.9	99.92	0.062	0.048
	200.0	200.0	100.0	0.081	0.041

[a] The average of five replicates.

Table 2. Analytical parameters for the determination of RAB and PAN drugs obtained by using KIO_3 reagent

Parameters	RAB	PAN
λ_{max} (nm)	520	520
Conc. Range (μg ml^{-1})	10–400	5–400
ϵ (l.mol^{-1}.cm^{-1})	1.34×10^3	1.64×10^3
Time (min)	25	25
T (°C)	25	25
[KIO_3] (ml)	1	1
Sandell Sensitivity (μg cm^{-2})	0.00284	0.00263
Slope	0.0006	0.0004
Intercept	0.0296	0.034
r^2	0.9998	0.9999
SD	0.017–0.446	0.019–0.129
RSD	0.006–0.559	0.007–0.501
LOD (μg ml^{-1})	6.76	5.699
LOQ (μg ml^{-1})	4.54	6.997

of the proposed method. The limits of detection (LOD) and limits of quantification (LOQ) were also calculated and their low values indicate the sensitivity of the proposed method. The proposed method can be applied successfully to the pharmaceutical preparations of the drugs that were studied. Table 3 shows the results obtained during the determination of RAB and PAN drugs in the dosage forms. The results are compared with those obtained by applying the official methods for PAN[29] and RAB[30] drugs. The results obtained were compared statistically by their percentage recovery with those obtained by official method on samples of the same batch. It is clear from the data listed in Table 3 that the percentage recovery values obtained using the proposed method (99.51–99.90 and 99.95–100.0) are higher than those obtained using the official method (98.50 and 98.94%) for RAB and PAN, respectively. There is no significant difference between accuracy and precision of the proposed and the official methods.

Spectrophotometric determination of OMP, RAB and PAN via ion-pair formation

Omeprazole, RAB and PAN form ion-pair complexes in an acidic buffer with dyestuffs such as bromocresol purple (BCP), bromophenol blue (BPB) and bromocresol green (BCG) and these complexes are quantitatively extracted into 1,2–dichloroethane. The absorption spectra of the ion-pair complexes extracted into 1,2–dichloroethane are shown in Figures 3A–C. These figures show that the ion–pairs of OMP attain their maxima at 385 and 570 nm with BPB, 400 and 570 nm with BCG and 400 nm with BCP.

As for RAB, λ_{max} is found to be at 405 and 570 nm with BPB, 405 and 560 nm with BCG and at 405 and 520 nm with BCP. Ion-pairs of PAN show maximum absorbance at 570 nm with BPB, 405 and 580 nm with BCG and at 395 nm with BCP reagent. The reagent blank under similar conditions showed no absorption.

The effect of solvents on the extraction and absorbance of the ion pairs formed was studied using different solvents. The results indicated that 1,2-dichloroethane, methylene chloride and chloroform can be used for the extraction of the ion pairs formed and 1,2-dichloroethane was chosen for having the highest molar absorptivity. Figure 4A shows the increase in absorbance with time up to 40 minutes for OMP with BPB, BCG and BCP reagents. The optimum time for the completion of the reaction of RAB with BPB or BCP was 20 minutes and 40 minutes with BCG (Figure 4A). For PAN, it was 40 minutes with BCG or BCP and 30 minutes with BPB (Figure 4A). The absorbance values remained almost unchanged with increasing time. The results indicate that ion pairs needed these time intervals for their complete formation. The absorbance of the extracted ion–pairs was measured at different temperatures in the range from 0 to 60 °C. The results show that the absorbance generally increased with an increase in temperature and attained maximum value at 40 °C for OMP, RAB or PAN drugs using BPB, BCG or BCP reagents. The temperature is slightly increased or decreased above this temperature (Figure 4B).

Table 3. Determination of RAB and PAN drugs in pharmaceutical preparations using KIO_3 reagent

		Proposed		Official			
		[Drug] μg ml^{-1}		[Drug] mg ml^{-1}		% Recovery ± SD	
Drug	**Name of Preparation**	*Taken*	*Found*	*Taken*	*Found*	*Proposed*	*Official*
RAB	Pariet	80	79.61	50	49.25	99.51 ± 0.046	98.50 ± 0.063
		200	199.8			99.90 ± 0.045	
PAN	Pantopi	80	80.03	200	197.88	100.0 ± 0.11	98.94 ± 0.448
		200	199.9			99.95 ± 0.08	

• RSD (n = 4) = 0.023–0.058% and 0.040–0.137% for RAB and PAN, respectively, using the proposed method.
• RSD (n = 4) = 0.128 and 0.226% for RAB and PAN drugs, respectively, using the official methods.

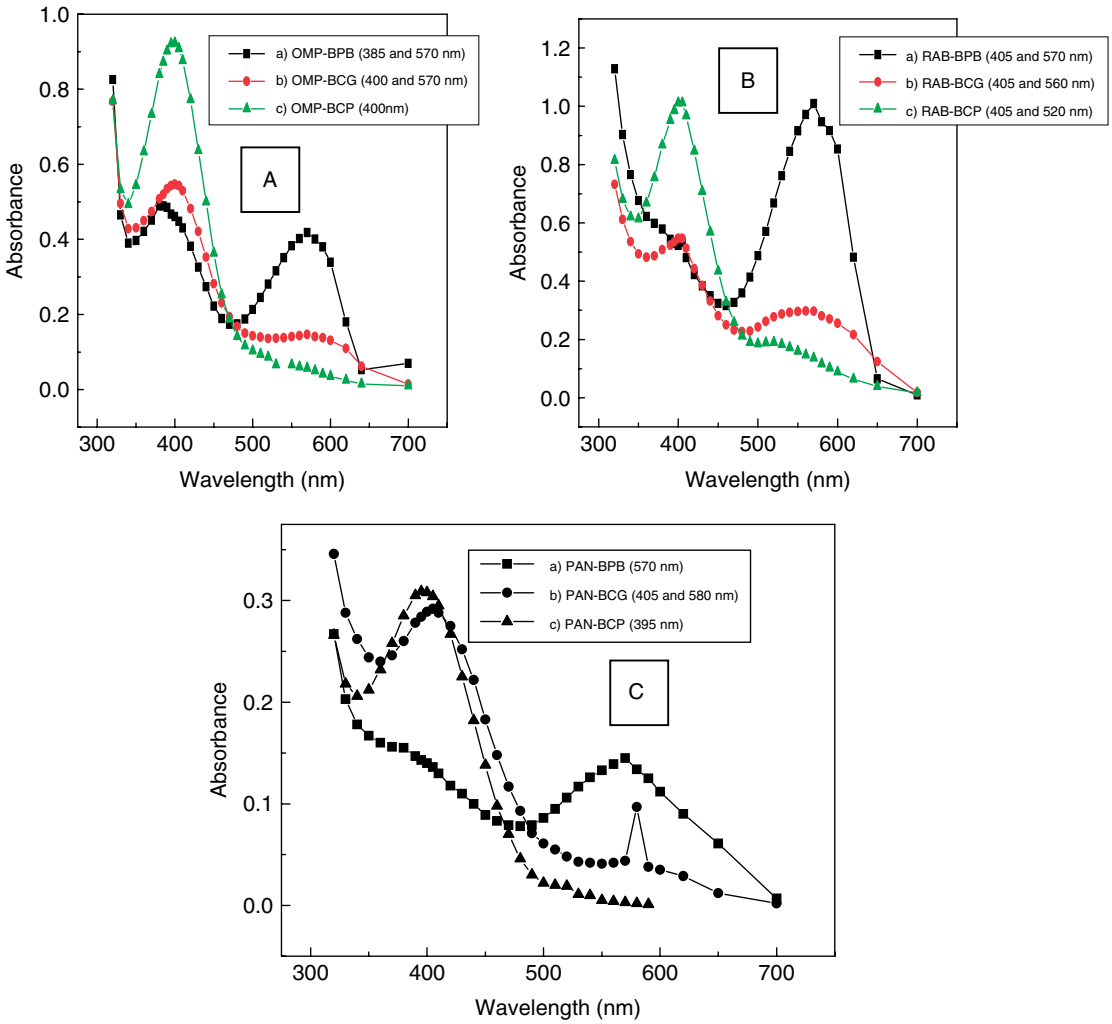


Figure 3. Absorption spectra of (A) OMP-; (B) RAB- and (C) PAN-ion-pairs using BPB, BCG and BCP reagents.

The concentrations of OMP, RAB and PAN were kept constant (20 μg ml^{-1}) and the concentrations of BPB, BCG and BCP reagents were varied from 0.1–2.5 ml (0.02% w/v). It was found that 1.75, 1.5 and 1.0; 1.5 and 1.5 and 1.0, and 1.0, 1.0 and 1.0 ml of BPB, BCG or BCP reagents, respectively, were sufficient for complete reaction with OMP, RAB and PAN (Table 4). The ion–pairs were found to be formed in an acidic medium in the pH range from 4–5 and specifically at pH = 4.6 for OMP, RAB and PAN with BPB, BCG or BCP reagents (Table 4).

In order to establish the molar ratio between diltiazem hydrochloride and the dyestuffs used, the continuous variation[31] and molar ratio[32] methods were applied. In these methods, solutions of drugs and dyestuff with identical molar concentrations were mixed in varying volume ratios or in such a way that the total volume of each mixture was the same. The absorbance of each solution was measured and plotted against the molar ratio of the drugs, [drugs]:[dyestuff] (Figure 4C). These measurements showed that 1 : 1 complexes were formed with each dyestuff.

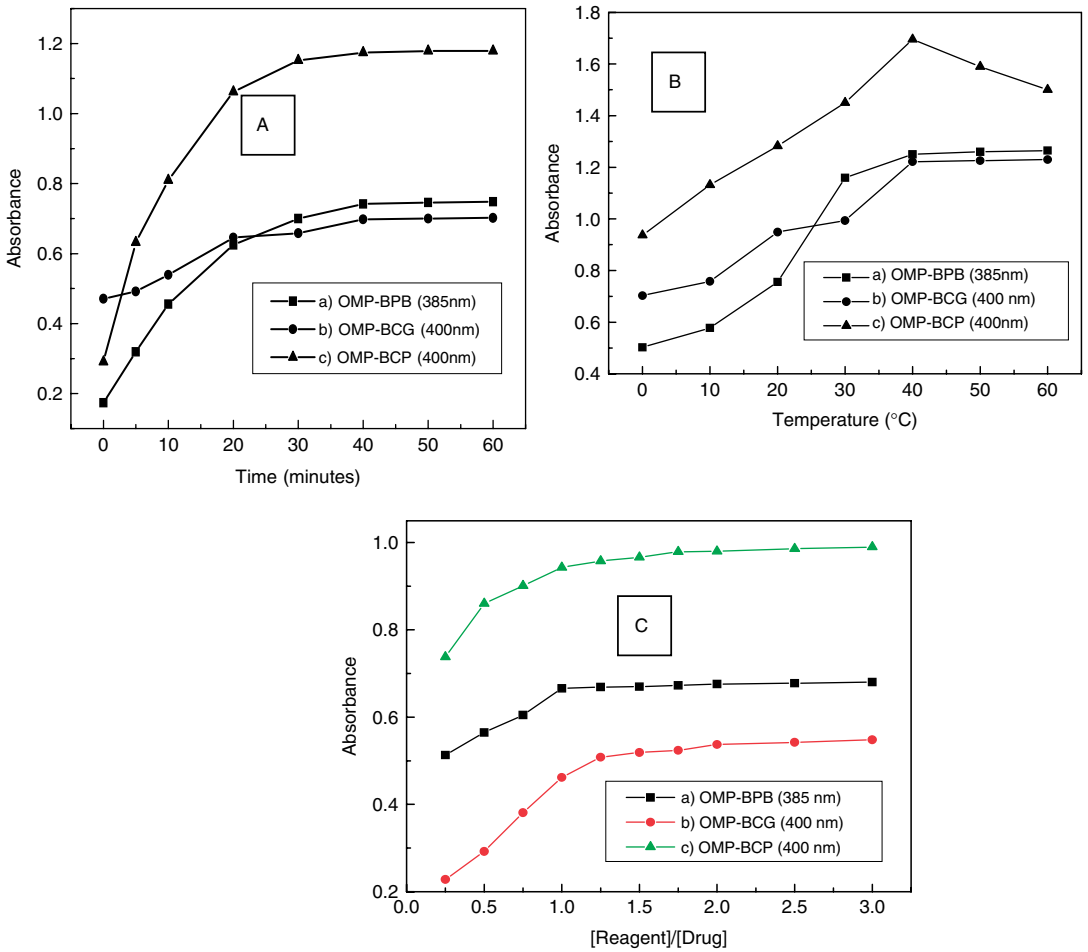


Figure 4. Effect of (A) time; (B) temperature and (C) stoichiometric ratio using molar ratio method.

Omeprazole, RAB and PAN contained a tertiary amino group, which is protonated in an acid medium, while a sulfonic acid group is present in BTB; that was the only group undergoing dissociation in the pH range 1–5. Bromophenol blue, BCG and BCP are examples of sulfonephthalein types of dye. The colour of such dyes is due to the opening of the lactoid ring and the subsequent formation of the quinoid group. It is supposed that the two tautomers are present in equilibrium but, due to the strongly acidic nature of the sulfonic acid group, the quinoid body predominates. Finally the protonated drugs, OMP^+, RAB^+ or PAN^+, form ion pairs with the dyestuffs, which are quantitatively extracted into 1,2-dichloroethane. Possible reaction mechanisms are given in Scheme 2.[33]

Validity of Beer's law

Under the above conditions of the proposed method, Beer's law was obeyed over the concentration range from 10–50, 10–150 and 10–250 μg ml^{-1} for OMP, RAB and PAN, respectively, using the BPB reagent. Using the BCG reagent, the concentration ranges were found to be 10–60 μg ml^{-1} for OMP and 10–150 μg ml^{-1} for both RAB and PAN drugs. Finally, using the BCP reagent, the concentration ranges were found to be 5–40, 10–60 and 10–100 μg ml^{-1} for OMP, RAB and PAN drugs, respectively (Table 4). The linear regression equations, Sandell's sensitivity and the correlation coefficient are tabulated in Table 4. In order

Table 4. Analytical parameters for the determination of OMP, RAB and PAN drugs using BPB, BCG and BCP reagents

Drugs	Parameters	BPB	BCG	BCP
OMP	λ_{max} (nm)	385	400	400
RAB		405	405	405
PAN		570	405	395
OMP	[Drug] (μg ml^{-1})	10–60	10–60	5–40
RAB		10–150	10–150	10–60
PAN		10–250	10–150	10–100
OMP	∈ ($l.mol^{-1}.cm^{-1}$)	4.56×10^3	5.80×10^3	
RAB		4.73×10^3	3.00×10^3	7.86×10^3
PAN		1.30×10^3	2.90×10^3	12.00×10^3
				4.30×10^3
OMP	Time (min)	40	40	40
RAB		20	40	20
PAN		30	40	40
OMP	T (°C)	40	40	40
RAB		40	40	40
PAN		40	40	40
OMP	pH	4.6	4.6	4.6
RAB		4.6	4.6	4.6
PAN		4.6	4.6	4.6
OMP	[Reagents] (mL)	1.75	1.5	1

Table 4. (*Continued*)

Drugs	Parameters	BPB	BCG	BCP
RAB		1.5	1.5	2
PAN		1	1	1
OMP	Sandell Sensitivity	0.0076	0.0060	0.0044
RAB	($\mu g\ cm^{-2}$)	0.0081	0.00127	0.0032
PAN		0.003226	0.00151	0.00101
OMP	Linear relation: Slope	0.014	0.016	0.023
RAB		0.0103	0.0071	0.0292
PAN		0.003	0.007	0.009
OMP	Intercept	0.008	0.008	−0.00213
RAB		0.021	0.008	0.018
PAN		0.0011	−0.0006	0.0093
OMP	r^2	0.9999	0.9999	0.9999
RAB		1.00	0.9992	0.9998
PAN		0.9993	0.9999	0.9998
OMP	SD	0.024–0.093	0.021–0.520	0.073–0.154
RAB		0.013–0.120	0.014–0.500	0.034–0.560
PAN		0.017–0.220	0.018–0.130	0.026–0.550
OMP	RSD	0.060–0.899	0.085–1.494	0.300–1.531
RAB		0.010–0.300	0.023–0.399	0.057–1.404
PAN		0.011–0.367	0.025–0.391	0.032–1.196
OMP	LOD ($\mu g\ ml^{-1}$)	0.77	1.00	0.46
RAB		1.19	1.85	1.30
PAN		7.96	1.34	1.65
OMP	LOQ ($\mu g\ ml^{-1}$)	2.57	3.33	1.52
RAB		3.97	6.16	3.75
PAN		8.53	4.76	5.51

to prove the validity and applicability of the proposed method and the reproducibility of the results obtained, five replicate experiments were carried out at two concentrations of OMP, RAB and PAN. It was found that the between–day relative standard deviations for different concentrations of the drugs obtained from experiments carried out over a period of four days were less than 1%, (Table 5), which indicates that the proposed method is highly reproducible and can be successfully applied to determine the studied drugs via ion pair formation. The limit of detection (LOD) does not exceed 7.96 $\mu g\ ml^{-1}$ for all the proposed chelates whereas the limit of quantitation (LOQ) was between 1.52 and 8.53 $\mu g\ ml^{-1}$ (Table 4).

Application

The validity of the proposed method was tested for the determination of OMP, RAB and PAN in dosage forms manufactured by local companies. The concentration of the drugs in the dosage forms was calculated from the appropriate calibration graphs. The determination of drugs in the dosage forms was compared with those obtained by applying the official methods for OMP,[34] PAN,[29] and RAB[30] (Table 6). The results obtained were compared statistically for percentage recovery with those obtained by official method on samples of the same batches and by means of F-tests and *t*-tests at the 95% confidence level. In all cases, the average results obtained by the proposed methods and the reference method were statistically identical, as the difference between the average values had no significance at 95% confidence level. The proposed methods are simple, sensitive and reproducible and can be used for routine analysis of OMP, RAB and PAN drugs in pure form and in formulations.

Table 5. Between–day precision for the determination of OMP, RAB and PAN drugs using (a) BPB, BCG and (c) BCP reagents

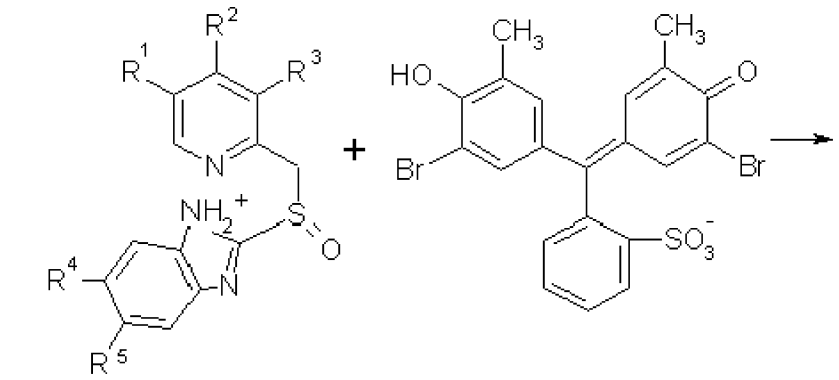
Compound	[Drug] taken $\mu g\ ml^{-1}$	[Drug] found[a] $\mu g\ ml^{-1}$	% Recovery	SD	RSD(%)
(a) using BPB					
OMP	40.00	39.96	99.90	0.074	0.185
	100.0	99.99	99.99	0.134	0.134
RAB	40.00	40.04	100.1	0.270	0.674
	80.00	80.04	100.1	0.200	0.249
PAN	10.00	10.02	100.2	0.140	1.397
	100.0	99.99	99.99	0.110	0.110
(b) using BPB	20.00	19.97		0.110	0.551
OMP	50.00	49.94	99.85	0.090	0.180
			99.88		
RAB	50.00	49.98	99.96	0.083	0.166
	100.0	99.96	99.96	0.102	0.102
	50.00	49.98	99.96	0.140	0.280
PAN	80.00	79.98	99.98	0.090	0.113
(c) using BPB	10.0	9.990	99.90	0.073	0.730
OMP	50.0	50.12	100.2	0.400	0.798
RAB	20.0	19.99	99.95	0.080	0.400
	40.0	39.82	99.55	0.360	0.900
PAN	10.0	10.09	100.9	0.078	0.773
	50.0	49.97	99.94	0.103	0.206

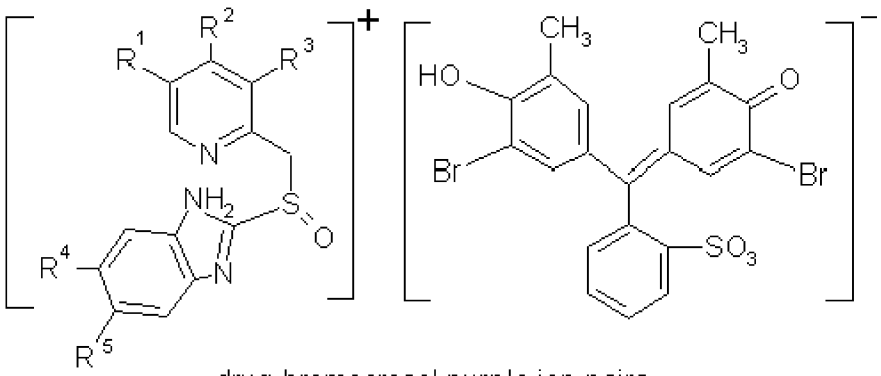
[a] The average of five replicates.

Conclusion

Only OMZ can be determined by non-selective titrimetric official method with standard NaOH in the British Pharmacopoeia.[2] Most of the reported methods are HPLC,[5–11] which requires complicated instrumentation. The electrochemical methods are less sensitive.[4,16] In addition the conventional UV methods[19,20] suffer from interference due to UV absorbing compounds in the determination of the drugs being studied. The few reported visible spectrophotometric methods are mainly concerned with charge transfer complexation with different electron acceptors, which give similar reactions with all basic compounds, or are concerned with the reducing activity of OMZ[21–23] or metal chelate formation,[26] where the linear range is narrow compared with the proposed methods.

As a general conclusion, the two spectrophotometric methods can readily be used for routine analysis in bulk form and in pharmaceutical formulations as they offer simple systems with short analytical time, good reproducibility and accuracy. It is obvious from the results that RAB and PAN drugs can be determined in a wider concentration range via an oxidation reaction with KIO_3 reagent (10–400 and 5–400 $\mu g\ ml^{-1}$ for RAB and PAN, respectively) rather than using the ion-pair formation reaction. So the oxidation process using KIO_3 is more sensitive to low concentration of the drugs than the ion-pair process.





In case of OMP: $R^1 = R^3 = Me$; $R^2 = R^5 = OMe$ and $R^4 = H$.

In case of RAB: $R^1 = R^4 = R^5 = H$; $R^2 = O(CH_2)_3OCH_3$ and $R^3 = Me$.

In case of PAN: $R^1 = R^5 = H$; $R^2 = R^3 = OMe$ and $R^4 = F_2CHO$.

Scheme 2. Structure of OMP-, RAB- and PAN-reagents ion-pairs.

Table 6. Determination of OMP, RAB and PAN drugs in pharmaceutical preparations using BPB reagent

Drug	Name of Preparation	Proposed [Drug] µg ml^{-1} Proposed method		Official [Drug] mg ml^{-1} Official method		% Recovery ± SD	
		Taken	*Found*	*Taken*	*Found*	*Proposed*	*Official*
(a) using BPB OMP	Omepak	30.00	29.94	100.0	99.16	99.80 ± 0.110	99.16 ± 0.286
		50.00	49.99			99.98 ± 0.140	
RAB	Pariet	30.00	29.95	50.00	49.25	99.83 ± 0.112	98.50 ± 0.063
		70.00	69.97			99.96 ± 0.102	
PAN	Pantopi	70.00	69.99	200.0	197.9	99.99 ± 0.160	98.95 ± 0.448
		100.0	99.90			99.90 ± 0.150	
(b) using BCG OMP	Omepak	30.00	29.98	100.0	99.16	99.93 ± 0.104	99.16 ± 0.286
		50.00	49.97			99.94 ± 0.090	
RAB	Pariet	10.00	9.970	50.00	49.25	99.70 ± 0.060	98.50 ± 0.063
		60.00	59.92			99.87 ± 0.090	
PAN	Pantopi	20.00	19.99	200.0	197.9	99.95 ± 0.160	98.95 ± 0.448
		100.0	99.85			99.85 ± 0.210	

Table 6. (*Continued*)

Drug	Name of Preparation	Proposed [Drug] μg ml^{-1} Proposed method Taken	Proposed [Drug] μg ml^{-1} Proposed method Found	Official [Drug] mg ml^{-1} Official method Taken	Official [Drug] mg ml^{-1} Official method Found	% Recovery ± SD Proposed	% Recovery ± SD Official
(c) using BCP	Omepak	10	9.97	100	99.16	99.70 ± 0.130	99.16 ± 0.286
OMP		20	19.99			99.95 ± 0.103	
RAB	Pariet	20	19.93	50	49.25	99.67 ± 0.120	98.50 ± 0.063
		40	39.95			99.88 ± 0.160	
PAN	Pantopi	10	10.05	200	197.9	100.5 ± 0.180	98.95 ± 0.448
		30	29.80			99.33 ± 0.360	

• RSD (%) for the proposed method is 0.280–0.368, 0.146–0.374 and 0.150–0.229 for OMP, RAB and PAN drugs, respectively. RSD (%) for the proposed method is 0.180–0.347, 0.150–0.602 and 0.210–0.800 for OMP, RAB and PAN drugs, respectively. RSD (%) for the proposed method is 0.515–1.303, 0.401–0.602and 1.208–1.790 for OMP, RAB and PAN drugs, respectively.
• RSD (%) for the official method is 0.288, 0.128 and 0.226 for OMP, RAB and PAN drugs, respectively. RSD (%) for the official method is 0.288, 0.128 and 0.226 for OMP, RAB and PAN drugs, respectively. RSD (%) for the official method is 0.288, 0.128 and 0.226 for OMP, RAB and PAN drugs, respectively.

References

[1] M. E Wolff (Ed.), *Burger's Medicinal Chemistry and Drug Discovery vol. 2*, Therapeutic Agents, 5th ed., Wiley: New York, **1996**, Chapter 27.
[2] *British Pharmacopoeia*, HMSO: London, **1993**, p. 1590.
[3] *The Merck Index*, 12 edn, Merck & Co. Inc.: Whitehouse Station, NJ, **1996**, pp. 6977–7149.
[4] S McClean, E Okane, V. N Ramachandran, W. F Smyth, *Anal. Chim. Acta* **1994**, *292*, 81.
[5] A Brandstrom, N.-A Bergman, P Lindberg, I Grundevik, S Johansson, L Tekenbergs-Hjelte, K Ohlson, *Acta Chem. Scand.* **1989**, *43*, 549.
[6] M Mathew, V Das Gupta, R. E Bailey, *Drug Dev. Ind. Pharm.* **1995**, *21*(8), 965.
[7] A Ekpe, T Jacobsen, *Drug Dev. Ind. Pharm.* **1999**, *25*(9), 1057.
[8] X. Y Xu, J. H Lu, M. L Wang, C Xu, R. L Wang, L. Y He, *Yaowu-Fenxi-Zazhi* **1997**, *17*(3), 169.
[9] G. W Sluggett, J. D Stong, J. H Adams, Z Zhao, *J. Pharm. Biomed. Anal.* **2001**, *25*(34), 357.
[10] M Tanaka, H Yamazaki, *Anal. Chem.* **1996**, *68*(9), 1513.
[11] A El-Gindy, F El-Yazby, M. M Maher, *J. Pharm. Biomed. Anal.* **2003**, *31*(2), 229.
[12] S Ray, P Kumar, *Indian Drugs* **1994**, *31*(11), 543.
[13] S Mangalan, R. B Patel, B. K Chakravarthy, *J. Planar Chromatogr. Mod. TLC* **1991**, *4*(6), 492.
[14] Y Zhang, X. Y Chen, Q Gu, D. F Zhong, *Anal. Chim. Acta* **2004**, *523*(2), 171.
[15] J. C Huang, Y Xu, S Gao, L Rui, Q. X Guo, *Rapid Commun. Mass Spectrom.* **2005**, *19*(16), 2321.
[16] E. X Cao, Y. H Zeng, *Fenxi Kexue Xueboa* **2001**, *17*(2), 110.
[17] A Tivesten, S Folestad, V Schonbacher, K Svensson, *Chromatographia* **1999**, *49*, (suppl. 1), 57.
[18] N Ozaltin, A Kocer, *J. Pharm. Biomed. Anal.* **1997**, *16*(2), 337.
[19] S. N Dhumal, P. M Dikshit, I. I Ubharay, B. M Mascaren has, C. D Gaitonde, *Indian Drugs* **1991**, *28*(12), 565.
[20] C. V Garcia, J Sippel, L. L Sfair, S. S Garcia, A Jablonski, M Steppe, E. E. S Schapoval, *J. AOAC. Int.* **2005**, *88*(4), 1081.
[21] N. M EL-Kousy, L. I Bebawy, *J. AOAC Int.* **1999**, *82*(3), 599.
[22] A. A. M Moustafa, *Bull. Fac. Pharn. Cairo Univ.* **1999**, *37*(2), 9.
[23] C. S. P Sastry, P. Y Naidu, S. S. N Murty, *Talanta* **1997**, *44*(7), 1211.
[24] K Karljikovic-Rajic, D Novovic, V Marinkovic, D Agbaba, *J. Pharm. Biomed. Anal.* **2003**, *32*(4–5), 1019.
[25] A El-Gindy, F El-Yazby, M. M Maher, *J. Pharm. Biomed. Anal.* **2003**, *31*(2), 229.
[26] F Salama, N El-Abasawy, S. A. A Razeq, M. M. F Ismail, M. M Fouad, *J. Pharm. Biomed. Anal.* **2003**, *33*(3), 411.
[27] J. E Collector, *Ann. Chim.* **1960**, *5*, 415.
[28] Z. A El Sherif, M. A El-Ries, *J. Drug Res. Egypt* **2000**, *23*, 105.
[29] N Rahman, S. N Hejaz-Azmi, *J. Pharm. Biomed. Anal.* **2000**, *24*, 33.
[30] *Analytical Profile of Drug Substances and Excipients* Ed. K. Florey, **2002**, 29, 213.
[31] P Jop, *Ann. Chim.* **1928**, *9*, 133.
[32] J. H Yoe, A. L Jones, *Indust. Eng. Chem. Anal. Ed.* **1944**, *16*, 14.
[33] N Rahman, S. N Hejaz-Azmi, *J. Pharm. Biomed. Anal.* **2000**, *24*, 33.
[34] *British Pharmacopeia*, Stationery Office: London, **2007**, Vol. II, 1521.