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Quantization of Buspirone Hydrochloride in Pure and Pharmaceutical Formulations by Spectrophotometric Method

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Abstract. A simple and sensitive method is described for the determination of buspirone hydrochloride in bulk drug and in formulations employing spectrophotometric technique. The method is based on the interaction of buspirone hydrochloride with ammonium molybdate in acidic media and the absorbance is measured at 700 nm. Beer's Law is obeyed in the range of 5 µg to 350 µg/ml and RSD is 0.96 % for buspirone hydrochloride. Analytical data for the determination of pure compound is presented along with the application of the proposed method for the analysis of pharmaceutical formulation.

Keywords: buspirone hydrochloride, ammonium molybdate, spectrophotometry.

Introduction

Buspirone hydrochloride is an anxiolytic azaspirodecane dione (Fig. 1). It is reported to be largely lacking in sedative, anticonvulsant and muscle relaxant actions. Adverse effects can include dizziness, nausea, headache, nervousness, light headedness, excitement, paraesthesias, sleep disturbances, chest pain, tinnitus, sore throat and congestion. Buspirone is reported to produce less sedation and to have a lower potential for dependence than the benzodiazepines (Sean, 2002).

The analytical techniques being employed for the determination of buspirone hydrochloride are reviewed hereunder. In reverse phase HPLC, the recovery of buspirone hydrochloride was not 100% (Franklin, 1990), while in HPLC procedure the RSD values were higher, < 7.6% (Pehourcq, 2004), > 8% (Foroutan *et. al.,* 2004) and < 9% (Du *et. al.,* 2003) for buspirone hydrochloride, whereas the eluent was monitored at 254 nm (Li *et al.,* 2004) by using lidocaine as the internal standard with pH adjusted to 4 (Zaxariou and Panderi, 2004). In the spectrophotometric method, extraction in chloroform is carried out prior to the determination (Sane *et al.,* 1993) and then molybdenum content of the complex was determined via atomic absorption spectrometry (Aboul-Kheir *et al.,* 2002). Long and tedious methods are involved in LC-tandem mass spectrometry (Chew *et al.,* 2006, Green *et al.,* 2004), GC-MS (Qiao *et al.,* 1996) and gas chromatography with nitrogen-phosphorus detection (Lai *et al.,* 1997) in which either pretreatment of sample is required or have high relative standard deviation.

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During the studies, it was found that buspirone hydrochloride reacts with ammonium molybdate in acidic media to give greenish blue colour having maximum absorbance at 700 nm. The reaction obeys Beer's Law from 5 µg to 350 µg/ml. The colour reaction has not been reported in the literature. The present method is simple, accurate, precise and sensitive. Contents of other drugs have also been determined by this method.

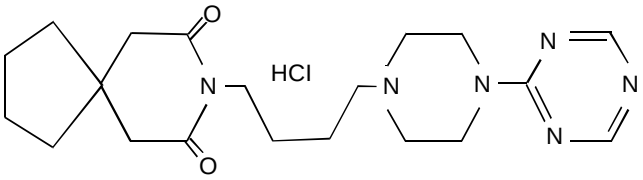

Fig. 1. Structural formula of buspirone hydrochloride.

Materials and Methods

Apparatus and reagent. Cecil CE-2041 spectrophotometer with 1 cm quartz cell was used to measure the absorbance and graduated pipettes were employed. Analytical grade chemicals and doubly distilled water were used. Standard solution (w/v) (1.0 mg/ml) of buspirone hydrochloride was prepared by dissolving buspirone hydrochloride (100 mg) in distilled water and the volume was made up to 100 ml with distilled water to give a stock solution, which was diluted further as required. A 10% (w/v) ammonium molybdate (BDH) as well as 2N sulphuric acid were prepared in distilled water.

General procedure. To an aliquot containing 5 µg to 350 µg/ml of buspirone hydrochloride, 2 ml of 8N sulphuric acid and 0.7 ml of 10% ammonium molybdate were added. The con-

tents were heated for 7 min in a water bath at 100 °C, then cooled and the volume was made upto 10 ml with distilled water. The resulting absorbance of the colour was measured at 700 nm, employing all reagents except buspirone hydrochloride as a blank. The experiment was repeated with different volumes of standard buspirone hydrochloride solution and a calibration curve was prepared (Fig. 2). The colour reaction obeys Beer's Law from 5 µg to 350 µg/ml of buspirone hydrochloride.

Procedure for studying the interfering compounds. To an aliquot containing 1.0 mg/ml of buspirone hydrochloride, different amounts of various compounds (1 mg/ml) were added individually until the solution showed the same (± 0.01) absorbance as that of pure buspirone hydrochloride solution without the addition of the organic compound, under experimental conditions, as described in the general procedure. The value was calculated as the percentage of organic compound with respect to the amount of buspirone hydrochloride.

Procedure for determination of buspirone hydrochloride in pharmaceutical preparations: *Tablets*. Tablets containing buspirone hydrochloride were powdered, weighed, dissolved in water and filtered. The filtrate was diluted with distilled water to get 1.0 mg/ml solution of buspirone hydrochloride. An aliquot containing 5 µg to 350 µg/ml was taken; the procedure was followed as described above and the absorbance was measured at 700 nm. The quantity of buspirone hydrochloride per tablet was calculated from the standard calibration curve.

Results and Discussion

Absorption spectrum of coloured complex. Buspirone hydrochloride reacted with ammonium molybdate when heated for 7 min at 100 °C in acidic media to give greenish blue complex, the absorption spectra of which under optimum conditions lie at 700 nm (Fig. 3).

Effect of temperature and heating time. Studies for the effect of temperature show that at 100 °C the colour intensity was maximum (Fig. 4). Below this temperature, the colour was unstable and it did not develop at room temperature. The colour remained stable for more than 24 h. A water bath was used to carry out the temperature studies. The effect of heating time on colour intensity (Fig. 5) shows that heating for 7 min at 100 °C gave the maximum colour; above and below this time and temperature, the colour intensity decreased and was unstable. The contents of the test tube were cooled to room temperature prior to dilution and measurement of absorbance.

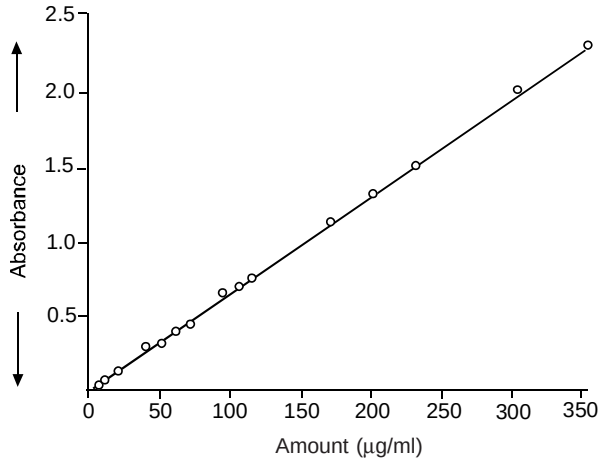

Fig. 2. Calibration curve of buspirone hydrochloride with ammonium molybdate.

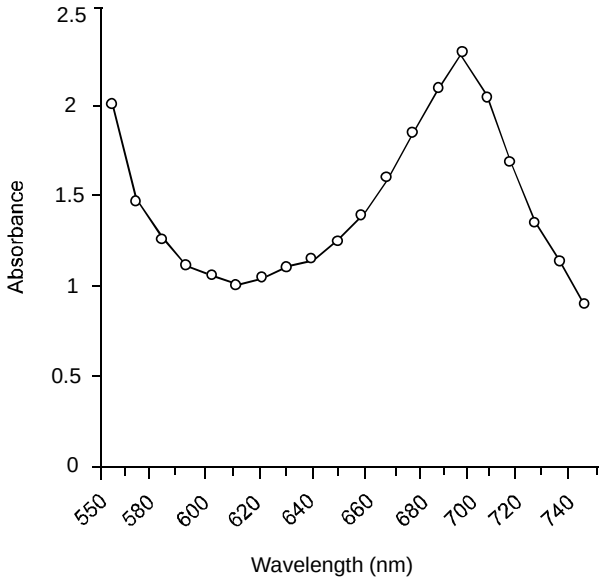

Fig. 3. Absorption spectra of buspirone hydrochloride with ammonium molybdate.

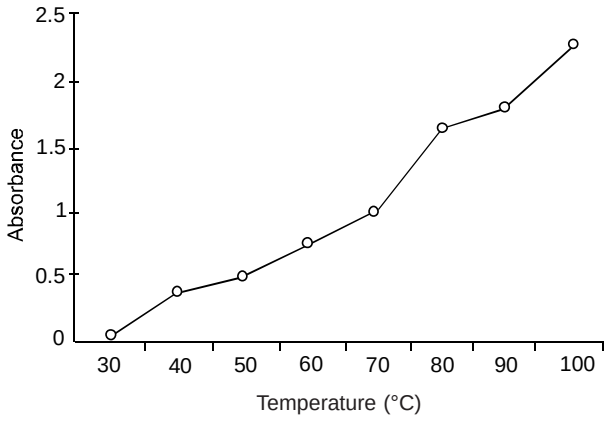

Fig. 4. Effect of temperature.

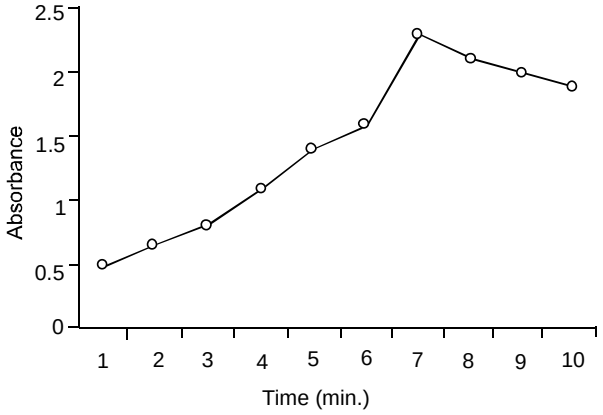

Fig. 5. Effect of heating time.

Effect of colour producing reagent. Ammonium molybdate was used as the colour producing reagent. It was found that 70 mg/ml of ammonium molybdate gave maximum colour (Fig. 6). If the concentration of ammonium molybdate was altered, the colour intensity diminished and the colour became unstable. The probable mechanism of the colour reaction is that the electron of nitrogen from buspirone hydrochloride is taken up by the H^+ ion forming a nitrogen ion (Cotton and Wilkinson, 1980) which in turn reacts with molybdate ion giving a charge transfer stable complex having a maxima at 700 nm.

Effect of pH. Effect of pH is shown in Fig. 7. Maximum colour intensity was obtained at pH 1.08. This pH was maintained by addition of 2 ml of 8N sulphuric acid.

Effect of organic solvents. Different organic solvents such as chloroform, *n*-hexane, xylene, acetone, benzene, dichloromethane and alcohol were tested for colour extraction and stability but none was effective and, therefore, no organic solvent was employed in the study.

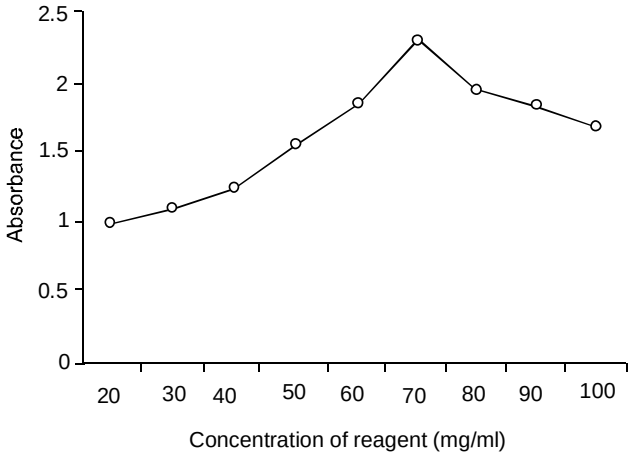

Fig. 6. Effect of reagent.

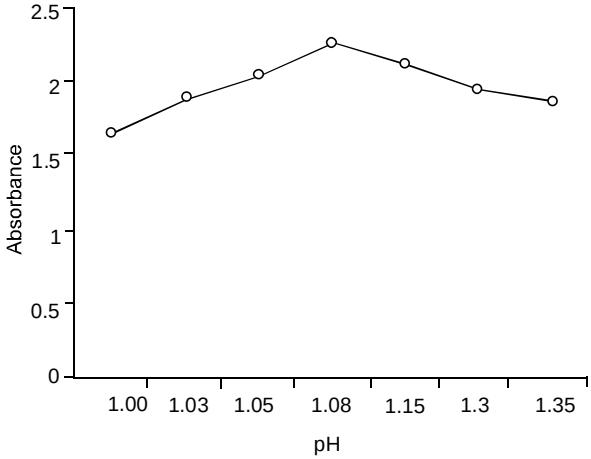

Fig. 7. Effect of pH.

Analytical figures of merit. The results for the determination of buspirone hydrochloride are shown in Table 1 and 2, which show the sensitivity, validity and repeatability of the method. It is also reasonably precise and accurate, as the amount taken from identical samples is known and the amount found by the above procedure does not exceed the relative standard deviation (0.96%) which is the replicate of five determinations. The optimization has been done at lower analyte concentration. The calibration graph is linear in the range 5 µg to 350 µg/ml. The calculated molar absorptivity was 0.2774×10^4; the regression was calculated by the method of least squares from ten points (Christian, 2004) each of which was the average of five determinations. The regression coefficient of determination (r^2) comes out to be 0.9938.

Interferences. The quantitative assessment of tolerable amounts of different organic compounds under the experimen-

Table 1. Determination of buspirone hydrochloride from pure solution

Buspirone hydrochloride taken (µg/ml)	Buspirone hydrochloride found* (µg/ml)	Relative standard deviation (%)
10	10.4	0.96
20.5	19.9	0.50
50	49.0	0.204
70	70.1	0.142
90	90.5	0.110
100	99.0	0.101
150	149.50	0.066
200	210.50	0.047
250	250	0.04
350	349	0.03

* = every reading is an average of five independent measurements.

Table 2. Determination of buspirone hydrochloride in pharmaceutical preparations

Drug	Trade name	Pharmaceutical preparation	Amount present (Manufacturer's specifications) (mg)	Amount found*	Recovery (%)
Buspirone–HCl	Buspar**	Tablet	5	4.99	99.8
Buspirone–HCl	Busron***	Tablet	5	4.95	99

* = every reading is an average of five determinations;** = Bristol–Myers Squibb Australia (Pvt.) Ltd.;*** = S.J.8G. Fazul Ellahie (Pvt.) Ltd., Karachi, Pakistan

tal conditions is given in Table 3. Various amounts of diverse interfering compounds were added to a fixed amount of buspirone hydrochloride (1.0 mg/ml) and the recommended procedure for the spectrophotometric determination was followed.

Applications. The proposed method is successfully applied for the quality control of pure buspirone hydrochloride and in the pharmaceutical dosage form as shown in Table 4.

Table 3. Quantitative assessment of tolerable amounts of other drugs

Drugs	Maximum amount not interfering* (%)
Aspirin	90
Paracetamol	100
Loratadine	50
Metaclopramide HCl	40
Mefanamic acid	50
Carbamazepine	45
Chloroquine phosphate	20
Lorazepam	50
Metformin HCl	100
Terbutaline sulphate	20
Domperidone	30
Indomethacin	10
Procyclidine HCl	25

* = value is the percentage of the drug with respect to 100/µg ml of buspirone hydrochloride that causes ± 0.01 change in absorbance.

Conclusion

The new spectrophotometric method for the determination of buspirone hydrochloride is simple, reliable and sensitive. The colour reaction does not require stringent conditions or several reagents or solvents. The method can be successfully applied to the microdetermination of buspirone hydrochloride either in pure or pharmaceutical preparations. The method is precise and other compounds like Paracetamol, Metformin hydrochloride and Terbutaline sulphate do not interfere.

Table 4. Optical characteristics, precision and accuracy of the proposed method

Parameters	Values
λ_{max} (nm)	700
Molar absorptivity (per mol/cm)	0.2774×10^4
Regression equation (Y^*)	
Slope (b)	0.6773
Intercept (a)	0.0014
Regression coefficient of determination (r^2)	0.9938
Relative standard deviation (%)**	0.96
Range of error (confidence limit) at 95% confidence level (%)	4.52 ± 0.0248%

* = Y = a + bc, where c is the concentration of analyte (µg/ml) and Y is the absorbance unit; ** = calculated from five determinations.

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