

Development and Validation of Spectrophotometric Method for simultaneous estimation of Meclizine and Folic Acid in Bulk and Pharmaceutical Dosage Forms

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ABSTRACT

An UV spectrophotometric method using simultaneous equation was developed for the simultaneous determination of meclizine and folic acid in a binary mixture. In the proposed method, the signals were measured at 390.0 nm and 237.0 nm corresponding to absorbance maxima of and folic acid in methanol respectively. Linearity range was observed in the concentration range of 2-12 µg/ml for both the drugs. Concentration of each drug was obtained by using the absorptivity values calculated for both drugs at two wavelengths, 390.0 nm and 237.0 nm and solving the simultaneous equation. The method was validated and proposed method was fast, accurate and precise so it can be used for regular quality control of the drug.

Keywords: Meclizine, Folic acid, Simultaneous equation, Spectrophotometry, Analysis

INTRODUCTION

Meclizine HCl is piperazine 1-[(4-chlorophenyl) phenylmethyl]-4-[(3-methylphenyl) methyl]-dihydrochloride monohydrate is an antiemetic agent used in post-operative vomiting^[1, 3]. (Figure 1) a piperazine derivative and antihistamine with anti muscarinic and central sedative properties, mainly used for its antiemetic action and in the prevention and treatment of nausea and vomiting associated with a variety of conditions. Folic acid is chemically 4-(2-amino-4-hydroxypteridin-6-yl) methyl amino benzoyl-L-glutamic acid, part of the vitamin B group (vitamin B₉) is a water soluble vitamin (Figure 2). It is one of the most important coenzyme of the haemopoietic systems that control the generation of ferrohaeme^[4-5]. Marketed tablet formulations of these agents play an important role in the treatment of persistent nausea and vomiting during pregnancy.

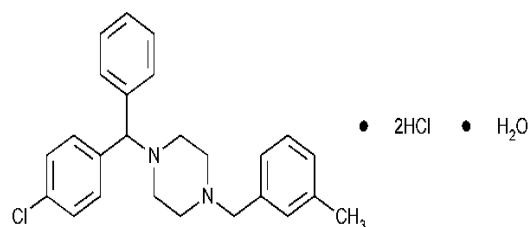


Figure 1: Structure of Meclizine

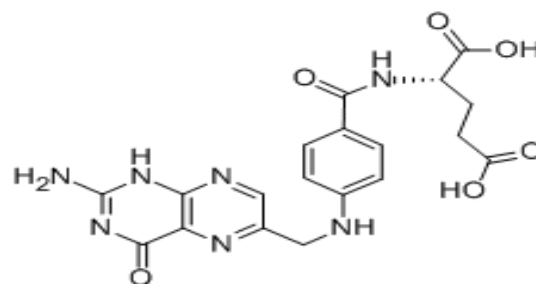


Figure 2: Structure of Folic acid

The review of literature reveals that there were analytical methods of two drugs individually in pharmaceutical dosage forms and even in biological samples and few methods reported for either of one drug with combination of another drug. Few analytical methods like RP-HPLC, HPTLC, HPLC, Spectroscopic methods have been reported for the determination of meclizine and its combination with other drugs in pharmaceutical preparations^[6-10]. Estimation of folic acid in combination with other drugs by spectrophotometric methods and HPLC has been reported^[11-14], but there is no work in the literature reported about the simultaneous determination of meclizine and folic acid in a binary mixture for the analysis of pharmaceutical formulation. Thus there is need to develop a simple rapid and economical method for routine analysis of meclizine and folic acid. The objective of present study was to develop and validate simple, sensitive, accurate, precise, rapid and economical method for estimation of Meclizine and folic acid in bulk and in pharmaceutical formulations.

MATERIALS AND METHODS

Instruments

- (a) Spectrophotometer- Double beam UV–Visible spectrophotometer with 1 cm matched quartz cell Model UV-2450 Shimadzu.
 (b) Electronic Balance- Shimadzu.

Reagents and Chemicals

Meclizine Hydrochloride and folic acid reference standard were kindly provided by Hetero Pharmaceuticals, Hyderabad for providing gift sample of working standard. Methanol of analytical grade was used as a solvent. All chemicals and reagents used were of analytical reagent grade.

Marketed Preparation

The brand name of marketed combined tablet formulation is PNV PLUS containing Meclizine Hydrochloride 25 mg and Folic acid 2.5 mg manufactured by Yash Pharma. Lab. Pvt. Ltd.

Study of Overlain Spectra and Selection of Wavelength

Solutions of Meclizine Hydrochloride and Folic acid were scanned between 200 and 400nm. From the overlay spectra (Figure 3) two wave lengths,

390.0nm and 237.0nm were selected and absorptivity values E (1%, 1cm) of both the drugs at both wavelengths were determined for formation of simultaneous equation.

$$C_x = (A_2 a_{y1} - A_1 a_{y2}) / (a_{x2} a_{y1} - a_{x1} a_{y2}) \quad (1)$$

$$C_y = (A_1 a_{x2} - A_2 a_{x1}) / (a_{x2} a_{y1} - a_{x1} a_{y2}) \quad (2)$$

Where, A_1 and A_2 are absorbances of mixture at 390nm and 237nm respectively, a_{x1} and a_{x2} are absorptivities of Meclizine Hydrochloride at λ_1 and λ_2 respectively and a_{y1} and a_{y2} are absorptivities of Folic acid at λ_1 and λ_2 respectively. C_x and C_y are concentrations of Meclizine Hydrochloride and Folic acid respectively.

PREPARATION OF SOLUTIONS

Meclizine Hydrochloride Standard Stock Solution

Accurately weighed Meclizine Hydrochloride (10mg) was transferred in 100 ml volumetric flask. The drug was dissolved in methanol with sonication and final volume was adjusted with methanol up to mark to prepare a 100 μ g/ml stock solution (Figure 3).

Meclizine Hydrochloride Working Standard Solution

From the above stock solution (100 μ g/ml), an accurately measured 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml was transferred into separate 10 ml volumetric flask and final volume was adjusted with methanol up to mark to prepare 2-12 μ g/ml solutions.

Folic acid Standard Stock Solution

Accurately weighed Folic acid (10mg) was transferred in 100 ml volumetric flask. The drug was dissolved in methanol with sonication and final volume was adjusted with methanol up to mark to prepare a 100 μ g/ml stock solution.

Folic acid Working Standard Solution

From the above stock solution (100 μ g/ml), an accurately measured 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml was transferred into separate 10 ml volumetric flask and final volume was adjusted with methanol up to mark to prepare 2-12 μ g/ml solutions.

Sample Solution

Transfer powder exactly equivalent to laboratory mixture containing 25 mg of Meclizine Hydrochloride and 2.5mg of Folic acid to a 100 ml volumetric flask.

Add about 60 ml of methanol and sonicate for 15 minutes solution was filtered through Whatmann No.1 filter paper. The residue was washed with 10ml methanol three times and make up volume with methanol. From this solution take 1ml and dilute up to 50ml with methanol. Again take 1ml and dilute up to 10ml with methanol.

METHOD VALIDATION

Linearity

The linearity was evaluated by linear regression analysis. The calibration curve was obtained with concentrations of pure Meclizine Hydrochloride and Folic acid solution ranging from 2-12 μ g/ml and 2-12 μ g/ml respectively for the chromatographic method.

Precision

The precision of the procedure was determined by repeatability (intraday). Intraday precision was evaluated by assaying same concentration and during the same day. Repeatability of sample measurement was carried out in six different sample preparations from same homogenous blend of sample. Another replicate determination on three different days to estimate inter day precision.

Accuracy

Recovery studies were performed to validate the accuracy of developed method. To a pre analysed sample solution, a definite concentration of standard drug was added and recovery was studied. 80%,100% and 120% of pure drug solutions were added to the pre analyzed samples.

Limit of Detection and Limit of Quantification

The limits of detection (LOD) and limit of quantification (LOQ) were calculated based on the standard deviation of the response and the slope by using calibration curves.

Ruggedness

Ruggedness of the method was determined by analysis of aliquots from homogeneous slot by two analyst using same operational and environmental conditions.

Analysis of Laboratory Mixture

The absorbances of solutions were recorded at 390.0nm and 237.0nm against blank. Concentration of each drug was obtained by solving the simultaneous equation. (Table5).

RESULT AND DISCUSSION

In this simultaneous equation method, the overlain spectra of drugs showed the λ max of 390.0nm and 237.0nm for Meclizine Hydrochloride and Folic acid respectively. Both the drugs obeyed linearity range 2-12 μ g/ml and correlation coefficient (r^2) were found to be <1 in both cases. The data of regression analysis of the calibration curves is shown in Table 1.

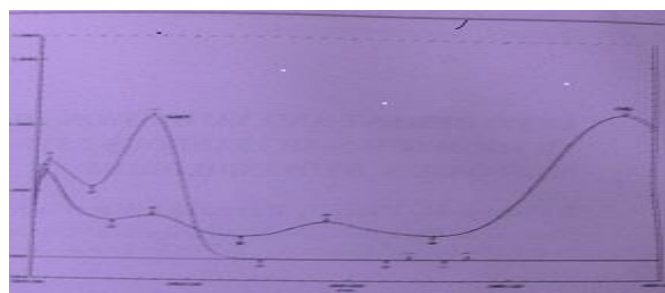


Figure 3: Overlay UV Spectra of Meclizine and Folic acid

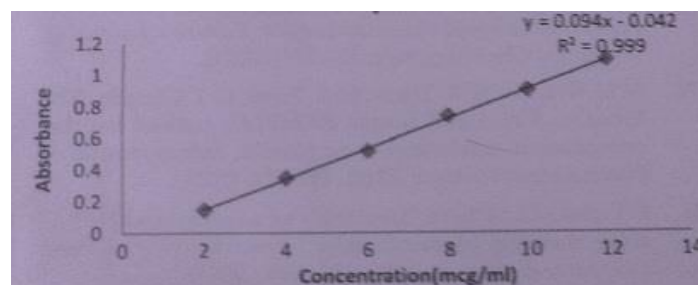


Figure 4: Calibration Curve for Meclizine Hydrochloride

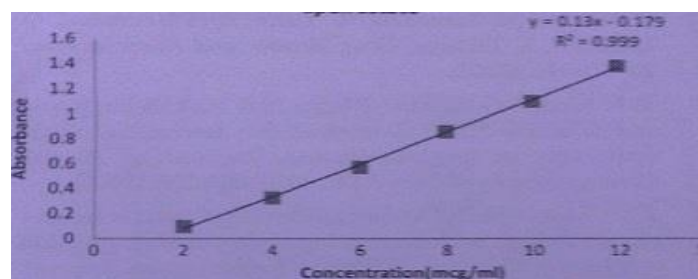


Figure 5: Calibration Curve for Folic acid

Table 1
Data of Regression Analysis and Calibration Curve

Drug	Linearity range	Y= mx+c		r ² *
		Slope*	Intercept*	
MEC	2-12µg/ml	0.129	0.178	0.9988
FOL	2-12µg/ml	0.093	0.041	0.9986

*= Average result of six replicate samples (Meclizine and Folic acid)

The absorptivity values were calculated and along with absorbances, these values were submitted in equation (1) and (2) to obtain concentration of drugs. The percentage purity of drugs in laboratory mixture was found to be 99.77±0.667% for Meclizine and 99.76±0.207 % for Folic acid. The accuracy of the method was determined by performing recovery study by standard addition method. The results were summarized in Table 2. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The results were summarized in Table 3. The LOD for Meclizine and Folic acid were found to be 0.067µg/ml and 0.069µg/ml respectively, while LOQ were 0.201µg/ml and 0.209µg/ml respectively. The method was found to be rugged as the percentage purity of the drugs determined by two different analysts and results were shown in Table 4. Marketed formulation was analyzed with the proposed method and the percentage purity of meclizine was found to be 99.72% w/w and for folic acid it was found to be 99.95% w/w in Table 6.

Table 2
Results of Recovery Studies

Drug	Conc. of Form. (µg/ml)	Conc. of Std. added (µg/ml)	Conc. Recover (µg/ml)	% recovery± SD*
MEC	3	2.4	5.37	99.87%±0.281
	3	3	5.97	99.61%±0.253
	3	3.6	6.54	99.79%±0.086
FOL	10	8	17.96	99.87±0.083
	10	10	19.98	99.94±0.100
	10	12	21.97	99.91±0.093

*=Average result of six replicate samples (Meclizine and Folic acid)

Table 3
Results of Intra Day & Inter Day Precision

Drug	Intraday		Inter day	
	Mean %assay*	%RSD*	Mean %assay*	%RSD*
MEC	98.82% ± 0.288	0.291	99.65%±0.164	0.165
FOL	100.15% ± 0.391	0.382	99.79%±0.381	0.381

*= Average result of six replicate samples (Meclizine and Folic acid)

Table 4
Results of Ruggedness Study

Drug	Analyst-I		Analyst-II	
	Mean %assay*	%RSD*	Mean %assay*	%RSD*
MEC	98.87%±0.252	0.251	99.77%±0.260	0.262
FOL	99.83%±0.128	0.125	99.96%±0.208	0.208

*= Average result of six replicate samples (Meclizine and Folic acid)

Table 5
Analysis of Laboratory Mixture

Laboratory Mixture	Drug	Amount taken found (ug/ml)	Amount found (µg/ml) ±SD*	%Amount found±SD*
1	MEC	3	2.98±0.021	99.77±0.667
	FOL	10	9.97±0.182	99.76±0.207

*= Average result of six replicate samples (Meclizine and Folic acid)

Table 6
Assay of Meclizine and Folic acid

Drug substance	Label claim		Percentage purity (% w/w)
	Taken	Found	
Meclizine	25	24.982	99.72
Folic acid	2.5	2.478	99.95

ACKNOWLEDGEMENT

The authors are thankful to the Management, Sarada Vilas College of Pharmacy for their kind help and providing necessary facilities.

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