SPECTROPHOTOMETRIC DETERMINATION OF PIZOTIFEN MALEATE IN BULK DRUG AND TABLETS USING N-BROMOSUCCINIMIDE AND THREE DYES

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ABSTRACT

Objective*:* Three sensitive spectrophotometric methods are presented for the assay of pizotifen maleate (PZT) in bulk drug and pharmaceutical formulation (tablets) using N-bromosuccinimide (NBS) and three dyes, methyl orange, amaranth and indigo carmine, as reagents.

Methods: The methods involve the addition of a known excess of NBS to drug in acid medium, followed by determination of unreacted oxidant by reacting with a fixed amount of methyl orange and measuring the absorbance at 522 nm (method A), amaranth and measuring the absorbance at 507 nm (method B) or indigo carmine and measuring the absorbance at 610 nm (method C).

Results: In all methods, the amount of NBS reacted corresponds to the amount of drug and the measured absorbance is found to increase linearly with the concentration of drug which is corroborated by the correlation coefficients of 0.9998- 0.9999. The systems obey Beer's law for 0.4-4.4, 0.2-3.2 and 0.2-4.0 µg mL^{-1}for methods A, B and C, respectively. The limits of detection and quantification are also reported. Intra-day and inter-day precision and accuracy of the methods have been evaluated.

Conclusion: The methods were successfully applied to the assay of PZT in tablets preparations and the results were statistically compared with those of the reference method by applying Student's t-test and F-test. No interference was observed from the common tablet excipients. The accuracy of the methods was further ascertained by performing recovery studies via standard-addition method.

Keywords: Spectrophotometry; Pizotifen maleate; N-bromosuccinimide; Methyl orange; Amaranth; Indigo carmine; Tablets.

INTRODUCTION

Pizotifen malate (PZT), chemically known as 9, 10-dihydro-4-(1-methylpiperidin-4-ylidene)-4H benzo [4,5] cyclohepta [1, 2-b] thiophene hydrogen malate (Fig. 1) [1]. Pizotifen is a sedating antihistamine that has strong serotonin antagonist and weak antimuscarinic properties. It also antagonises the action of tryptamine. Pizotifen is used, usually as the malate, for the prophylaxis of migraine and for the prevention of headache attacks during cluster periods. It is not effective in treating an acute attack [2]. The drug is official in British Pharmacopoeia [1], which describes a potentiometric titration with perchloric acid in anhydrous acetic acid medium.
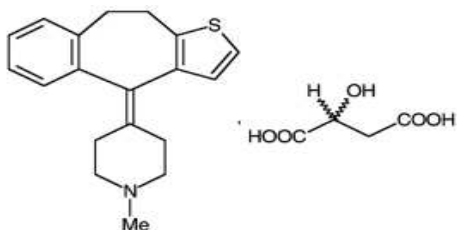

Fig. 1: The chemical structure of pizotifen malate (PZT)

Several analytical methods have been reported for the determination of PZT in pure drug, pharmaceutical dosage forms and in biological samples using high performance liquid chromatography[3–7], atomic absorption spectroscopy [8], spectrophotomety [8, 9] and spectrofluorimetry [9].

Several visible spectrophotometric methods based on colour reactions involving the amino or thiophene of the pizotifen molecule

can be found in the literature. El-Kousy and Bebawy [8] have developed three methods for the assay of PZT in bulk drug and in tablets; the first method was based on extraction of drug-cobalt thiocyanate ternary complex with methylene chloride and estimation by indirect atomic absorption method via the determination of the cobalt content in the complex after extraction in 0.1M hydrochloric acid at 240.7 nm in concentration ranges from 10 – 74 µg mL^{-1}. The second method is based on the formation of orange red ion pair by the reaction of PZT and molybdenum thiocyanate with absorption maxima at 469.5 nm in dichloromethane in the concentration ranges 3.5-25 µg mL^{-1}. The third method was a charge transfer reaction between PZT and 2,3-dichloro-5,6-dicyano-p-benzoquinone in acetonitrile medium at 588 nm in concentration range 10-80 µg mL^{-1}. Dessouky et al., have determined PZT in tablets using three spectrophotometric and one spectrofluorimetric methods, the first spectrophotometric method was based upon measuring the absorbance of the investigated drug at λ = 317 nm after its treatment with concentrated sulfuric acid in concentration ranges 2.0 – 8.0 µg mL^{-1}. The second method comprised a reaction between formaldehyde and PZT in the presence of concentrated sulfuric acid and measured at λ = 480 nm in concentration ranges 12 - 60 µg mL^{-1}. In the third method, PZT was determined spectrophotometrically by applying the first derivative technique (D$_1$). Quantitative determination was carried out by measuring the first derivative (D$_1$) of the trough at λ = 238 nm in concentration ranges 2.4 - 28 µg mL^{-1}. The spectrofluorimetric method involved the reaction of the cited drug and citric acid/acetic anhydride system and measuring the relative fluorescence intensity of the reaction product at 485 nm after excitation at 385 nm in the concentration range 0.3 – 6.0 µg mL^{-1} [9].

However, the reported spectroscopic techniques suffer from some other disadvantage such as poor sensitivity, dependence on critical experimental variables, tedious and time-consuming extraction steps, heating step, and/or use of expensive reagent or large amounts of organic solvents.

From the foregoing paragraphs, it is clear that N-bromosuccinimide (NBS) despite its strong oxidizing power, versatility, high oxidation potential and high stability in solution has not been applied for the assay of PZT in pure form and tablets. This paper describes for the first time the application of acidic N-bromosuccinimide (NBS) to the spectrophotometric determination of PZT using methyl orange, amaranth and indigo carmine as chromogenic agents.

N-bromosuccinimide (NBS) has earlier been widely applied for the assay of a variety of pharmaceuticals [10–16]. The proposed methods have the advantages of speed and simplicity besides being accurate and precise, and can be adopted by the pharmaceutical laboratories for industrial quality control.

MATERIALS AND METHODS

Apparatus

All absorption spectra were made using Kontron Unikon 930 (UV-Visible) spectrophotometer (German) with a scanning speed of 200 nm/min and a band width of 2.0 nm, equipped with 10 mm matched quartz cells.

Materials and Reagents

All chemicals and reagents used were of analytical or pharmaceutical grade and all solutions were prepared fresh daily. Double distilled water was used throughout the investigation.

Materials

Pharmaceutical grade pizotifen maleate (PZT) was supplied from (*Novartis*, Egypt). Mosegor tablets, labeled to contain (0.5 mg PZT per tablet) were purchashed from local commercial markets.

Standard PZT solution

A stock standard solution of PZT (100 µg mL^{-1}) was prepared by dissolving an exact weight (10 mg) of pure drug in bidistilled water and diluted to 100 mL with bidistilled water in a 100 mL measuring flask. The solution was diluted stepwise to get working concentration of 10 µg mL^{-1}. The standard solutions were found stable for at least one week without alteration when kept in an amber coloured bottle and stored in a refrigerator when not in use.

Reagents

-      N-bromosuccinimide (NBS): An approximately 0.01M NBS solution was prepared by dissolving about 1.8 g of chemical (Sigma-Aldrish) in water with the aid of heat and diluted to one liter with water and standardized iodometrically [17]. The solution was kept in an amber coloured bottle and was diluted appropriately to get 100 µg mL^{-1} NBS for use in all methods. The NBS solution was stored in a refrigerator when not in use.

-      Potassium bromide, KBr (1.0% w/v).

-      Hydrochloric acid (5.0 M): A 5.0 mol L^{-1} of HCl was prepared by diluting 43 mL of concentrated acid (Merck, Darmstadt, Germany, Sp. gr. 1.18, 37%) to 100 mL with bidistilled water and standardized as recommended previously   [18] prior to use.

-      Methyl orange (50 µg mL^{-1}): A 500 µg mL^{-1} dye solution was first prepared by dissolving accurately weighed 58.8 mg of dye (Sigma-aldrish, 85% dye content) in water and diluting to 100 mL in a calibrated flask and filtered using glass wool. It was further diluted to obtain a working concentration of 50 µg mL^{-1}.

-      Amaranth (200 µg mL^{-1}): A 1000 µg mL^{-1} stock standard solution was first prepared by dissolving accurately weighed 112 mg of dye (Sigma-aldrish, 90% dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5.0-fold to get the working concentration of 200 µg mL^{-1}.

-      Indigo carmine (200 µg mL^{-1}): A 1000 µg mL^{-1} stock standard solution was first prepared by dissolving accurately weighed 112 mg of dye (Sigma-aldrish, 90% dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5.0-fold to get the working concentration of 200 µg mL^{-1}.

Recommended general procedures

Different aliquots (0.4 - 4.4 mL), (0.2 - 3.2 mL) and (0.2-4.0 mL) of a standard 10 µg mL^{-1} PZT solution for methods A, B and C, respectively were transferred into a series of 10 mL calibrated flasks by means of a micro burette and the total volume was adjusted to 5.0 mL by adding adequate quantity of water. To each flask were added 1.0 mL each of 5.0 M HCl; 1.0 mL of NBS solution (100 µg mL^{-1}) and 1.0 mL of 1.0% KBr were added successively. The flasks were stoppered, content mixed and let stand for 15 min with occasional shaking. Finally, 1.0 mL of (100 µg mL^{-1}) methyl orange and (200 µg mL^{-1}) amaranth or indigo carmine solution was added (accurately measured) and the volume was diluted to the mark with water and mixed well. The absorbance of each solution was measured at 522, 507 and 610 nm for methods A, B and C respectively after 5.0 min against a reagent blank.

In all methods, a standard graph was prepared by plotting the absorbance versus the concentration of drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation derived using Beer's law data.

Procedure for pharmaceutical formulations (tablets)

The contents of twenty Mosegor tablets (0.5 mg PZT per tablet) were weighed accurately and ground into a fine powder. An accurate weight equivalent to 0.5 mg PZT was dissolved in 20 mL of 0.2 M HCl with shaking for 5.0 min and filtered using a Whatman No. 42 filter paper.. The filtrate was diluted to the mark with 0.1 M HCl in a 50 mL measuring flask to give and 10 µg mL^{-1} stock solution of PZT for analysis by spectrophotometric methods A, B and C, respectively. A convenient aliquot was then subjected to analysis by the spectrophotometric procedures described above. Determine the nominal content of the tablets either from a previously plotted calibration graph or using the corresponding regression equation.

RESULTS

Absorption spectra

A close examination of the literature search presented in the introduction reveals that NBS has not yet been used for the spectrophotometric determination of GMF or MX**F**. NBS is a strong oxidizing agent and perhaps the most important positive bromine containing organic compound; it is used for the specific purpose of brominating alkenes at the allylic position [19].
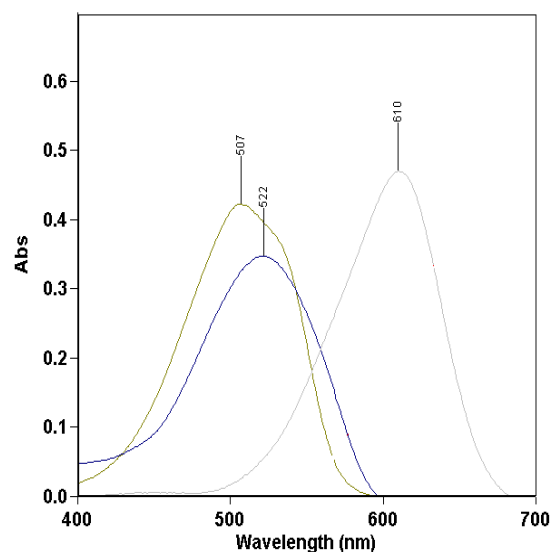

Fig. 2: Absorption spectra for the unreacted oxidant that determined by reacting with a fixed amount of dyes and measuring the absorbance at 522, 507 and 610 nm for methods A, B and C, respectively.

The present work involves the bromination of PZT by NBS followed by determination of surplus NBS after allowing the bromination reaction to complete. The ability of NBS to oxidize PZT and bleach the colors of methyl orange, amaranth and indigo carmine dyes has been used for the indirect spectrophotometric assay of the drugs. In the three methods, the drugs are reacted with a known excess of NBS in acid medium and the unreacted oxidant is determined by reacting with a fixed amount of dyes and measuring the absorbance at 522, 507 and 610 nm for methods A, B and C, respectively, the absorbance increased linearly with increasing concentration of drug (Fig. 2).

Effect of acid concentration

The hydrochloric acid was found most appropriate. The effect of HCl was studied and 0.25-3.0 mL of 5.0 M HCl in a total volume of 5.0 mL was found to have constant effect on both reactions (i.e. Drug with NBS, and residual NBS with dyes). The results presented in Fig. 3 indicated that, at 1.0-3.0 mL of 5.0 M HCl, there was almost same absorbance values were obtained in the presence of PZT, the absorbance values obtained were constant and were almost the same as those of the reagent blank. At the acid volumes less than 1.0 mL, reaction led to go slower and incomplete. Therefore, 1.0 mL of 5.0 M HCl was used though out the study (Fig. 3).
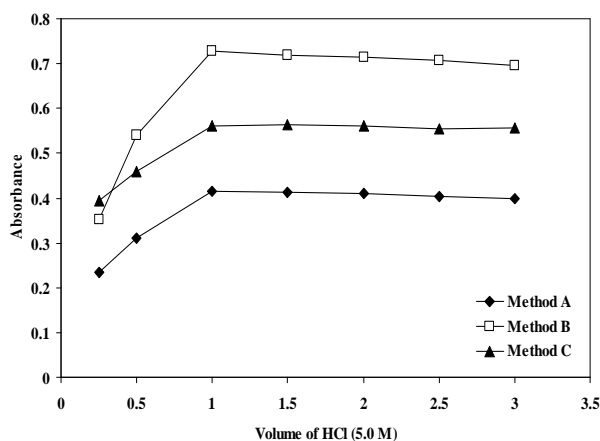

Fig. 3: Effect of volume of HCl (5.0 M) of the oxidation product of PZT with NBS and dyes.

Effect of reagents

Preliminary experiments were performed to determine the maximum concentrations of the dyes spectrophotometrically in acid medium, and these were found to be 10, 20 and 20 $\mu g\ mL^{-1}$ for methyl orange, amaranth and indigo carmine, respectively. A NBS concentration of 10 $\mu g\ mL^{-1}$ was found to irreversibly destroy the red colour of 10 $\mu g\ mL^{-1}$ methyl orange, whereas 10 $\mu g\ mL^{-1}$ NBS was required to destroy the red and blue colours of 20 $\mu g\ mL^{-1}$ amaranth and indigo carmine, respectively in HCl medium. Hence, different concentrations of drugs were reacted with 1.0 mL of 100 $\mu g\ mL^{-1}$ NBS in all methods before determining the residual NBS as described under the respective procedures. 1.0 mL of KBr (1.0%) was chosen as optimum volume in 10 mL total volume to accelerate the oxidation process.

Effect of time and temperature

The reaction time between PZT and NBS was studied by standing the drug solution after mixing with NBS for different intervals of time in the presence of 1.0 mL of 5.0 M HCl and the results indicated that time of 5.0-10 min was required to complete of the reaction. Therefore, a 10 min reaction time was fixed as optimum after the addition of NBS. A sufficient time to completely bleach dyes due to unreacted NBS was found to be 5.0 min, and the same was fixed in all subsequent studies. Raising the temperature does not accelerate the

oxidation process and does not give reproducible results, so the optimum temperature is the ambient (25±1 °C). The measured colour was found to be stable for several hours in the presence of the reaction product/s in the three methods.

Effect of sequence of addition

Drug–acid–NBS–KBr-(dye) is the optimum sequence of addition; other sequences gave lower absorbance values under the same experimental conditions.

Method of validation

The proposed methods have been validated for linearity, sensitivity, precision, accuracy, selectivity and recovery.

Linearity and sensitivity: Under the optimum conditions a linear correlation was found between absorbance λ_{max} and concentration of PZT in the range of (0.2-4.4 $\mu g\ mL^{-1}$). The calibration graph is described by the equation:

A = a + b C (1)

(where A = absorbance, a = intercept, b = slope and C = concentration in $\mu g\ mL^{-1}$) obtained by the method of least squares. Correlation coefficient, intercept and slope for the calibration data are summarized in Table 1. For accurate determination, Ringbom concentration range [21] was calculated by plotting log concentration of drug in $\mu g\ mL^{-1}$ against transimittance % from which the linear portion of the curve gives accurate range of microdetermination of PZT and represented in Table 1. Sensitivity parameters such as apparent molar absorptivity and Sandell's sensitivity values, as well as the limits of detection and quantification, were calculated as per the current ICH guidelines [22] and illustrated in Table 1. The high molar absorptivity and lower Sandell sensitivity values reflect the good and high sensitivity of the proposed methods. The validity of the proposed methods was evaluated by statistical analysis [23] between the results achieved from the proposed methods and that of the reported method. Regarding the calculated Student's *t*-test and variance ratio *F*-test (Table 1), there is no significant difference between the proposed and reported method [8] regarding accuracy and precision.

The limits of detection (LOD) and quantification (LOQ) were calculated according to the same guidelines using the formulas [22, 23]:

$$LOD = 3.3\sigma/s \text{ and } LOQ = 10\sigma/s \text{ (2)}$$

Where σ is the standard deviation of five reagent blank determinations, and s is the slope of the calibration curve.

Accuracy and precision

In order to evaluate the precision of the proposed methods, solutions containing three different concentrations of PZT were prepared and analyzed in six replicates. The analytical results obtained from this investigation are summarized in Table 2. The low values of the relative standard deviation (% R.S.D) and percentage relative error (% R.E) indicate the precision and accuracy of the proposed methods. The percentage relative error is calculated using the following equation:

$$\% R.E. = \left[\frac{found - taken}{taken} \right] \times 100$$

(3)

The assay procedure was repeated six times, and percentage relative standard deviation (% R.S.D) values were obtained within the same day to evaluate repeatability (intra-day precision), and over five different days to evaluate intermediate precision (inter-day precision). For the same concentrations of drugs inter- and intra-day accuracy of the methods were also evaluated. The percentage recovery values with respect to found concentrations of each drug were evaluated to ascertain the accuracy of the methods. The recovery values close to 100% as compiled in Table 2 shows that the proposed methods are very accurate.

Table 1: Analytical and regression parameters of proposed oxidation spectrophotometric methods for determination of PZT

Parameters	Method A	Method B	Method C
Beer's law limits, $\mu g\ mL^{-1}$	0.4 – 4.4	0.2 – 3.2	0.2 – 4.0
Ringboom limits, $\mu g\ mL^{-1}$	0.8 – 4.0	0.4– 2.8	0.4– 3.6
Molar absorptivity, x 10^4 L mol^{-1} cm^{-1}	2.8547	4.2193	6.5343
Sandell sensitivity, ng cm^{-2}	10.35	7.0	4.52
Regression equation,[a]			
Intercept (a)	0.0027	- 0.0033	0.0026
Standard deviation of intercept (S_a)	0.0085	0.0045	0.0076
Slope (b)	0.0942	0.2302	0.1394
Standard deviation of slope (S_b)	0.0055	0.005	0.0062
Correlation coefficient, (r)	0.9998	0.9999	0.9998
Mean ± SD	100.10 ± 1.08	99.40 ±0.90	99.90 ±1.30
RSD%	1.08	0.91	1.30
RE%	1.13	0.95	1.37
Limit of detection, $\mu g\ mL^{-1}$	0.11	0.05	0.055
Limit of quantification, $\mu g\ mL^{-1}$	0.37	0.167	0.183
Calculated *t*-value [b]	0.63	0.55	0.27
Calculated *F*-value [b]	1.54	1.07	2.23

[a] $A = a + bC$, where C is the concentration in $\mu g\ mL^{-1}$, A is the absorbance units, a is the intercept, b is the slope., [b] The theoretical values of t and F are 2.57 and 5.05, respectively at confidence limit at 95% confidence level and five degrees of freedom (p= 0.05).

Table 2: Results of intra-day and inter-day accuracy and precision study for PZT obtained by the proposed methods.

Method	PZT taken ($\mu g\ mL^{-1}$)	Recovery %	Precision RSD % [a]	Accuracy RE %	Confidence Limit [b]
	Intra-day				
A	1.0	99.60	0.64	-0.40	0.996 ± 0.004
	2.0	99.10	1.35	-0.90	1.982 ±0.012
	4.0	99.80	1.80	-0.20	3.992 ± 0.027
B	1.0	100.50	0.90	0.50	1.005 ± 0.009
	2.0	100.90	1.12	0.90	2.018 ± 0.019
	3.0	99.30	1.74	-0.70	2.976 ± 0.048
C	1.0	99.00	0.46	-1.0	0.99 ± 0.005
	2.0	100.30	1.05	0.30	2.006 ±0.015
	4.0	101.20	1.50	1.20	4.048 ± 0.033
	Inter-day				
A	1.0	99.60	0.72	-0.45	0.996 ± 0.006
	2.0	100.20	1.40	0.20	2.004 ±0.015
	4.0	99.70	1.60	-0.30	3.988 ± 0.040
B	1.0	99.10	0.75	-0.90	0.991 ± 0.009
	2.0	99.30	1.65	-0.70	1.986 ± 0.029
	3.0	100.25	1.27	0.25	3.008 ± 0.071
C	1.0	100.40	0.90	0.40	1.004 ± 0.005
	2.0	100.90	1.10	0.90	2.018 ±0.013
	4.0	99.30	1.40	-0.70	3.972 ± 0.031

[a] RSD%, percentage relative standard deviation; RE%, percentage relative error. [b] Mean ± standard error.

Table 3: Results of method robustness and ruggedness (all values in %RSD) studies

Methods	Nominal amount concentration ($\mu g\ mL^{-1}$)	RSD% Robustness Variable alerted [a]		Ruggedness	
		Acid volume (n=3)	Reaction time (n=3)	Different analysts (n=3)	Different instruments (n=3)
A	1.0	1.10	0.90	0.90	0.88
	2.0	1.50	1.25	1.20	0.75
	4.0	2.20	1.60	2.10	2.25
B	1.0	1.30	0.89	1.39	1.35
	2.0	1.80	1.40	1.80	1.50
	3.0	2.30	2.25	2.58	2.60
C	1.0	1.03	1.15	1.42	1.20
	2.0	1.57	1.74	2.50	1.60
	4.0	1.60	2.0	2.10	2.0

[a] Volume of 5.0 M HCl is (1.0±0.2 mL) and reaction time is (10±2.0 min) (after adding NBS) were used.

Robustness and ruggedness: For the evaluation of method robustness, volume of HCl and reaction time (between NBS and drug) were slightly varied deliberately. The analysis was performed with altered conditions by taking three different concentrations of

drug and the methods were found to remain unaffected as shown by the RSD values in the ranges of 0.89-2.30%. Methods ruggedness was expressed as the RSD of the same procedure applied by three different analysts as well as using three different instruments (spectrophotometers).

The inter-analysts RSD were in the ranges 0.90-2.58% whereas the inter-instruments RSD ranged from 0.75-2.60% suggesting that the developed methods were rugged. The results are shown in Table 3.

Recovery studies

To study the reliability and accuracy of the proposed methods, a standard addition technique was followed. This study was performed by spiking a fixed amount of tablet preparation to three different levels of pure drug. The total concentration was found by the proposed methods. The determination with each level was repeated three times and the percent recovery of the added standard (pure drug) was calculated from:

$$\% \text{ Recovery} = \frac{[C_F - C_T]}{C_P} \text{ x } 100 \tag{4}$$

where C_F is the total concentration of the analyte found, C_T is a concentration of the analyte present in the tablet preparation, C_P is a concentration of analyte (pure drug) added to tablet preparation. Results of this study presented in Table 4 revealed that the accuracy of the proposed methods was unaffected by the various excipients present in tablets.

Table 4: Results of recovery experiments for Mosegor tablets by standard addition method.

Methods	Taken Conc. from tablet (µg mL⁻¹)	Pure drug added (µg mL⁻¹)	Total found (µg mL⁻¹)	Recovery% [a] ± SD
Method A	0.5	0.5	0.996	99.60 ± 0.77
		2.0	2.480	99.20 ± 0.90
		3.5	3.976	99.40 ± 0.79
Method B	0.5	0.5	0.993	99.30 ± 1.10
		2.0	2.490	99.60 ± 0.60
		3.5	3.976	99.40 ± 0.58
Method C	0.5	0.5	1.006	100.60±0.80
		2.0	2.488	99.50±0.90
		3.5	3.968	99.20±1.16

[a] Mean value of three determinations

Table 5: Application of the proposed methods for the determination of PZT in Mosegor tablets

|	Proposed methods			Reported method [8]
	A	B	C	
Recovery ± RSD [a]	99.40± 0.84	99.70 ± 1.10	99.10 ± 0.97	99.30 ± 0.91
t-Value [b]	0.18	0.63	0.34	
F-Value [b]	1.17	1.46	1.14	

[a] Mean for six independent analyses. ,[b] The theoretical values of *t* and *F* are 2.57 and 5.05, respectively at confidence limit at 95% confidence level and five degrees of freedom (*p*= 0.05).

Application to formulations

The proposed methods were applied to the determination of PZT in tablets. The results in Table 5 showed that the methods are successful for the determination of PZT and that the excipients in the dosage forms do not interfere. The results obtained from the assay of PZT by the proposed methods and reference method [8] for the same batch of material is presented in Table 5. The results agreed well with the label claim and also were in agreement with the results obtained by the reference methods. When the results were statistically compared with those of the reference methods by applying the Student's t-test for accuracy and F-test for precision, the calculated t-value and F-value at 95% confidence level did not exceed the tabulated values of 2.57 and 5.05, respectively, for five degrees of freedom [23]. Hence, no significant difference existed between the proposed methods and the reference methods with respect to accuracy and precision.

DISCUSSION

PZT, when added in increasing amounts to a fixed amount of NBS, consumes the latter and there will be a concomitant fall in its concentration. When a fixed amount of each dye is added to decreasing amounts of NBS, a concomitant increase in the concentration of dye results. This is observed as a proportional increase in the absorbance at the respective wavelengths of maximum absorption with increasing concentration of drug as indicated by the correlation coefficients ranged from of 0.9992-0.9998.
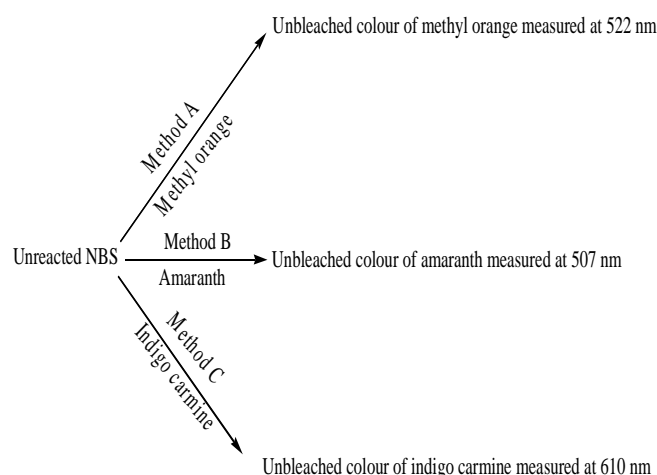
Scheme 1: Tentative reaction scheme for the proposed spectrophotometric methods.

The tentative reaction scheme of spectrophotometric methods is shown in Scheme 1. The bromination of PZT will take place in position α to the carbonyl group [20].

Drug + Known excess of NBS $\xrightarrow{\text{H}^+}$ Reaction product of drug + Unreacted NBS

CONCLUSION

Three methods have been developed for determination of PZT in bulk drug and in its tablets and validated as per the current ICH guidelines. The present spectrophotometric methods are characterized by simplicity since they do not involve any critical experimental variable and are free from tedious and time-consuming extraction steps and use of organic solvents unlike many previous methods. The proposed methods have additional advantages of ease of operation and possibility of carrying them out with a common laboratory instrument unlike many other instrumental methods reported for PZT. They are characterized by high selectivity and comparable sensitivity with respect to the existing methods. The accuracy, reproducibility, simplicity, and cost-effectiveness of the methods suggest their application in the quality control laboratories where the modern and expensive instruments are not available.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests with the company name used in the paper.

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