



Research Article

OPTIMIZATION OF QUANTITATIVE ANALYSIS OF BUCLIZINE HYDROCHLORIDE USING SPECTROPHOTOMETRY IN BULK DRUG AND PHARMACEUTICAL FORMULATIONS

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Received: 01 July 2010, Revised and Accepted: 06 Aug 2010

ABSTRACT

Development and validation of an analytical spectral calibration method to quantify Buclizine hydrochloride (BUCZ), which is a piperazine derivative and used as a single active principle in pharmaceutical forms were done. The quantification of BUCZ was performed in the wavelength range of 620, 440, 560 nm. The developed methods were applied directly and easily to the analysis of the pharmaceutical tablet preparations. % RSD was found in the range of 0.4425 to 1.207%. The methods were completely validated and proven to be rugged. These validated UV-Vis spectrophotometric methods are potentially useful for a routine laboratory analysis because of its simplicity, rapidity, sensitivity, precision, and accuracy.

Keywords: Buclizine, Piperazine derivative, Spectrophotometric methods, Statistical analysis, Recovery studies.

INTRODUCTION

Buclizine as hydrochloride¹ (BUCZ) is a piperazine antihistamine [Figure 1] with antimuscarinic and central sedative properties. Chemically BUCZ is 1-[(4-chlorophenyl) Phenyl methyl] -4-[(4-(1,1 dimethyl ethyl) phenyl) methyl] piperzine; It is mainly used for the prevention of motion sickness when it should be given at least 30 minutes before traveling and it is also used in combination with analgesics to treat migraine attacks.

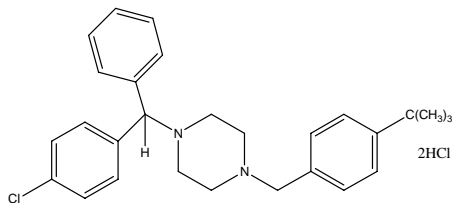


Fig. 1: Buclizine

A very few physico-chemical methods appeared in the literature for the assay of BUCZ in biological fluids, and pharmaceutical formulations. Most of them are based on RP-HPLC²⁻⁴, RP-LC⁵ and UV-Visible spectrophotometry⁶⁻⁸. The analytically useful functional groups in BUCZ has not been fully exploited for designing suitable visible spectrophotometric methods and so still offer a scope to develop few more visible spectrophotometric methods with better sensitivity, selectivity, precision and accuracy. Authors have developed simple and sensitive UV-Vis spectrophotometric methods in CHCl₃ for the estimation of BUCZ in pure or pharmaceutical formulations and adopted it as a reference method to compare the results obtained with the proposed methods.

Experimental

Instrumentation: An Elico made UV-Visible digital spectrophotometer with 1cm matched quartz cells were used for the spectral and absorbance measurements. An Elico LI-120 digital pH meter was used for pH measurements.

Preparation of standard drug solution: Buclizine as hydrochloride was prepared by dissolving an appropriate amount of its salt (Buclizine Hydrochloride) equivalent to 100 mg of free base in 20 ml of water, adding 10 ml of 0.1 M NaOH solution and extracting the separated base with chloroform (4 × 20 ml). The combined chloroform extract was washed with water, dried over anhydrous sodium sulphate and made upto 100 ml with chloroform and this stock solution was diluted step wise with chloroform to get the working standard solutions of 400 µg/ml (M₁), 100 µg/ml (M₂), and 200 µg/ml (M₃).

Preparation of reagents: All the reagents were prepared by double distilled water and the reagents are AR grade.

Method (M₁): TA solution (Loba 0.2 %, 1.17 × 10⁻³ M); Prepared by dissolving 200 mg of Tannic acid in 100 ml of distilled water

PMAP solution (Loba, 0.3 %, 8.71 × 10⁻³ M): Prepared by dissolving 300 mg of P-N-methyl amino phenol sulphate in 100 ml of distilled water

Cr (VI) solution (BDH, 0.3 %, 1.01 × 10⁻² M): Prepared by dissolving 300 mg of Potassium dichromate in 100ml of distilled water

Buffer solution pH-3: Prepared by diluting a mixture of 250 ml of 0.2 M Potassium acid phthalate and 204 mg of 0.1M HCl to 1L with distilled water and the pH was adjusted to 3.0

Method (M₂): CTC solution (2.5 × 10⁻¹ M): Prepared by dissolving 7.25 g of cobaltous nitrate (BDH) and 3.8 g of ammonium thiocyanate (BDH) in 100 ml of distilled water.

Buffer solution (pH 2.0): Prepared by mixing 306 ml of trisodium citrate (0.1 M) with 694 ml of HCl (0.1M) and the pH of the solution were adjusted to 2.0.

Nitrobenzene (Qualigens): AR grade directly taken from the bottle.

Method (M₃): SNP Solution (E. Merck; 0.5 %, 1.678 × 10⁻² M): Prepared by dissolving 500 mg of sodium nitroprusside in 100 ml of distilled water.

HA Solution (Fluka; 0.5%, 7.195 × 10⁻² M): Prepared by dissolving 500 mg of hydroxylamine hydrochloride in 100 ml of distilled water.

Na₂CO₃ solution (Loba; 10%, 9.43 × 10⁻¹M): Prepared by dissolving 10 g of sodium carbonate in 100 ml of distilled water.

Recommending procedures: M₁: Aliquots of standard drug solution were delivered in to a series of centrifuge tubes and the volume in each tube was adjusted to 3.0 ml with 0.01 N HCl. Then 1.0 ml of Tannic acid was added and centrifuged for 5 min. The precipitate was collected through filtration and subsequently washed with 2 ml of distilled water. The filtrate and washings were collected in a 25 ml graduated test tube. Then 15 ml of pH 3.0 buffer and 1.5 ml of PMAP solution were successively added. After 2 min, 2.0ml of Cr (VI) solution was added and the volume was made upto the mark with distilled water. The absorbance was measured after 5 min at 560 nm against distilled water. A blank experiment was also carried out omitting the drug. The decrease in absorbance and in turn drug concentration was obtained by subtracting the absorbance of the test solution from the blank.

M₂: Into a series of 125 ml of separating funnels, aliquots of standard BUCZ solution were taken. Then 2.0 ml of buffer (pH 2.0) and 5.0 ml of CTC solutions were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0 ml with distilled water. To each separating funnel, 10.0 ml of nitrobenzene was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured at 620 nm against a similar reagent blank. The amount of BUCZ was computed from its calibration graph.

M₃: Aliquots of standard BUCZ solution were transferred into a series of 25 ml calibrated tubes. Then 1.0 ml of SNP and 1.0 ml of HA were added successively and kept aside for 5 min. Then 1.0 ml (9.43 × 10⁻¹M) of Na₂CO₃ solution was added and shaken for 15 min. The volume was made upto the mark with distilled water. The absorbance was measured after 10 min. at 440 nm against a similar reagent blank. The amount of BUCZ was computed from its calibration graph.

For pharmaceutical formulations: An accurately weighed portion of tablet powder equivalent to about 100 mg of BUCZ was transferred into a 100 ml volumetric flask. Added about 80 ml of warm chloroform and shaken well for about 20 min. the contents were diluted with chloroform upto the mark and mixed thoroughly. The solution was filtered the filtrate was evaporated to dryness. The residue was used for the preparation of standard solution as shown under standard solution preparation. These solutions were analysed as under procedures described from bulk solutions.

Reference Method: An accurately weighed portion of the powdered tablets equivalent to 100 mg of drug was dissolved in 30 ml of chloroform, shaken well and filtered. It was evaporated to dryness. The residue was dissolved in chloroform. Solution was diluted to 100 ml with chloroform to get 1mg/ml. The above solution was further diluted to with chloroform to get 75 µg/ml solution. The absorbance of the solution was determined at λ_{max} 272 nm. The quantity drug was computed from the Beer's law plot of the standard drug in Chloroform.

RESULTS AND DISCUSSION

Chemical reactions of methods

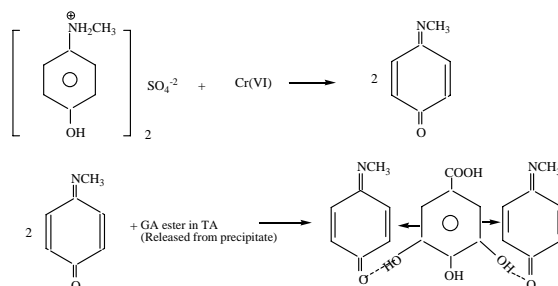
M₁: The method involves two steps. First step is the quantitative precipitation of BUCZ with TA. Second step is the formation complex between the released TA from adduct and PMAP – Cr (VI). The probable sequence of reactions based on analogy is given in scheme 1.

M₂: The colored complex formed between BUCZ and CTC can be attributed to cyclic tertiary nitrogens in BUCZ. The probable sequence of reaction based on analogy is presented in scheme 2.

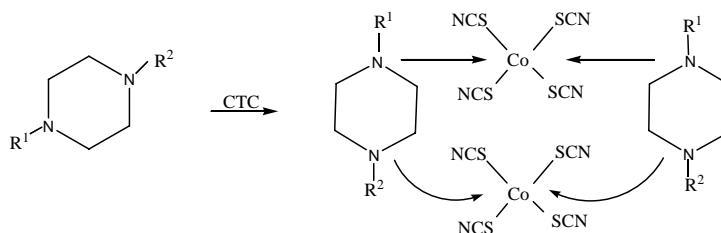
M₃: In this method BUCZ acts as an electron donor SNP in presence of hydroxylamine and alkali exists as aqua ferricyanide [Fe (CN)₅ H₂O]³⁻. The color obtained may be due to the formation of [Fe (CN)₅ M]³⁻, where M is a compound exhibiting legating properties. Based on the analogy, the probable sequence of reactions are presented in scheme 3.

Step I: BUCZ + TA → BUCZ – TA (Adduct) + TA (unreacted)

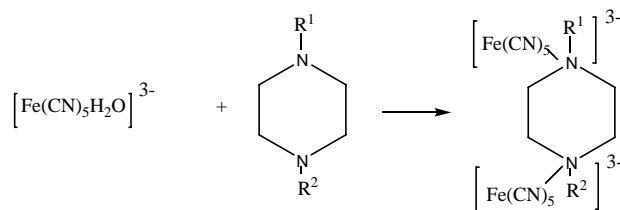
Step II:



Scheme 1



Scheme 2



Scheme 3

Table 1: Optical and regression characteristics, precision and accuracy of the proposed methods for BUCZ

Parameter	M ₁	M ₂	M ₃
λ_{\max} (nm)	560	620	440
Beer's law limits ($\mu\text{g/ml}$)	8-48	5-30	4-24
Detection limit ($\mu\text{g/ml}$)	2.475	3.054	3.809
Molar absorptivity (1 mol/cm)	4.366×10^3	8.173×10^3	1.9104×10^4
Sandell's sensitivity ($\mu\text{g/cm}^2/0.001$ absorbance unit)	0.2377	0.1564	8.886×10^{-2}
Optimum photometric range ($\mu\text{g/ml}$)	12.6-48	10-30	12-24
Regression equation ($Y=a + bc$)			
slope (b)	0.0221	0.019755	0.03619
Standard deviation on slope (S_b)	2.518×10^{-4}	1.113×10^{-2}	3.224×10^{-2}
Intercept (a)	1.4×10^{-2}	1.625×10^{-3}	2.5×10^{-3}
Standard deviation on intercept (S_a)	6.682×10^{-3}	1.845×10^{-1}	4.277×10^{-2}
Standard error on estimation (S_e)	6.371×10^{-3}	1.759×10^{-1}	4.079×10^{-2}
Correlation coefficient (r)	0.9989	0.9611	0.9646
Relative standard deviation (%)	1.072	1.207	0.4425
% Range of error (confidence limits)			
0.05 level	1.232	1.388	0.5088
0.01 level	1.933	2.176	1.7979

* Average of six determinations considered

Table 2: Assay of BUCZ in pharmaceutical formulations (Tablets)

Formulations*	Amount taken (mg)	Amount found by proposed Methods**			Reference method	Percentage recovery by proposed methods***		
		M ₁	M ₂	M ₃		M ₁	M ₂	M ₃
Tablet I	25	25.12 \pm 0.33	24.74 \pm 0.42	25.04 \pm 0.39	24.95 \pm 0.51	99.85 \pm 0.84	99.47 \pm 0.75	99.72 \pm 0.99
		F = 2.388	F = 1.474	F = 1.710				
		t = 0.7010	t = 0.7821	t = 0.3464				
Tablet II	25	24.63 \pm 0.53	25.12 \pm 0.37	24.56 \pm 0.44	24.92 \pm 0.62	99.52 \pm 0.61	99.43 \pm 0.74	99.73 \pm 0.98
		F = 1.368	F = 2.807	F = 1.176	25.12 \pm 0.47	99.96 \pm 0.98	99.67 \pm 0.97	99.89 \pm 0.61
		t = 0.8735	t = 0.6997					
Tablet III	25	24.85 \pm 0.35	24.91 \pm 0.42	24.78 \pm 0.31	24.90 \pm 0.82	99.82 \pm 0.97	99.90 \pm 0.43	99.75 \pm 0.53
		F = 1.803	F = 1.252	F = 2.298				
		t = 1.140	t = 0.8173	t = 1.509				
Tablet IV	26	24.43 \pm 0.73	25.12 \pm 0.65	25.28 \pm 0.54	24.90 \pm 0.82	99.82 \pm 0.97	99.90 \pm 0.43	99.75 \pm 0.53
		F = 1.261	F = 1.591	F = 2.305				
		t = 1.050	t = 0.5184	t = 0.9678				

**Average \pm standard deviation of six determinations, the *t*-and *F*-test values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit, $F = 5.05$, $t = 2.57$

***Recovery of 10mg added to the pre-analyzed pharmaceutical formulations (average of three determinations)

Validation of methods: The optimum conditions for the color development of methods M₁ to M₃ were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the colored species. The optical characteristics such as Beer's law limits, molar absorptivity and sandell's sensitivity for the three methods are given Table 1. The precision of the method to the drug was found by measuring the absorbance of 6 separate samples containing known amounts of drug and the results obtained are incorporated in Table 1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) and standard error of estimation (Se) for each system. The accuracy of the methods was ascertained by comparing the results by proposed and reference methods (UV) statistically by the *t*-and *F*-tests Table 2. The comparison shows that there is no significant difference between the results of studied methods and those of the reference ones. The similarity of the results is obvious evidence that during the application of these methods the excipients present in pharmaceutical formulations do not interfere in the assay of proposed methods. As an additional check of accuracy of the proposed methods, recovery experiments were carried out. The recovery of the added amounts of standard drug was studied at 3 different levels. Each level was repeated 6 times. From the amount of drug found, the percentage recovery was calculated from the

amount of drug found. The high λ_{\max} values of all the proposed methods have a decisive advantage since the interference from the associated ingredients should be generally less at higher wavelengths than at lower wavelengths. Thus the proposed visible spectrophotometric methods are simple and sensitive with reasonable precision, accuracy and constitute better alternatives to the existing ones to the routine determination of BUCZ in bulk forms and pharmaceutical formulations.

CONCLUSION

The proposed methods exploit the various functional groups in BUCZ molecule. The concomitants which do not contain the functional groups chosen in the present investigation do not interfere in the color development by the proposed methods. Thus the proposed methods are simple, sensitive and selective with reasonable precision and accuracy and constitute better alternatives to the reported ones in the assay of BUCZ in bulk drugs and pharmaceutical formulations.

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