Research Article

Drug Testing and Analysis

Received: 15 August 2009 Revised: 24 October 2009 Accepted: 29 November 2009 Published online in Wiley Interscience: 9 February 2010

(www.drugtestinganalysis.com) DOI 10.1002/dta.103

A sensitive spectrophotometric method for the determination of propranolol HCl based on oxidation bromination reactions

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Three new, simple, sensitive, rapid and economical spectrophotometric methods (A, B and C) have been developed for the determination of propranolol hydrochloride (PRO) in bulk drug and dosage forms. These methods are based on oxidation-bromination reaction of PRO by bromine, generated *in situ* by the action of acid on a bromate-bromide mixture, followed by determination of unreacted bromine by three different reaction schemes. In method A, the determination of the residual bromine is based on its ability to bleach the indigo carmine dye and by measuring the absorbance at 610 nm. The residual bromine (in method B), is treated with excess of iron(II) and the resulting iron(III) is complexed with thiocyanate and the absorbance is measured at 480 nm. Method C involves treating the unreacted bromine with a measured excess of iron(II) and the remaining iron(II) is complexed with 1,10-phenanthroline and the increase in absorbance is measured at 510 nm. In all three methods, the amount of bromine reacted corresponds to the drug content. The different experimental parameters affecting the development and stability of the colour are carefully studied and optimized. Beer's Law is valid within a concentration range of 1–13, 4–12 and 2–9 μg ml^{-1} for methods A, B, and C, respectively. The molar absorptivity, Sandell's sensitivity, detection and quantification limits are calculated. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed methods. The proposed methods have been successfully applied to the determination of PRO in pharmaceutical preparations and the results were statistically compared with those of the official method by applying the Student's *t*-test and F-test.

Keywords: propranolol; spectrophotometry; bromate-bromide mixture; redox reactions; pharmaceutical formulations

Introduction

Propranolol (PRO), 1-[isopropylamino-3-[1-naphthyloxy]-2-propanol], is a β-adrenoceptor antagonist (β-blocker), which is widely used in the treatment of several diseases, such as cardiac arrhythmia, angina pectoris, sinus tachycardia, thyrotoxicosis, hypertrophic subaortic stenosis, and hypertension.[1] PRO is commercially employed in the form of hydrochloride and has also been suggested for use in a number of other conditions including dysfunctional labour and anxiety.[2] Because it is also used in low activity sports as a doping agent, which acts reducing cardiac frequency and contraction force, the International Olympic Committee included it in its list of forbidden substances. The assay procedures of propranolol in pure form and in pharmaceutical preparations listed in USP 24 NF 19,[3] and BP,[4] described potentiometric titration, spectrophotometric, and chromatographic methods.

The analytical techniques used to determine propranolol in pharmaceuticals and in biological fluids such as high performance liquid chromatography (HPLC),[5–7] are tedious, time-consuming, and require special and expensive apparatus. The other chromatographic methods, gas chromatography,[8,9] liquid chromatography,[10–12] and thin layer chromatography,[13] although simpler than HPLC methods, are less sensitive. Non-chromatographic methods such as UV derivative spectroscopy,[14,15] spectrofluorimetry,[16–20] flow injection-chemiluminescence,[21] capillary electrophoresis,[22–27] polarography,[28,29] and voltammetric,[30] are also relatively complicated in terms of assay procedure or the equipment required for analysis and are costly. Spectrophotometric techniques continue to be the most preferred method for routine analytical work because of their simplicity and reasonable sensitivity with significant economical advantages. Hence, many of spectrophotometric methods have been described for the determination of PRO.[31–42] Most of these methods suffer from limitations (Table 1). For instance, these involve low sensitivity,[31,39] the use of organic solvent and long standing for colour development,[32,37,40] or solvent extraction.[33]

The aim of this work is to develop simple, low-cost, sensitive, and diversely applicable indirect spectrophotometric methods for the determination of propranolol hydrochloride. These methods are based on the oxidation-bromination of PRO by bromine, generated *in situ* by the action of HCl on bromate-bromide mixture. Moreover, the proposed methods are free from interference by common additives and excipients. These merits, in addition to the use of simple reagents, suggest their utility for routine quality control.

Experimental

Apparatus

All the absorbance spectral measurements were made using spectroscan 80 D double-beam UV/Visible spectrophotometer

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Table 1. Comparison of the proposed methods with the reported methods for the determination of PRO

Reagent(s) Used	$\lambda_{max,\ nm}$	Beer's law Limit, $\mu g ml^{-1}$	Molar absorptivity, $\times 10^4$, $l.mol.^{-1}\ cm^{-1}$	Remark	Ref.
NBS, metol and INH in acetic acid medium	620	1.6–14	0.949	Absorbances were recorded after 30 min; the method has low sensitivity.	31
NBS and Celestine blue	540	0.4–3.0	4.29	Reaction mixture was allowed to stand for 10–20 min, in the first step and 20 min for the second step.	32
Carbon disulphide	435.4	40–60	0.689	Involved extraction and low sensitivity.	33
Iodine and π-acceptors	365–480	4–200	0.583–2.29	Uses organic solvent such as 1,2-dicloroethane, ethanol, acetonitrile and the reaction mixture required 5–40 min for complete colour development.	37
3-methylbenzothiazoline-2-one hydrazone	496	–	0.32	The method has low sensitivity and reaction mixture required 30 min for colour intensity reached a maximum.	39
Cu (II) and Co(II)	548, 614	–	0.0016, 0.0050	Reaction time required 15–60 min and uses organic solvent, DMSO.	40
B-BrO_3^- - Br^--Indigo carmine	610	1–13	3.42	No heating or extraction step involved, shorter contact time, more sensitive.	This work
C-BrO_3^- - Br^--Fe(III)-thiocyanate	480	4–12	8.8		This work
D-BrO_3^- - Br^--Fe(II)-1,10-phenanthroline	510	2–9	3.91		This work

(Biotech Sedico (Scientific Equipment Distribution) Ltd. Nicosia, Cyprus.), with wavelength range 190 nm ~ 1100 nm, spectral bandwidth 2.0 nm, with 10 mm matched quartz cells. An Orion Research Model 601 A/digital analyzer, pH-meter with a combined saturated calomel glass electrode was used for pH measurements.

Reagents and materials

All reagents and chemicals used were of analytical or pharmaceutical grade and all solutions were prepared fresh daily.

1. Standard solution of PRO
   Pharmaceutical grade propranolol hydrochloride was received from Kahira Pharmaceutical Company (Cairo, Egypt) which was reported to be 99.8% purity, as a gift and was used as received. A stock standard solution containing 20 mg of PRO was prepared by dissolving the weighed amount in distilled water. The solution of PRO (200 $\mu g\ ml^{-1}$) was diluted stepwise to obtain working concentration of 100 $\mu g\ ml^{-1}$.
2. Indigo carmine
   A 5×10^{-4} M of indigo carmine (Aldrich, Sigma-Aldrich Chemie, Steinheim, Germany.) was prepared by dissolving 23.31 mg of dye (98% purity) in water and diluting to 100 ml in a calibrated flask.
3. Bromate – bromide mixture
   A bromate-bromide solution equivalent 100 $\mu g\ ml^{-1}$ $KBrO_3$ and 10-fold excess of KBr was prepared by dissolving accurately weighed 10 mg of $KBrO_3$ and 0.1 g of KBr in water and diluting to the mark in a 100 ml calibrated flask.
4. Hydrochloric acid
   A 2.0 M of HCl was prepared by diluting 41.8 ml of concentrated acid (Merck, Darmstadt, Germany, sp. gr. 1.18, %37) to 250 ml with water.
5. Ammonium ferrous sulphate (AFS)
   A stock solution of 5×10^{-3} M AFS was freshly prepared by dissolving 0.1961 g from $(NH_4)_2Fe(SO_4)_2.6H_2O$ of the salt (Merck, Darmstadt, Germany) in 20 ml water containing 1.0 ml of 1.0 M H_2SO_4 and diluted to 100 ml with distilled water.
6. 1,10-phenanthroline
   A 0.2% of 1,10-phenanthroline monohydrate (Sigma Chemical Company, St Louis, MO, USA) solution was made up by dissolving the solid in 1.0 ml of 2.0 M HCl and diluted to 100 ml with water.
7. Ammonium thiocyanate
   A 1.0 M ammonium thiocyanate was prepared by dissolving 7.6666 g of the chemical (Merck, Darmstadt, Germany) in 100 ml water.
8. Ammonia solution
   A 1 : 1 ammonia solution was prepared by diluting 50 ml of strong ammonia with 50 ml of water.

Recommended Procedures and Calibration Curve

Method A: using indigo carmine

Aliquot of a standard solution of PRO (0.1, 0.3, 0.5, …. 1.3 ml, 100 $\mu g\ ml^{-1}$) was transferred into a series of 10 ml calibrated flasks. Then, 1.0 ml of 2.0 M HCl and 1.0 ml of bromate-bromide (100 $\mu g\ ml^{-1}$ in $KBrO_3$) solution was added and the mixture was left to stand for 5 min, with occasional shaking. Later 2.0 ml of 5×10^{-4} M indigo carmine was added to each flask and diluted to the mark with water. The absorbance was measured at 610 nm against reagent blank treated similarly, after 5 min. The amount of drug present in each pharmaceutical preparation was computed from the corresponding calibration graph or regression equation.

Method B: using thiocyanate

Into a series of 10 ml volumetric flasks, different aliquots (0.1, 0.2, 0.3, ... 1.2 ml, 100 μg ml^{-1}) of standard PRO solution were transferred using a micro burette. The solution was acidified by adding 1.0 ml of 2.0 M HCl and 1.4 ml of bromate-bromide (100 μg ml^{-1} in $KBrO_3$) solution was then added to each flask. The flasks were kept aside for 5 min, with periodic shaking. Then, 1.0 ml of 5×10^{-3} M AFS was added and mixed well. After 5 min, 2.2 ml of 1.0 M ammonium thiocyanate solution was added to each flask and the volume was brought up to the mark with distilled water. Absorbance was measured after 5 min at 480 nm against water blank. The calibration graph was drawn by plotting the decrease in the absorbance of thiocyanate complex against the amount of the drug. The amount of drug in each sample was calculated either from the calibration graph or the regression equation.

Method C: using 1,10-phenanthroline

Aliquots of standard drug solution (0.1, 0.2, 0.3, ... 0.9 ml of PRO, 100 μg ml^{-1}) were transferred into a series of 10 ml calibrated flasks, containing 1.0 ml of 2.0 M HCl and 1.0 ml of the bromate-bromide mixture (100 μg ml^{-1} in $KBrO_3$). The contents were mixed well and the flasks were allowed to stand for 5 min before adding 0.6 ml of 5×10^{-3} M AFS. After 5 min, 1.2 ml of 0.2% of 1,10-phenanthroine and 1.0 ml of 1 : 1 ammonia solution were added. The solutions in the calibrated flasks were made up to 10 ml with distilled water. The absorbance of the coloured product of oxidation was measured at 510 nm against the reagent blank treated similarly, after 10 min. The amount of drug in the sample was estimated from its calibration curve or regression equation.

Assay of Pharmaceutical Formulations

Tablets containing propranolol HCl, Inderal 10 and 40 labelled to contain 10 mg and 40 mg of propranolol hydrochloride per tablet, respectively. Ampoules containing propranolol HCl, Inderal ampoules labelled to contain 1.0 mg of propranolol HCl per ampoule. Tablets and ampoules were obtained from the local market.

Procedure for the tablets

Twenty tablets of drug were accurately weighed, finely powdered, and the average weight of tablet calculated. A portion of the powder equivalent to 20 mg of the PRO was dissolved in distilled water. The solution was filtered through Whatmann filter paper No. 42 and the filtrate was made up to 100 ml with distilled water. An aliquot of the solution was analyzed as described earlier.

Procedure for ampoules

The contents of 15 ampoules were mixed. An accurately measured volume of the solution equivalent to 10 mg was transferred into a 100 ml calibrated flask. It was completed to the mark with distilled water. The solution was then treated as described in recommended procedures. Determination of the nominal content of the ampoules was achieved either from the calibration curve or using the regression equation.

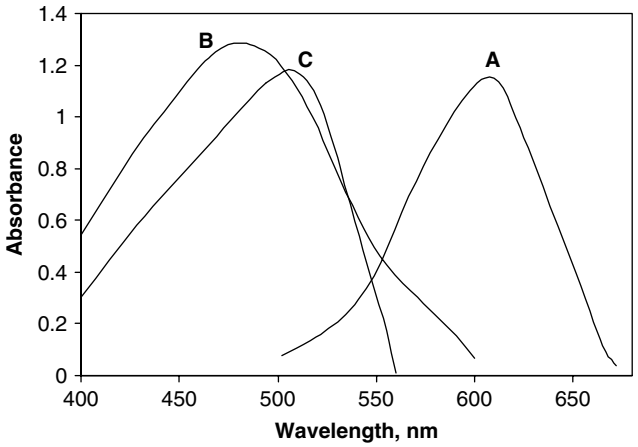

Figure 1. Absorption spectra of the oxidation product of PRO by bromate-bromide mixture with: (A) indigo carmine, (B) thiocyanate and (C) 1,10-phenanthroline.

Results and Discussion

Aqueous bromine solutions are unstable because of the high vapor pressure of bromine. Therefore, bromate-bromide mixture has been used for a long time as a way of generating bromine for analytical application and a number of bromination reactions have been used in the analysis of several pharmaceuticals.[43–49] The determination of PRO is based on oxidation-bromination reaction by a known excess of bromate in acid medium and in the presence of excess of bromide, followed by estimation of residual bromine by three different reaction schemes.

Optimization of the reaction conditions

The optimum conditions for the colour development of the methods were established by varying the parameters one at a time in each method, keeping the others fixed and observing the effect produced on the absorbance of the coloured species.

Method development

A comparison of acid, HCl, H_2SO_4, CH_3COOH and HNO_3 was examined. A 2.0 M of each acid was used in the mixed reagent solution. The results obtained indicate that the reaction in HCl medium provides the highest sensitivity. A 2.0 M hydrochloric acid was found adequate for the oxidation of the drug as well as the complex formation reactions. The variation in HCl concentration indicated that constant absorbance was obtained with 0.5–2.0 ml of 2.0 M HCl, subsequent studies were performed with 1.0 ml of 2.0 M HCl for methods A, B and C.

Method A: using indigo carmine

Propranolol underwent bromination with the brominating mixture in an acidic medium. After bromination was completed, the unreacted bromine was determined by reacting it with a fixed amount of indigo carmine dye. The method makes use of bleaching action of bromine on the dye; the decolouration being caused by the oxidative destruction of the dye and measuring the absorbance at 610 nm, Figure 1A.

In order to establish the experiment conditions in method A, PRO was allowed to react with BrO_3^- in the presence of indigo

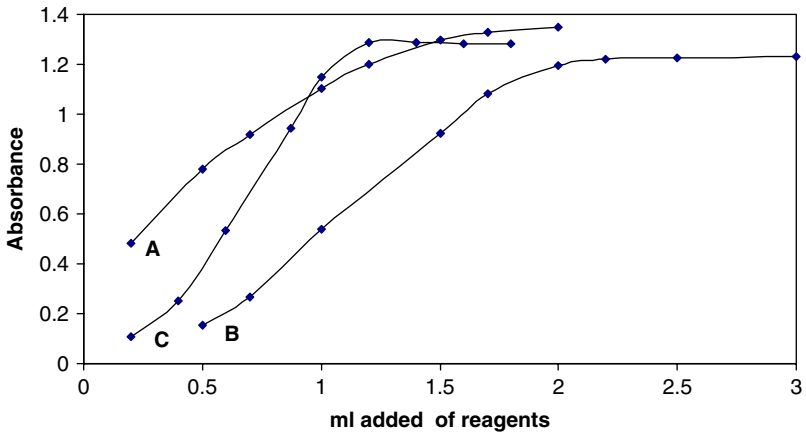

Figure 2. Effect of ml added of reagents: (A) 5×10^{-4} M indigo carmine, (B) 1.0 M thiocyanate, and (C) 0.2% 1,10-phenanthroline.

carmine and HCl. The effect of reagent concentrations (BrO_3^-, and indigo carmine), temperature, time, and order of addition of reagents was studied by means of control experiments. The effect of bromate concentration was optimized and the influence of KBr concentrations on sensitivity was investigated. The results showed that in the absence of bromide the sensitivity was a little poor. Therefore, the oxidation of PRO by bromate was accelerated when bromide was present in a relatively large amount.

Preliminary experiments were performed to fix the upper limits of indigo carmine dye which could be spectrophotometricaly determined in acid medium, and this was found to be 2.0 ml of 5×10^{-4} M of indigo carmine (Figure 2A). A bromate concentration of 100 μg ml^{-1} in the presence of a large excess of bromide was found to destroy the blue colour of indigo carmine. Therefore, 1.0 ml of BrO_3^- (100 μg ml^{-1} in $KBrO_3$) was adopted in the recommended procedure.

The effect of time and temperature of oxidation on the absorbance of the coloured species was studied by performing the oxidation at different temperatures over different time intervals. Oxidation times ranging from 2–5 min at room temperature (25 ± 2 °C) gave constant and reproducible absorbance values. A 5-min standing time was found to be necessary for the complete bleaching of the dye colour by the residual bromine. The absorbance of the measured colour was constant for a few days even in the presence of the reaction products. The order of addition of the reagents had no effect on the absorbance of the coloured species.

PRO, when added in increasing concentration to a fixed amount of *in situ* generated bromine, consumes the latter and there will be a concomitant decrease in its concentration. When fixed concentration of indigo carmine dye is added to decreasing concentrations of bromine, a concomitant increase in the concentration of dye is obtained. This is observed as a proportional increase in absorbance with increasing concentration of PRO (Figure 3A).

Method B: using thiocyanate

Complex formation reaction involving iron(III) and thiocyanate is a well known reaction that has been widely used for trace level determination of iron(III).[50] The present method is based on the oxidation-bromination of PRO with a solution of excess brominating mixture in hydrochloric acid medium. After bromination of the drug was ensured to be completed, the unreacted oxidant was reduced by a reaction with a fixed amount of iron(II) and subsequent formation of iron(III)–thiocyanate complex which is measured at 480 nm (Figure 1B).

The conditions for the determination of iron(III) by thiocyanate are well established through a number of preliminary experiments. Hence, experimental variables for the oxidation of PRO by bromate-bromide and its reduction by iron(II) were optimized. A 1.0 ml of 2.0 M HCl was used for the oxidation step which was complete in 5 min and the same acidic condition was used to reduce the residual bromine by iron(II) which was complete in 10 min; resulting iron(III). It was found that 2.0–2.5 ml of 1.0 M ammonium thiocyanate gave the maximum pronounced effect on the absorbance of iron(III)-thiocyanate complex (Figure 2B). Therefore, 2.2 ml of 1.0 M of ammonium thiocyanate was employed in the investigation.

Two blanks were prepared for this study. The reagent blank which contained optimum concentrations of all the reagents except PRO gave maximum absorbance. The other blank was prepared in the absence of bromate and drug to determine the contribution of other reagents to the absorbance of the system. Since the absorbance of the second blank was negligible, the absorbance measurement was made against water blank.

However, a slightly higher concentration of ammonium ferrous sulphate was used to ensure the complete reduction of residual oxidant. Hence, different concentrations of PRO were reacted with 1.4 ml of 100 μg ml^{-1} bromating mixture followed by the reduction of residual oxidant by 1.0 ml of 5×10^{-3} M AFS. Finally, complex formation reaction between the resulting iron(III) and thiocyanate was instantaneous under the described experimental conditions. Developed colour was stable for at least 60 min in the presence of reaction products. The influence of temperature was studied over the range of 25–100 °C. The results show that the absorbance was decreased when the temperature was higher than 25 °C. Therefore, the room temperature (25 ± 2 °C) was adopted for further experiments.

When a fixed concentration of bromate is reacted with increasing concentrations of PRO, there will be a proportional decrease in the concentration of the oxidant. The unreacted oxidant, when treated with a fixed concentration of iron(II) accounts for a proportional decrease in the iron(III) concentration. This is observed as a proportional decrease in the absorbance of iron(III)-thiocyanate complex on increasing the concentration of PRO (Figure 3B), which formed the basis for the assay of drug.

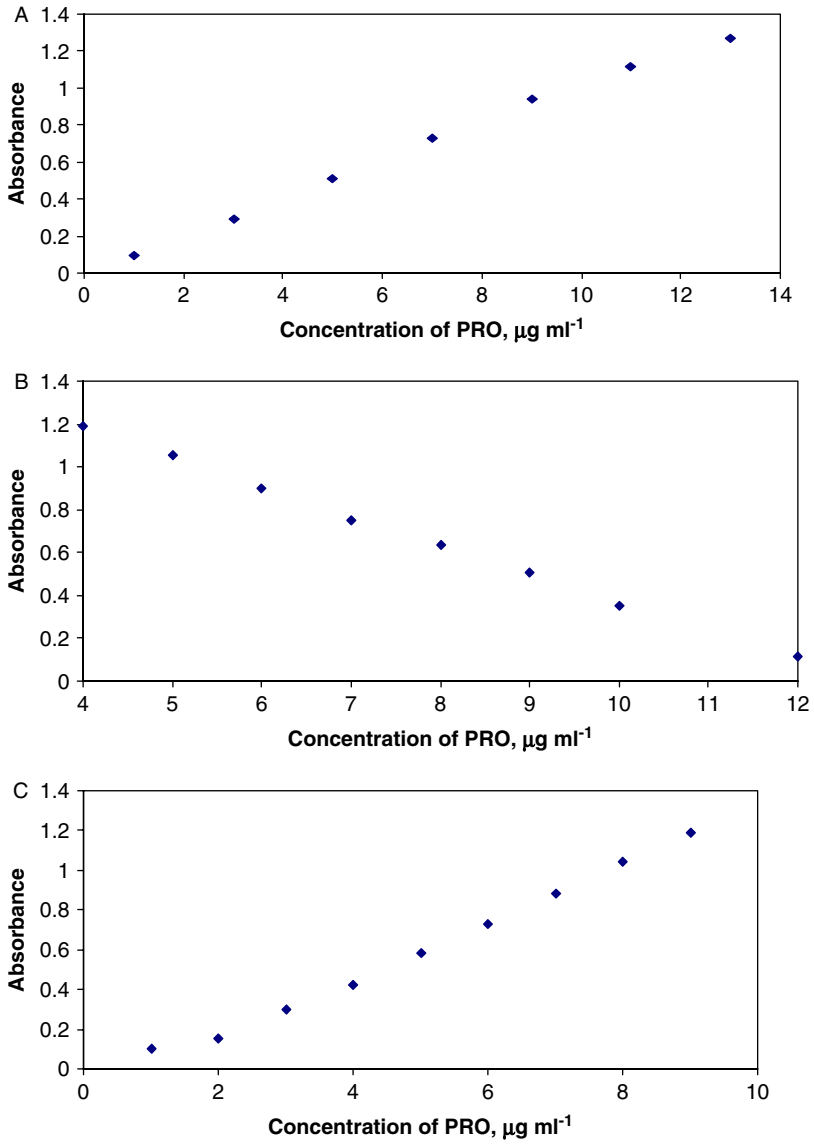

Figure 3. Beer's Law curves for methods A, B and C.

Method C: using 1,10-phenanthroline

It is known that 1,10-phenanthroline forms highly stable, intensely red-coloured, water-soluble chelates with iron(II). The complex formation stabilizes the iron(II) oxidation state, as the formal redox potential of complex (+1.06 V) is higher than that of the iron aqua-complex. This complex was applied to the determination of reducing substances by measuring the amount of ferrous.[50] Trace amounts of the reductants are conveniently measured this way through spectrophotometric determination of ferrous using 1,10-phenanthroline at 510 nm (Figure 1C).

The optimum reaction conditions for the quantitative determination of PRO, were established through a number of preliminary experiments. The results obtained showed that at least 1.0 ml of bromate-bromide mixture is required for maximum colour development in method C. The effects of 1,10-phenanthroline was studied by measuring the absorbance of solutions containing a fixed concentration of the PRO and varied amounts of the reagent separately. It was observed that the maximum colour intensity was obtained with 1.2 ml of the reagent (Figure 2C); after which a further increase in volume resulted in no change in the absorbance. Therefore, 1.2 ml of 0.2% 1,10-phenanthroline was sufficient to reach with the maximum drug concentration in the Beer's range.

The drug in varying concentrations, when treated with fixed and known concentrations of bromating mixture in acid medium, consumes the latter in proportionate concentrations for its oxidation, and there will be a concomitant decrease in the amount of oxidant. When the decreasing concentrations of oxidant are treated with fixed and known concentrations of iron(II) in the same acidic conditions, there will be a proportional increase in the concentration of iron(II). This is shown by the increase in the absorbance of phenanthroline complex formed with the residual iron(II). The absorbance measured at 510 nm was found to increase linearly with the increasing concentration of PRO (Figure 3C), serving as the basis for the determination of drug.

The formation of coloured complex was slow at room temperature and at low pH and required longer time for completion. Hence efforts were made to accelerate by carrying out the reaction at higher pH range (4.0–6.0). The pH of acidic

Table 2. Optical characteristics and statistical data for the regression equation of the proposed methods

Parameters	Units	Method A	Method B	Method C
Absorption maxima, λ_{max}	nm	610	480	510
Beer's law limits	μg ml^{-1}	1–13	4–12	2–9
Molar absorptivity	l mol^{-1} cm^{-1}	3.42×10^4	8.8×10^4	3.91×10^4
Sandell's sensitivity	ng cm^{-2}	8.649	3.361	7.56
Regression equation*				
Slope (b)		0.1281	0.1420	0.1438
Intercept (a)		−0.1227	1.201	−0.138
LOD	μg ml^{-1}	0.0150	7.93×10^{-3}	0.0154
LOQ	μg ml^{-1}	0.0499	0.0264	0.0512
Correlation coefficient (r)		0.9992	−0.9996	0.9995

* A = a + bC, where A is the absorbance and C concentration in μg ml^{-1}.

medium employed for the redox reaction was raised by adding 1.0 ml of 1 : 1 ammonia solution which was found to be optimum. Under these conditions, the absorbance of the complex remained constant at room temperature for more than 24 h.

Analytical Performance

The performance of the proposed methods was compared with that of other existing UV–visible spectrophotometric methods (Table 1). It is evident from Table 1 that the proposed methods are more sensitive than the other reported methods due to their higher molar absorptivities and present better accuracy with narrow linear dynamic range. The methods are found to be simple and can compete with other existing spectrophotometric methods in determining drug in lower concentrations. The order of performance of the proposed methods is B > C > A.

Linearity

Under the optimized experimental conditions, the optical characteristics such as the Beer's Law limits, molar absorptivity and Sandell's sensitivity for each method are given in Table 2. A regression analysis using the method of least squares was performed to evaluate the slope (b), intercept (a) and correlation coefficient (r) for each method; these are also presented in Table 2. The comparative study of the molar absorptivity, Sandell's sensitivity, and detection limit indicated good sensitivity of the proposed methods.

Sensitivity

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from background levels. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision, and variability. The values of LOD and LOQ are given in Table 2. The detection and quantification limits were calculated from the standard deviation of absorbance measurements from a series of 10 blank solutions. In this study, LOD and LOQ were calculated from calibration curves using Eqn (1).[51]

$$\text{LOD} = 3\,a/b;\ \ \text{LOQ} = 10\,a/b \qquad (1)$$

where *a*, is the standard deviation of the absorbance of the sample and *b*, is the sensitivity, namely the slope of the related calibration graphs. In accordance with the formula, the LOD and the LOQ were found to be 0.015, 7.93×10^{-3}, 0.0154 μg ml^{-1} and 0.0499, 0.0264, 0.0512 μg ml^{-1} for methods A, B and C, respectively.

Precision and accuracy

The inter- and intra-day precision and accuracy of the proposed spectrophotometric methods were studied. Precision of the methods expressed by percentage relative standard deviation (RSD%) and accuracy of the methods as percentage relative error (Er%) were estimated by measuring six determinations at three different concentrations of PRO within the linearity range (low, medium and high) by the proposed spectrophotometric methods. The percentage relative error calculated using the Euq (2).

$$\text{Er\%} = [(\text{founded} - \text{added})/\text{added}] \times 100 \qquad (2)$$

The inter- and intra-day precision and accuracy results are shown in Table 3. The results indicate that there are good accuracy and precision of the proposed spectrophotometric procedures for the analysis of PRO as a substance and in pharmaceutical preparations.

Effect of interferences

In order to evaluate the selectivity of the developed methods for the analysis of pharmaceutical preparations, the effect of the presence of several species, which can occur in real samples with propranolol was investigated. It was found that the presence of the common expicients of tablets (e.g., lactose, glucose, starch, sucrose, and fructose) or common degradation products does not interfere in the determination of the studied drug (Table 4). This fact indicates good selectivity of the proposed methods to determine the studied drug in raw material and dosage forms.

Analytical Applications

In order to confirm the feasibility of the proposed methods, PRO was determined in commercial tablets and ampoules. The results of the comparison of the proposed methods with the pharmacopoeia methods[4] are shown in Table 4. Six replicates determinations were made. For all samples assayed, the results obtained using official and proposed methods were compared by applying the *t*- and *F*-test at 95% confidence level. In all cases, the

Table 3. The inter- and intra-day precision and accuracy data for PRO obtained by the proposed methods (n = 6)

Methods	Inter-day				Intra-day		
	Taken μg ml^{-1}	Found μg ml^{-1}	Precision RSD %	Accuracy Er %	Found μg ml^{-1}	Precision RSD %	Accuracy Er %
A	3	2.99	0.984	−0.333	3.02	1.218	0.666
	7	6.98	0.907	−0.285	6.99	0.887	−0.142
	9	8.99	1.113	−0.111	9.05	1.206	0.555
B	4	3.99	0.387	−0.25	3.98	0.524	−0.50
	8	8.01	0.699	0.125	7.97	0.841	−0.375
	10	9.98	1.019	−0.20	10.03	0.645	0.30
C	2	2.01	0.601	0.50	1.99	0.624	−0.50
	6	5.98	0.599	−0.333	6.05	0.578	0.833
	8	7.97	0.379	−0.375	7.95	0.789	−0.625

n, number of determinations, RSD %, percentage relative standard deviation; Er %, percentage relative error.

Table 4. Determination of PRO in pharmaceutical formulations by the suggested spectrophotometric methods and B.P. method

Preparations	Nominal composition (mg)	Taken μg	Found μg	Recovery ± RSD[b], %			t[c]			F[c]		
				A	B	C	A	B	C	A	B	C
Inderal[a] tablets	10 mg PRO HCl/tablet	7	6.99	99.95 ± 0.079			2.17			1.08		
		8	8.01		100.1 ± 0.07			1.91			1.62	
		9	9			100 ± 0.067			2.18			1.22
Inderal[a] tablets	40 mg PRO HCl/tablet	7	6.99	99.98 ± 0.07			2.09			1.37		
		8	8.02		100.2 ± 0.044			2.26			1.56	
		9	8.99			99.95 ± 0.077			2.22			1.08
Inderal[a] ampoules	1 mg PRO HCl/ampoules	7	7.01	100.1 ± 0.065			2.26			1.59		
		8	8.01		100.06 ± 0.042			2.33			1.71	1.03
		9	8.99			99.95 ± 0.073			2.01			
		Official method		6.98 ± 0.082	7.99 ± 0.055	8.98 ± 0.074						

[a] Product of Kahira Pharmaceutical Company, Cairo, Egypt.
[b] Average of six determinations.
[c] Theoretical values at 95% confidence limit: $t = 2.57$, $F = 5.05$.

calculated *t* and *F* values did not exceed the theoretical values, indicating that there is no significant difference between methods concerning precision and accuracy in the determination of PRO in pharmaceutical formulations and also referring to the robustness of the proposed methods. The average recoveries obtained by the proposed methods ranged from 99.95 to 100.2% for all of the assayed samples. The proposed methods were successfully applied to the determination of PRO in tablets and ampoules can be used as a reliable and advantageous alternative to other previously reported methods for the routine analysis of PRO in quality control laboratories.

Conclusion

The proposed spectrophotometric methods for the determination of propranolol are simple, rapid, sufficiently sensitive, and yield reproducible results without involving critical maintenance of the experimental conditions. The proposed methods involve the addition of a measured excess of bromate-bromide in HCl medium and subsequent estimation of the residual bromine by three different reaction schemes. When the proposed methods are applied to the assay of pharmaceutical dosage forms, their advantage is that they do not require the removal of usual excipients since they were found not to interfere with the determination of PRO and can be used in the routine analysis of PRO in bulk samples and formulations with reasonable precision and accuracy.

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