Spectrophotometric Determination of Buclizine as Hydrochloride Using Various Chromogenic Reagents

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Abstract: Simple, accurate and reproducible UV spectrophotometric methods were established for the assay of buclizine (BUCZ) based on the formation of precipitation, charge transfer complex and inner complex formation. Method A involves the precipitation, charge transfer complex formation of BUCZ with tannic acid/ *p*-*N*-methyl aminophenol sulphate (PMAP)-Cr(VI), the complex formation with cobalt thiocyanate (CTC) in method B and inner complex formation of BUCZ with sodium nitroprusside hydroxylamine hydrochloride and sodium carbonate in method C were proposed. The optical characteristics such as Beers law limits, molar absorptivity and Sandell's sensitivity for the methods (A-C) are given. 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 Determination of BUCZ in bulk form and in pharmaceutical formulations were also incorporated.

Keywords: Estimation, Buclizine, Precipitating agent, Charge transfer complex.

Introduction

Buclizine¹ (as hydrochloride, BUCZ) is a piperazine antihistamine with antimuscarinic and central sedative properties. It is mainly used for its anti-emetic action, particularly in the prevention of motion sickness when it should be given at least 30 min. before traveling. It is also used in combination with analgesics to treat migraine attacks.

A very few physicochemical methods appeared in the literature for the assay of the proposed drug samples in biological fluids and pharmaceutical formulations. Most of them are based on visible spectrophotometric methods^{2,3}, HPLC⁴⁻⁶, GC^{7,8}, fluorimetry⁹⁻¹¹, LC-MS¹², GC-MS¹³⁻¹⁵ and TLC¹⁶, mass¹⁷. Existing analytical methods reveal that relatively little

attention was paid in developing visible spectrophotometric methods by exploiting the analytically useful functional groups. Hence there is a need to develop sensitive and flexible visible spectrophotometric methods which prompted the author to carry out in this accord.

Experimental

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

All the chemicals and reagents used were analytical grade and the aqueous solutions were freshly prepared with triple distilled water. A 1 mg/mL solution was prepared by dissolving 100 mg of pure BUCZ in 5 mL of 0.1N HCl followed by dilution to 100 mL with distilled water and the stock solution was diluted step wise with distilled water to get the working standard solutions of required concentrations. TA solution (Loba 0.2%, 1.17×10^{-3} M); PMAP solution, (Loba, 0.3%, 8.71×10^{-3} M), Cr(VI) solution (BDH, 0.3% 1.01×10^{-2} M), Buffer solution PH = 3 for method A, CTC solution, (2.5×10^{-1} M) Buffer solution (pH 2.0), Nitrobenzene (Qualigens) for method B and SNP Solution (E. Merck; 0.5%, 1.678×10^{-2} M) HA Solution, (Fluka; 0.5%, 7.195×10^{-2} M) Na_2CO_3 solution (Loba; 10%, 9.43×10^{-1} M) for method C were prepared.

Recommended Procedures

Method A

Aliquots of standard drug solution (0.5-3.0 mL 400 $\mu\text{g/mL}$) 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 2.0 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, 2.0 mL of Cr(VI) solution was added and the volume was made up to 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. The amount of drug was calculated from Beer's law plot (Figure 1).

Method B

Into a series of 125 mL separating funnels, aliquots of standard BUCZ solution (0.5-3.0 mL, 100 $\mu\text{g.mL}^{-1}$) were taken. Then 2.0 mL of buffer (pH 2.0) and 5.0 mL (2.5×10^{-1} M) 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 (Figure 2).

Method C

Aliquots of standard BUCZ solution (1.0-6.0 mL, 100 $\mu\text{g.mL}^{-1}$) were transferred into a series of 25 mL calibrated tubes. Then 1.0 mL (1.678×10^{-2} M) of SNP and 1.0 mL (7.195×10^{-2} M) of HA were added successively and kept aside for 5 min. Then 1.0 mL (9.43×10^{-1} M) of Na_2CO_3 solution was added and shaken for 15 min. The volume was made up to 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 (Figure 3).

Figure 1. Beer's law plot of BUCZ - TA/PMAP - Cr (VI)

Figure 2. Beer's law plot of BUCZ - CTC

Figure 3. Beer's law plot of BUCZ - SNP - HA

Structure of BUCZ

Buclizine (CAS 82-95-1): 1-[(4-chlorophenyl) Phenyl methyl] -4-[(4-(1,1 dimethyl ethyl) phenyl) methyl] piperazine;

Method A

Step II

Method B *Method C* **Results and Discussion**

The optimum conditions for the color development of methods A, B and C 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 list of proposed and reported methods was given in Table 1. The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for the methods (A-C) are given Table 2. The precision of the method to the drug was found by measuring the absorbance of six separate samples containing known amounts of drug and the results obtained are incorporated. 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.

Table 1. Proposed and reported visible spectrophotometric methods

Type of Reaction	Reagent	Method	Optical characteristics		
			λ_{max} nm	ϵ_{max} L.mole ⁻¹ cm ⁻¹	Beer's limits $\mu\text{g mL}^{-1}$
Precipitation/charge transfer complex formation	TA/Metol-Cr(VI)	A	560	4.366×10^3	8-48
Complex formation	CTC	B	620	8.173×10^3	5-30
Inner complex formation	SNP-HA	C	440	1.910×10^4	4-24

Table 2. Optical and regression characteristics, precision and accuracy of the proposed methods for BUCZ

Parameters	Method A	Method B	Method C
$\lambda_{\max}$, 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, $\text{Lmol}^{-1}\cdot\text{cm}^{-1}$	4.366×10^3	8.173×10^3	1.9104×10^4
Sandell's sensitivity ($\mu\text{g}\cdot\text{cm}^{-2}/0.001$ 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	4425
0.05 level	1.232	1.388	0.5088
0.01 level	1.933	2.176	1.7979
% Error in Bulk samples	-0.143	0.166	0.10

The accuracy of the methods was ascertained by comparing the results by proposed and reference methods statistically by the *t*- and *f*- tests. 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 are usually 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 for six times. From the amount of drug found, the % recovery was calculated in the usual way.

The higher $\lambda_{\max}$ 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 decreasing order of sensitivity ($\epsilon_{\max}$) among the proposed methods are (Method A > Method B > Method C) respectively. The concomitants which do not contain the functional groups chosen in the present investigation do not interfere in the color development by 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 form and pharmaceutical formulations (Table 3).

Table 3. Assay of BUCZ in pharmaceutical formulations.

Formulations	Amount taken, mg	Amount found by proposed Methods				Percentage recovery by proposed methods		
		Method A	Method B	Method C	Reference Method	Method A	Method B	Method C
Tablet I	25	25.04±0.39 F=1.710 t=0.3464	24.57±0.33 F=1.777 t=1.619	24.80±0.22 F=4.0 t=0.682	24.95±0.51	99.72±0.99	99.55±0.99	99.73±0.98
Tablet II	25	24.56±0.44 F=1.9855 t=1.176	24.63±0.42 F=3.0209 t=1.807	24.92±0.63 F=1.342 t=0.7895	24.92±0.62	99.73±0.98	99.85±0.61	99.82±0.44
Tablet III	25	24.78±0.31 F=2.298 t=1.509	24.72±0.43 F=1.6538 t=0.60	24.37±0.41 F=1.819 t=0.64	25.12±0.47	99.89±0.61	99.93±0.85	99.72±0.53
Tablet IV	25	25.28±0.54 F=2.305 t=0.9678	24.63±0.22 F=1.506 t=0.700	24.93±0.14 F=3.719 t=1.520	24.90±0.82	99.75±0.53	99.73±0.65	99.88±0.84

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