

Method Development of Mebeverine Hydrochloride by Using UV Spectrophotometric Method

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ABSTRACT

Objective: The aim of this study was to develop spectrophotometric method for the determination of mebeverine hydrochloride in bulk.

Method: Standard and working solutions of mebeverine hydrochloride were prepared then aliquots of working solutions of different concentrations were prepared then linearity, precision, accuracy, quantitation limit and detection limit were determined.

Result: The linearity for this method was found to be within the range of 12.5-200µg/ml. Correlation coefficient (r^2) was found to be 0.998. Regression equation was found to be $y = 0.0116x + 0.0544$.

Conclusion: A simple, specific and sensitive UV spectroscopy method was developed for the evaluation of mebeverine hydrochloride in bulk. The projected method may be duly applied for the analysis of mebeverine hydrochloride in bulk for routine analysis.

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INTRODUCTION

Mebeverine hydrochloride (MB.HCl) is “4-[ethyl (4-methoxy- α -methylphenethyl) amino] butylveratrate hydrochloride” which is shown in Figure 1. Its molecular formula (MF) is $C_{25}H_{35}NO_5.HCl$, its molecular weight (MW) is 466, and its melting point is 105 -107 °C. It is physically white or almost white; form of powder is crystalline, freely soluble in ethanol (96%) and water, though almost insoluble in diethyl ether. MB.HCl is an antispasmodic compound and its derivative “methoxybenzamine” with a direct action on smooth muscle of the gastrointestinal (GI) tract. It is commonly prescribed in the treatment of abdominal ache and spasm related with gastrointestinal (GI) disorders such as mucous colitis. It has been clinically prescribe for the treatment of (IBS) irritable bowel syndrome for

several years.¹⁻⁵ Mebeverine is indicated for apparent antispasmodic action. MB main metabolites such as “mebeverine alcohol” and “veratric acid”, do not appear to acquire any action on smooth muscles.⁶ When administered orally at doses of 135-270 mg three times a day, it do not show distinctive anticholinergic side effects, for instance blurred vision, dry mouth and impaired micturition.⁷ Mebeverine administered intramuscularly shows a stronger effect on motility of colon in man than when given through oral route.⁵ Literature survey reveals that just a small number of analytical methods have been stated for quantitative evaluation of mebeverine hydrochloride in pharmaceutical formulations including TLC^{8,9}, HPTLC¹⁰, HPLC¹¹⁻¹³, LC¹⁴ micro LC¹⁵ UV^{16,17} and researcher also studied quantitative

estimation of mebeverine hydrochloride by using acidic dyes such as bromothymol blue (BTB), fast green FCF (FG FCF), and cobalt thiocyanate (CTC) in extracting solvents benzene (BTB and CTC) and chloroform (FG FCF) by Visible Spectrophotometry.¹⁸ Spectrophotometric methods are popular because of their high sensitivity and low expenses.^{19,20}

METHODOLOGY

EXPERIMENT

Materials

Active of mebeverine, 0.1 N NaOH, distilled water. Freely soluble in ethanol (96%); Very soluble in water.

Glass wares

Glass wares used in this experiment are volumetric flask, stirrer, beakers, pipette and measuring cylinder. All of the glass ware used were made up of Pyrex material. Initially all the glass wares were rinsed with chromic acid then with water and finally washed with freshly prepared distilled water.

Instruments

Weighing Balance used for weighing the drug was 'Pioneer OHAIUS' (article PA214C) and Spectrophotometer ('PG Instrument', T80 ultraviolet-visible spectrometer) with a cuvette (quartz) was used for the measurement of absorbance of mebeverine hydrochloride dilutions.

Selection of wavelength detection

By using UV spectrophotometer in the range of 200-400nm the scanning of the solution of mebeverine hydrochloride (active drug) was carried out. It was examined that mebeverine hydrochloride demonstrated maximum absorbance at 246nm which was selected as the detection wavelength for the drug.

Standard stock solution of Mebeverine hydrochloride

50 mg of drug (Mebeverine hydrochloride) was dissolved in DI water/ethanol (96%) to prepare the standard stock

solution and finally adjusted the final volume with same solvent in 25 ml of volumetric flask to acquire a solution of 50µg/ml of mebeverine.

Working stock solutions of Mebeverine hydrochloride

Aliquots of working stock solutions of mebeverine hydrochloride were prepared with DI water/ethanol (96%) to acquire the concentration in range of 12.5-200µg/ml of the drug (mebeverine hydrochloride).

Method validation

The tools for the method validated for a drug (mebeverine hydrochloride) are as follows

1. Accuracy,
2. Precision,
3. Linearity,
4. Quantitation limit (LOQ) and
5. Detection limit (LOD).

Linearity

The precise volume of the 'standard stock solution of mebeverine hydrochloride' were taken in 5 separate volumetric flasks (25 ml) and dilute the aliquots of stock solution up to the final volume mark with ethanol (96%) to obtain ultimate concentration of 12.5, 25, 50, 100 and 200µg/ml of mebeverine hydrochloride. absorbance versus concentrations values were plotted to construct the calibration curves and to calculate the regression equation for mebeverine hydrochloride.

Precision

The response of the mebeverine hydrochloride aliquots was estimated six times at the wavelength of 246nm for the repeatability studies and their results are repeated in terms of relative standard deviation. Intermediate Precision consists of the intra-day and inter-day precision, this studies were executed by estimating the comparable responses three times (on the same day and on 3 different days) and the results are demonstrated in terms of % relative standard deviation.

Accuracy

Calculating the recoveries of mebeverine hydrochloride was determined for the accuracy of the method. The accuracy of the

method was carried out by standard additions at three different levels i.e. 80%, 100% and 120%. The 'mean percentage recovery' was estimated and calculated.

Limit of detection (LOD) and limit of quantitation (LOQ)

The limit of detection (LOD) is calculated by the following formula:

$$3.3\sigma/S$$

The limit of quantitation (LOQ) is calculated by the following formula:

$$10\sigma/S$$

Where, ' σ ' is the (RSD) relative standard deviation of the response and 's' is the slope of the analyte by forming calibration curve.

RESULT AND DISCUSSION

The results for validation parameters (Accuracy, precision, linearity, quantitation limit and detection limit) are shown in table 1, the result of interday and intraday precision are shown in table 2 and the result of recovery studies is shown in table 3 and data for calibration curve is shown in table 4. Linearity range for mebeverine is 12.5- 25 $\mu\text{g/ml}$, 25-50 $\mu\text{g/ml}$, 50-100 $\mu\text{g/ml}$ and 100-200 $\mu\text{g/ml}$ at selected wavelength of 246nm. The coefficient of correlation for mebeverine at 246nm is 0.998. mebeverine showed good regression values at the respective wavelengths of 246nm and the results of recovery study reveals that any small alteration in the mebeverine concentration in the solution can be correctly determined by the projected method. The reliability and validity of projected method are determined by recovery studies. Precision is calculated by studying the repeatability precision. Result of repeatability shows intraday precision and the precision under the same operating conditions over a small interval of time. In both inter-day and intra-day precision study for mebeverine % RSD are NMT 2.0% indicates good repeatability and intermediate precision (Table 2).

CONCLUSION

The projected spectrophotometric method is precise, simple, accurate, economic, rapid and

validated in terms of accuracy, precision, linearity and reproducibility. Proposed method can be proficiently used for evaluation of mebeverine hydrochloride in bulk.

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Table 1. Validation parameters result

Parameter	Result
Linearity Range (mg/ml)	200-12.5
Correlation Coefficient (r^2)	0.998
Slope (m)	0.0116
Intercept	0.0544
Accuracy	100.433
Interday precision (% RSD)	1.046
Intraday precision (% RSD)	0.978
LOD (μg)	0.43469
LOQ (μg)	1.31724

Table 2. Interday precision and Intraday precision

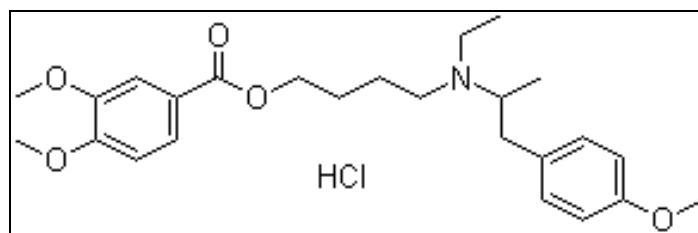
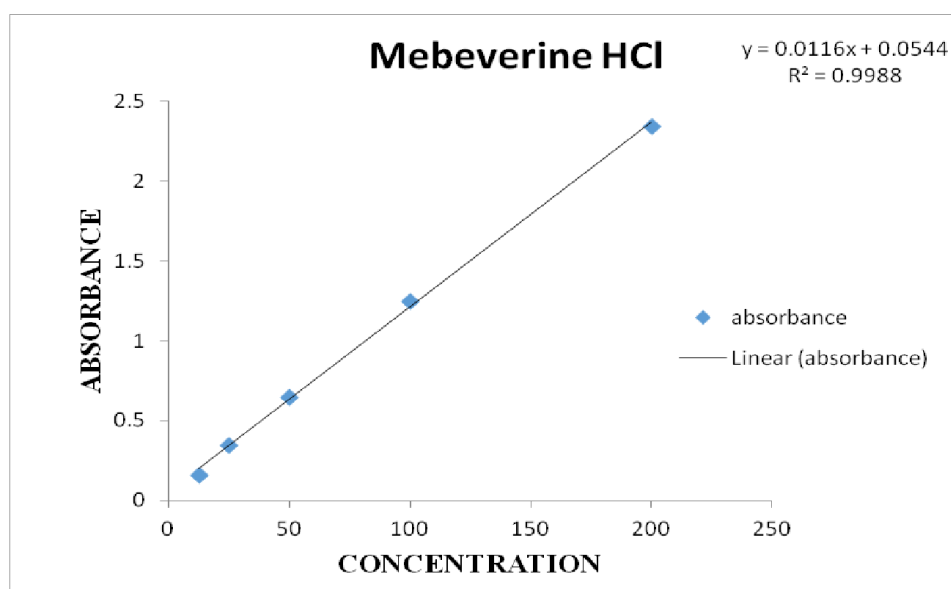
Interday and intraday precision of Mebeverine Hcl					
Drugs	Conc.	Inter-day		Intra-day	
	mg mL ⁻¹	%RSD	%Recovery	%RSD	%Recovery
	Mebeverine Hcl	200	0.23	102.01	0.50
	100	0.81	102.48	0.90	101.00
	50	1.56	101.59	1.30	101.60
	25	1.67	101.96	1.20	101.20
	12.5	0.96	103.03	0.99	102.20

Table 3. Recovery studies

Accuracy			
Drugs	Conc.	%RSD	% Recovery
Mebeverine HCl	80%	1.10	100.20
	100%	1.22	100.90
	120%	1.22	100.20

Table 4. Data for calibration curve

Mebeverine HCl	Absorbance
200	2.349
100	1.25
50	0.65
25	0.35
12.5	0.16

**Figure 1.** Structure of mebeverine hydrochloride**Figure 2.** Calibration curve of mebeverine hydrochloride