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Original Article

A STABILITY INDICATING UV SPECROPHOTOMETRIC METHOD FOR DETERMINATION OF METOCLOPRAMIDE HYRDROCHLORIDE

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ABSTRACT

A stability indicating method has been developed for specific determination of Metoclopramide HCl in bulk by UV spectrophotometry in presence of its degradation products. The method is simple, accurate, precise, and robust. Linearity range for the method is 10-50µg/ml at detection wavelength of 272 nm. The LOD and LOQ values were found to be 3.26µg/ml and 9.89µg/ml respectively.

Keywords: Metoclopramide hydrochloride, Stability indicating, UV Bulk, Forced degradation.

INTRODUCTION

Metoclopramide HCl, 4-amino-5-chloro-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide hydrochloride, is an antiemetic drug. It inhibits gastric smooth muscle relaxation produced by dopamine and therefore increases cholinergic response of gastrointestinal tract. [1,2]

Knowledge of the stability of the molecule helps in selecting proper formulation and package as well as providing proper storage conditions and shelf life, which is essential for regulatory documentation. Forced degradation is a process that involves degradation of drug products and drug substances at conditions more severe than accelerated conditions and thus generates degradation products that can be studied to determine the stability of the molecule [3]. The presently available literature reveals few analytical methods for determination of Metoclopramide HCl by HPLC [4,5], UV spectrophotometry [6,7], LC-MS [8], in plasma [9].

The objective of this work was to develop a validated Stability indicating assay method for the determination of Metoclopramide hydrochloride in presence of its degradation products generated by subjecting the drug to forced degradation conditions under acid, alkali, thermal and oxidative stress as per the guidelines[10] and to establish the inherent stability of Metoclopramide hydrochloride.

MATERIALS AND METHODS

Metoclopramide hydrochloride was supplied by IPCA Laboratories, Aurangabad as the gift sample. Its identity and purity were confirmed by recording the FTIR spectra. Solvent used was Deionized water from the water treatment plant (SG) of the Institute. The reagents used were Hydrochloric acid (Qualigens), Sodium hydroxide & Hydrogen Peroxide 50% solution.

Apparatus

UV Spectrophotometer- Shimadzu Japan UV 1700, FT-IR- Thermo electron co.(IR 200) Prestige 21 and analytical balance (Schimadzu AUX 220).

Method

Spectrophotometric conditions

Spectrophotometric analysis was carried out at ambient temperature. Solvent used was deionized water; standard solution of 50µg/ml was analyzed at 272 nm.

Preparation of stock and standard solution

Accurately weighed 100mg of standard Metoclopramide HCl was transferred to 100 ml volumetric flask to make a stock solution of 1000µg/ml. Suitable aliquots were taken into 100 ml volumetric flask to make standard solutions in the range of 10-50 µg/ml.

Preparation of calibration curve

The calibration curve was prepared in the concentration range 10-50µg/ml by analyzing each solution in triplicate and plotting the concentration (µg/ml) against absorbance. The correlation coefficient and equation of the line were determined. The spectrum of fresh drug solution (50µg/ml) is shown in fig1 and the calibration curve in fig 2. The data is shown in table 2.

Forced degradation studies

The forced degradation of MTD was done in each of the stress condition at a concentration of 1 mg/ml. The degradation was confirmed in each case by recording the changes in the ultraviolet spectra of each stressed sample comparing it with that of fresh drug solution.

A. Acidic stress

100 mg of MTD was refluxed in 1 N Hydrochloric acid for 4 hours in a water bath at 70°C.

B. Alkaline stress

100 mg of MTD was refluxed in 1 N sodium hydroxide for 4 hours in a water bath at 70°C.

C. Thermal stress

100 mg of MTD was kept in solid state at 70°C for 4 hours in an oven equipped with temperature control probe.

D. Oxidative stress

100 mg of MTD was dissolved in 3% and 6% Hydrogen peroxide separately and kept at room temperature for 24 hours in amber colored stoppered vials.

RESULTS AND DISCUSSION

Recording of spectrum of standard solution

The spectrum of standard drug was recorded with 50µg/ml solution, and scanned in the range of 400-200 nm. 272 nm was found to be the suitable wavelength for analysis.

Degradation behavior of MTD

The amount (percent) of MTD remaining undegraded under each stress condition was determined from the absorbance of the fresh drug sample relative to that of stressed drug sample. The results are shown in table 7.

Method validation

A. Accuracy

Accuracy of the method was evaluated by spiking the drug at three concentration levels (8, 10 & 12µg/ml) to the original 10 µg/ml solution. The percent recovery of the added drug was calculated from the linearity plots. The results are shown in table 1.

B. Linearity and range

The linearity of the method was established by preparing a calibration curve in water in the range 10-50µg/ml. Triplicates of each of the solution were analyzed and calibration curve recorded. The mean (n=3) absorbance was plotted against concentration (µg/ml). The correlation coefficient and equation of line were determined. The results are shown in fig2 and table 2.

C. Precision

The Interday and intraday precision was determined by calculation of the % RSD values on triplicates of each concentration. The mean (n=3) absorbance of each concentration was compared with that of the second run on the same day (intraday) and with that on the next day (interday) and the percent relative deviation calculated. The results are shown in table 3.

D. Specificity

The Specificity of the method was established through the determination of the drug in the presence of its degradation products with high degree of precision. The spectrum homogeneity was confirmed by analyzing the ratio chromatograms at the wavelengths 271 nm and 273 nm.

E. Ruggedness [16]

Mean absorbance (n=3) was measured for the 10µg/ml solution analyzed by two different analysts on different days and the percent relative deviation between two trials was calculated. The results are shown in table 4.

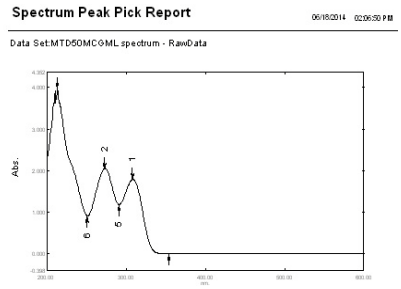

Fig. 1: Spectrum of fresh standard solution of Metoclopramide HCl (50µg/ml)

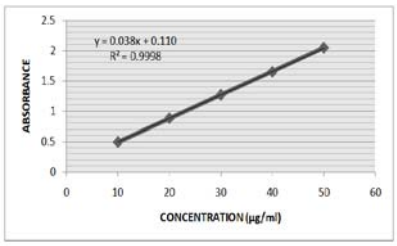

Fig. 2: Calibration curve of Std MTD

F. Robustness

Deliberate changes in the detection wavelength were made. Three replicates of each deviation were analyzed and the %RSD between the mean (n=3) absorbance and that obtained under optimized spectrophotometric conditions were determined. The results are shown in table 5.

G. Limit of detection and limit of quantitation

The limit of detection and limit of Quantitation was calculated based on standard deviation (σ) and the slope (S) of the calibration plot, using the formulae LOD= 3.3σ/s and LOQ=10σ/S as defined by ICH. The LOD was found to be 3.26µg/ml and LOQ 9.89µg/ml.

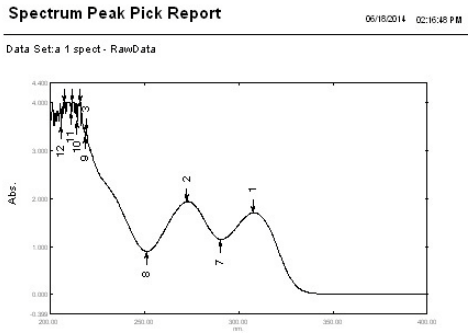

Fig. 3: Spectrum of Acid degraded MTD

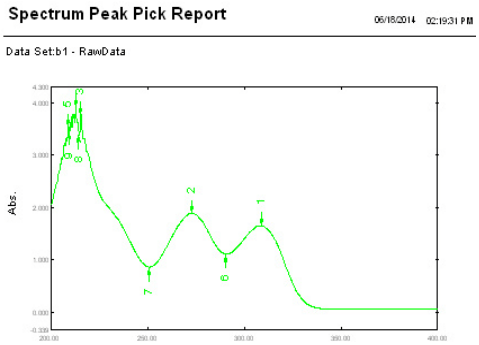

Fig. 4: Spectrum of base degraded MTD

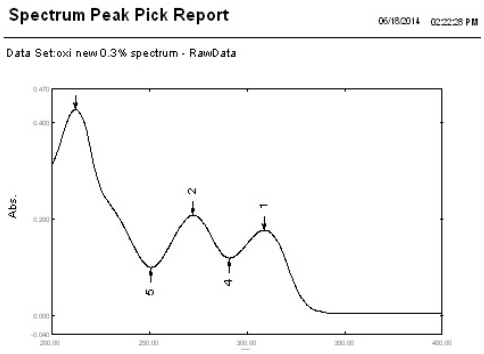

Fig. 5: Spectrum of oxidatively (0.3%) degraded MTD

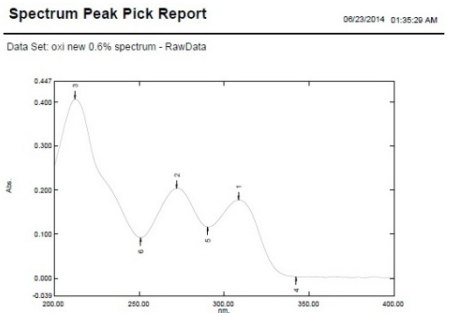

Fig. 6: Spectrum of Oxidatively (0.6%) degraded MTD

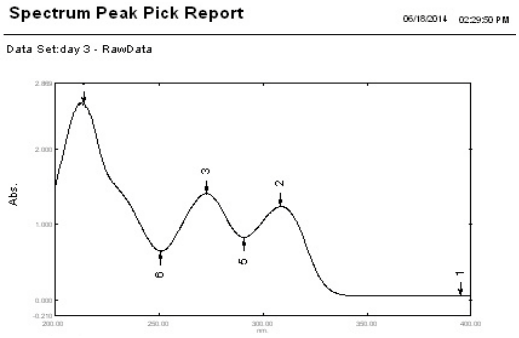

Fig. 7: Spectrum of thermally Degraded MTD

H. System suitability

The system suitability parameters Linearity and range, accuracy, precision and specificity were determined and are shown in table 6.

Table 1: Results of recovery studies

Preanalyzed Sample Solution (µg/ml)	Level of Addition	Drug recovered (µg/ml)	% Recovery	%RSD
MTD10	80	17.92	99.55	0.435
	100	20.02	100.1	0.698
	120	22.03	100.13	0.333
Average %RSD				**0.488**

Table 2: Linearity Study of MTD at 272 nm

S. No.	Conc.	Absorbance Mean±S. D.	%RSD
1	10	0.498±0.0032	0.642
2	20	0.883±0.001	0.113
3	30	1.269±0.0015	0.118
4	40	1.648±0.0005	0.030
5	50	2.045±0.0005	0.024

Table 3: Results of Intra-day and Inter-day precision studies

Drug	Intra-day Precision			Inter-day Precision	
	Conc.	Mean±S. D.	%RSD	Mean±S. D.	%RSD
MTD	10	9.99±0.036	0.360	10.005±0.028	0.279
	20	19.91±0.035	0.175	19.98±0.077	0.385
	30	30.02±0.015	0.050	29.97±0.063	0.210
	40	40.07±0.056	0.139	39.96±0.148	0.370
	50	49.70±0.045	0.092	49.84±0.197	0.395
Average %RSD			**0.163**	**Average %RSD**	**0.327**

Table 4: Results of ruggedness studies

Drug	Amount Taken (µg/ml)	Analyst I		Analyst II	
		Amount Found	%RSD	Amount Found	%RSD
MTD	10	9.96±0.025	0.25	9.99±0.0152	0.152
MTD	10	**Instrument I**		**Instrument II**	
		10.01±0.047	0.47	9.80±0.045	0.459

Table 5: Results of Robustness studies

Drug Amount Taken (µg/ml)	WL-1 (271 nm) Amount %RSD Found	WL-2 (272 nm) Amount %RSD Found	WL-3 (273 nm) Amount %RSD Found
MTD 10	9.88±0.02 0.202	9.96±0.025 0.25	9.99±0.045 0.45

Table 6: System suitability parameters

Validation Parameter	Values
Range	10-50µg/ml
Linearity-	
Regression equation (y=mx+C)	y = 0.038x + 0.110
and Correlation coefficient r^2	r^2 = 0.9998
LOD	3.26µg/ml
LOQ	9.89µg/ml
Recovery (% RSD)	0.488
Intra-Day Precision	0.163
Inter-Day Precision	0.327
Inter-Analyst	0.201
Inter-Instrument	0.464

Table 7: % Drug Degraded under each stress condition

S. No.	Stress Condition	Absorbance	% Drug degraded	% Drug Remain
1	Fresh Solution	2.045	0	100
2	Acidic	1.927	5.78	94.22
3	Basic	1.859	9.10	90.90
4	Oxidative (0.3%)	0.290	85.82	14.18
5	Oxidative (0.6%)	0.262	87.19	12.81
6	Thermal	1.639	19.86	80.14

CONCLUSION

A validated stability indicating assay method has been developed for the determination of Metoclopramide hydrochloride in bulk. The results show that the developed method was accurate, precise, simple, economic, fast and specific. Metoclopramide HCl is most prone to degradation under oxidative (6%) stress, followed in order by the stress oxidative (3%), thermal, basic, and acidic.

ABBREVIATIONS

MTD: Metoclopramide HCl.

CONFLICT OF INTERESTS

Declared None

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