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DEVELOPMENT & VALIDATION OF UV SPECTROPHOTOMETRIC METHODS FOR THE ESTIMATION OF MECLIZINE HCL BY ABSORPTION MAXIMA, FIRST ORDER DERIVATIVE AND AUC IN BULK AND ITS TABLET DOSAGE FORM

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ABSTRACT

The present work describes three simple, precise and economical UV methods have been developed for the estimation of Meclizine Hcl in bulk and pharmaceutical dosage form. Method A shown the absorbance maxima at 230 nm, method B area under curve method which involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 225-235 nm respectively and in the first order derivative spectra showed sharp peak at 259 nm for method C. The developed methods were founded to be linear in the concentration range of 2-20 µg/ml. The developed methods were validated by following the analytical performance parameters suggested by ICH. All the validation parameters were within the acceptable range. As economical solvent is used, these methods were used for routine analysis of Meclizine Hcl in bulk and pharmaceutical formulation.

KEYWORDS: Absorption Maxima, Area under curve, Derivative Spectroscopy, Meclizine Hcl, Meclizine Hcl Tablet Dosage form.

INTRODUCTION

Meclizine Hcl has its actions as antagonist at H_1-receptors; meclizine also possesses anticholinergic, central nervous system depressant, and local anesthetic effects. Meclizine depresses labyrinth excitability and vestibular stimulation and may affect the medullary

chemoreceptor trigger zone. Meclizine Hcl is 1-[(4-chlorophenyl)-phenylmethyl]-4-[(3 methylphenyl) methyl] piperazine. Meclizine Hcl is White or off white crystalline powder with a molecular weight of 390.948 g/mol. The molecular formula of Meclizine Hcl $C_{25}H_{27}ClN_2$ and chemical structure is given below (fig.1). Meclizine Hcl is practically insoluble in sparingly soluble in aqueous solutions. It is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide.

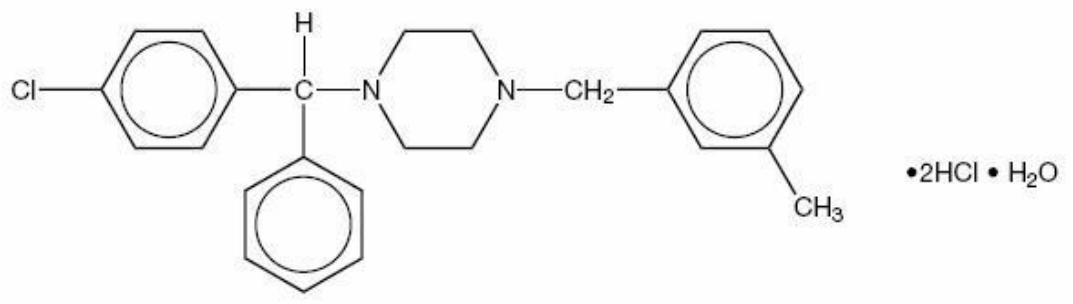

Fig. 1 chemical structure of Meclizine Hcl

Available literature states few HPLC methods for the estimation of Meclizine Hcl at 254 nm. Though HPLC method is highly sensitive and accurate but cost of analysis is too high. But there is no work in the literature reported about the Derivative method and Area under curve method by using UV spectroscopy for the analysis of Meclizine Hcl in pharmaceutical formulation. Thus there is need to develop a simple rapid and economical method for routine analysis of Meclizine Hcl. The objective of present study was to develop and validate simple, sensitive, accurate, precise, rapid and economical method for estimation of Meclizine Hcl in bulk and in pharmaceutical formulations as per ICH guidelines [10, 11].

MATERIALS AND METHODS

Drug samples

Meclizine hydrochloride working standard drug (99.37) was obtained from Hetro Pharmaceutical, Hyderabad, India. Meclizine hydrochloride tablets (antivert-45 mg) were purchased from local pharmacy.

Chemicals & solvents

Methanol of AR grade was purchased from mark fine chemicals (Mumbai, India). Double distilled water, 0.1 N HCL, were used for the study.

Instrumentation

UV Visible spectrophotometer Shimadzu model 1800 was employed with spectral band width of 1 nm attach with computer loaded shimadzu UV Pc software (UV probe) version 2.31 and using a pair of 10mm matched quartz cells. Shimadzu Analytical balance was used for the weighing of samples.

Preparation of standard stock solution and calibration curve

Accurately weight 10 mg of meclizine hydrochloride working standard in 10 ml volumetric flask containing 5 ml of methanol shaken for 5 min then remaining volume made with methanol. The final concentration obtained was 1000µg/ ml. it was further diluted with 0.1 N HCL to get concentration 100 µg/ml. From this a series of aliquots were prepared to get concentration ranging from 2,4,6,8,10,12,14,16,18,20,µg/ ml in 10ml volumetric flask using 0.1 N HCL solution.

Method A: Absorption Maxima Method

By appropriate dilution of stock solution and scanned in spectrum mode from 400-200nm, the maximum wavelength 230nm was selected for the analysis. The calibration curve for Meclizine Hcl was plotted in the concentration v/s absorbance as shown in Fig no 2 and. From this regression equation was calculated. This equation was used to estimate the Meclizine Hcl in tablet dosage forms.

Method B: Area under curve Method

Area under curve (AUC) method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 225nm and 235nm. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. The wavelength range is selected on the basis of repeated observations so as to get the linearity between the area under curve and concentration as shown in Fig no 3. From this regression equation was calculated. This equation was used to estimate the Meclizine Hcl in tablet dosage forms.

Method C: First order derivative method

It involves the conversation of a normal spectrum to its zero, first, second or higher derivative spectrum. In derivative spectrophotometry, spectra are obtained by plotting the first or a higher order derivative of absorbance with respect to wavelength as a function of wavelength.

Often, these plots reveal spectral details that are lost in an ordinary spectrum. In addition, concentration measurements of an analyte in the presence of interference or of two or more analytes in a mixture can sometimes be made more easily or accurately using derivative methods. In this method, 20µg/ml solution of Meclizine Hcl was prepared by appropriate dilution of standard stock solution and scanned from 200-400 nm. The absorption spectra thus obtained were derivatized from zero to second order. First order derivative spectra of the drug showed a sharp peak at 254 nm, which was selected for its quantitation. The concentration of Meclizine Hcl present in the test solution was determined against the calibration curve as shown in Fig no 3 in quantitation mode.

Analysis of marketed formulations

For the estimation of Meclizine Hcl in the commercial formulations, 5tablets each containing 40mg of Meclizine Hcl were weighed and average weight was calculated. The tablets were crushed and powdered in glass mortar. For analysis of the drug, quantity of powder equivalent 10mg of Meclizine Hcl was transferred to 10ml volumetric flask and dissolved in sufficient quantity of Methanol and volume made up to the mark with Methanol to obtain concentration of 1000µg/mL of Meclizine Hcl. Then the solution was filtered through whatman filter paper no.41. Further dilution of the solution was made in 0.1N HCL to get required concentration of 10µg/ml. The concentration of Meclizine Hcl in formulation was determined by above developed methods. The assay procedure was repeated 6 times (n=6) for each method.

VALIDATION

The methods were validated according to ICH guidelinesQ2 (R1) to study linearity, accuracy and precision by using above three methods.

Linearity

A linear relationship was found for the three methods between the absorbance and the concentration of Meclizine Hcl in the range of 2-20µg/ml. The correlation coefficient for these methods A, B, C was 0.991, 0.997, and 0.999 indicating linearity ($r2 > 0.999$) (Table No.2)

Precision

The precision of the method was expressed in terms of % relative standard deviation (% RSD). The % RSD values for three methods A, B, C found to be less than 2 for intraday and

inter day precision, the precision results showed good reproducibility. The results are expressed in Table. 3.

Accuracy

Accuracy for the methods A, B, C were established at 80, 100, 120% levels by the addition of standard drug of Meclizine Hcl to pre analyzed samples. The results were given in Table no.4.

Limit of Detection and Limit of Quantitation

LOD and LOQ values were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determination, Y intercept and its standard deviation was computed. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation (LOQ) were determined on the basis of response and slope of the regression equation. The results were given in Table no.2

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for the analysis of Meclizine Hcl in bulk and in pharmaceutical dosage form. The absorbance Maxima of Meclizine Hcl was found at 230 nm (Method A) and the wavelength range for area under curve (Method B) was 225-235 nm. The first order derivative spectroscopy method sharp peak at 254nm (Method C) was selected for the analysis. Linearity for detector response was observed in the concentration range of 2-20 µg/ml for Method A, Method B, Method C. standard deviation and coefficient of variance for six determinations of tablet sample using all the methods were to be less than ± 2.0 indicating the good precision of all the methods. The validation of proposed methods were further confirmed by recovery studies, the %recovery values vary from 97- 99%. Based on results obtained it was found that the proposed methods were accurate, precise, reproducible and can be employed for routine quality control of Meclizine Hcl tablet dosage form.

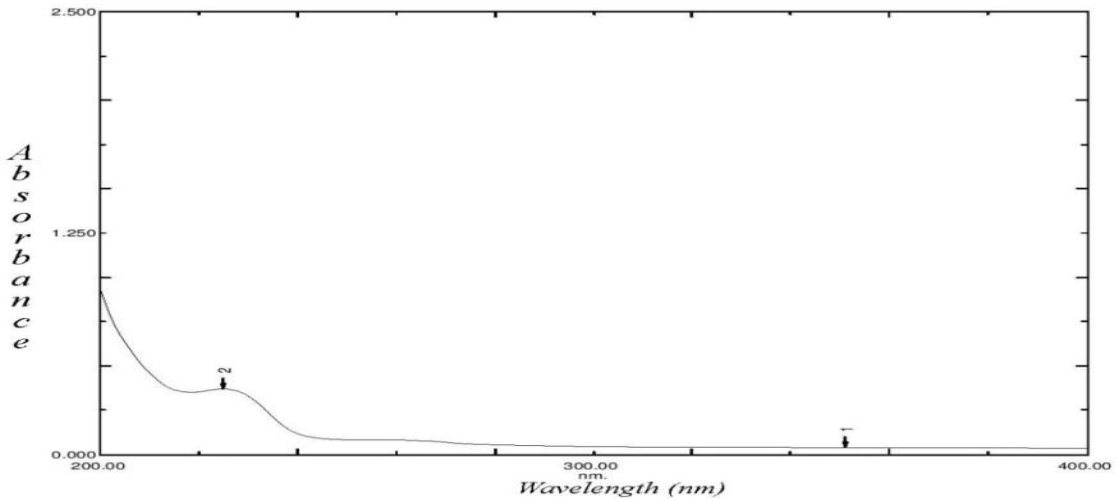

Fig. 2: Absorption Maxima Spectrum of Meclizine Hcl

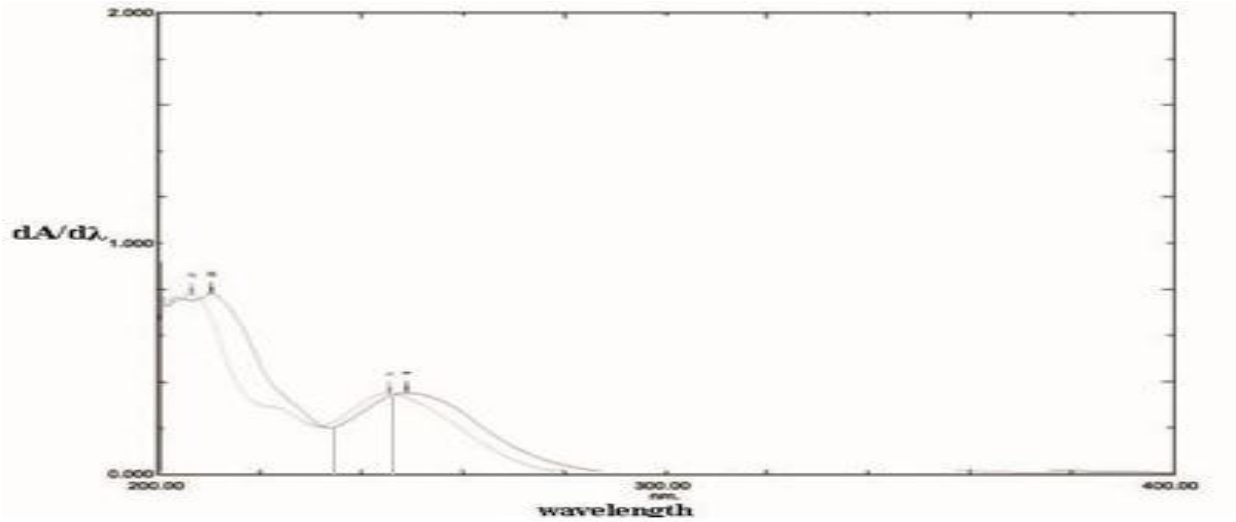

Fig. 3: UV-Spectrum of Meclizine Hcl indicating AUC

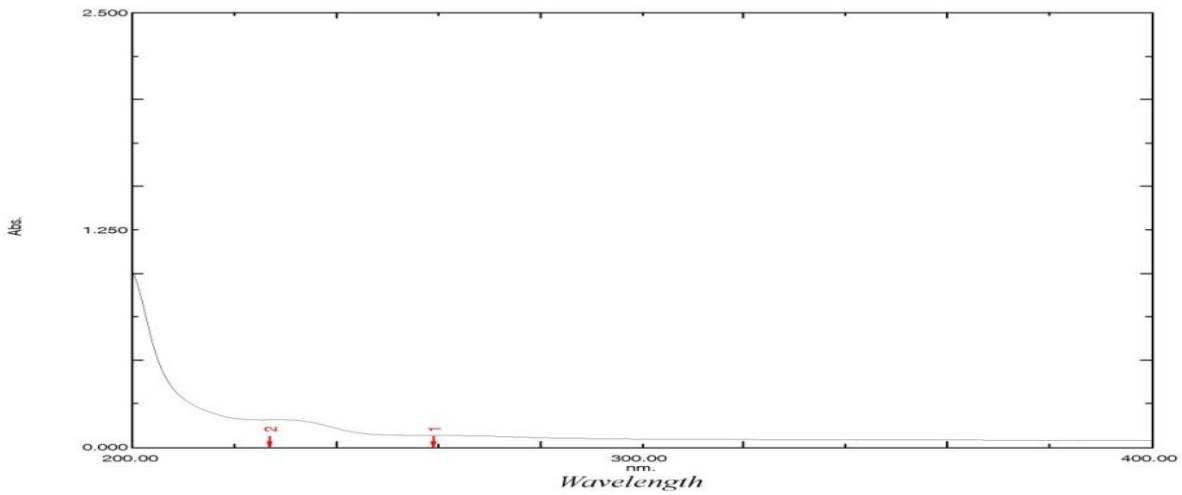

Fig. 4: First order derivative spectrum of Meclizine Hcl

Table No .1: Result of Marketed Formulation Analysis

Method	Label claim (mg/tablet)	Test concentration (µg/ml)	Concentration found (µg/ml) n=6	% of assay
A	45	10	9.75	97.5
B	45	10	9.81	98.1
C	45	10	9.93	99.3

Table No- 2: optical characteristics of Meclizine Hcl

Parameter	Method A	Method B	Method C
λmax	230nm	225-235nm	227nm, 254nm
Beers limit(µg/ml)	2-20µg/ml	2-20µg/ml	2-20µg/ml
Correlation coefficient (r^2)	0.991	0.997	0.999
Slope(a)	0.501	4.85	0.567
Intercept(b)	0.005	0.034	0.001

Table No-3: Intraday and Inter day data of Precision of Meclizine Hcl

Method	Label Claim (mg)	Intraday precision % RSD (n=3)	Inter-day precision %RSD (n=3)	
			Day I	Day II
A	45mg	0.55	0.49	0.52
B	45mg	0.62	0.52	0.60
C	45mg	0.83	0.78	0.80

Table No-4: Recovery data of Meclizine Hcl

Concentration Taken (µg/ml)	Recovery Levels %	Amount Added (µg/ml)	Amount Found (µg/ml)			% Recovery		
			A	B	C	A	B	C
4	50	2	5.89	5.93	5.99	97	98	99
4	100	4	7.88	7.95	7.97	97.2	98	99
4	150	6	9.87	9.92	9.97	97.7	98	99

CONCLUSION

The proposed UV spectrophotometric methods were found to be simple, sensitive, accurate, precise and economical and can be used in the determination of Meclizine Hcl in bulk and pharmaceutical dosage forms in a routine manner.

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