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Research Article

SECOND DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF METFORMIN HYDROCHLORIDE IN BULK AND IN TABLET DOSAGE FORM

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ABSTRACT

A simple, economic, sensitive, precise and accurate second derivative spectrophotometric method has been developed for determination of Metformin hydrochloride in bulk and in tablet dosage form. The quantitative determination of the drug was carried out using the second derivative values measured at 233.8 nm. Calibration graph constructed at 233.8 nm was linear in concentration range of 4-20 µg/ml with correlation coefficient 0.9979. The method was validated as per ICH guidelines and can be used for determination of Metformin hydrochloride in tablet dosage form.

Keywords: Metformin hydrochloride, Derivative spectrophotometry, Tablet, Validation.

INTRODUCTION

Metformin hydrochloride is a biguanide class of antidiabetic drug, chemically is N,N-dimethylimidodicarbonimidic diamide hydrochloride. The anti-diabetic Metformin hydrochloride indicated for the relief of signs and symptoms of Type-2 diabetes mellitus or non-insulin dependent diabetes mellitus (NIDDM), and hyperglycemia.

In present study, an attempt has been made to develop a simple, sensitive and efficient second derivative spectrophotometric method for estimation of Metformin hydrochloride in tablet dosage form.

Experimental

Chemicals and Reagents

Metformin hydrochloride working standard was kindly provided by Cadila Pharmaceuticals Ltd., Ahmedabad (India), and was used as received. A commercial tablet formulation was purchased from the local market.

Distilled water used as a solvent.

MATERIAL AND METHODS

Instrument

A double beam UV-VIS Spectrophotometer (UV CE7400, Cecil, UK) Spectral bandwidth of 1 nm and wavelength accuracy of ±0.5 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (XB120A, Precisa, Switzerland).

Preparation of Standard Stock Solution

Accurately weighed Metformin hydrochloride (10.0 mg) was transferred to 100 ml volumetric flask, dissolved in about 50 ml of distilled water and volume was up-to 100 ml with distilled water to obtain stock solution of drug concentration of 100µg/ml.

Determination of wavelength of maximum amplitude (D^2 value) of Metformin hydrochloride

10 ml of above solution was diluted to 100 ml with the same solvent to get the concentration of 10 µg/ml. The UV spectrum of final solution obtained was scanned in the range of 200 to 400 nm against distilled water as a blank. The λ_{max} was found 233.8 nm. The UV spectrum of Metformin hydrochloride is shown in Fig. 1.

Preparation of calibration curve for Metformin hydrochloride

From standard stock solution of Metformin hydrochloride 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 ml solutions were pipetted out in a series of ten 100 ml volumetric flasks. The volumes in each flask were made up to 100 ml with solvent (distilled water), to obtain final solutions contained 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 µg/ml of drug.

Calibration curve was constructed from absorbance measure at 233.8 nm (against distilled water as blank) for standard containing 2-20 µg/ml of Metformin hydrochloride shown in Fig. 2

Estimation of Metformin hydrochloride in tablets

The powder of 20 Metformin hydrochloride tablets (label claim 500 mg) of the same batch no. were triturated and mixed properly. Accurately weighed 119.4 mg powder [equivalent to 100 mg of Metformin hydrochloride] was transferred in 100 ml volumetric flask containing small quantity of reference solvent (Distilled water). Ultrasonic water bath was used for 20 minutes to complete dissolution. The solution were diluted to volume and filtered through whattman filter paper no. 40. Further suitable dilutions were made to obtain six replicates of 10 µg/ml solutions. These solutions were analyzed and percent recovery of Metformin hydrochloride tablet was determined. Recovery data for estimation of Metformin hydrochloride in Metformin hydrochloride tablets are summarized in Table 2.

Method Validation

Specificity: Commonly used excipients present in selected tablet formulation were spiked into a preweighed quantity of drug. The absorbance was measured and calculations determined the quantity of the drug.

Linearity: A calibration curve was constructed at optimum experimental conditions using D^2 values versus concentration in the range of 4-20 µg/ml. Regression analysis using the method of least square was made for slope (0.0005), intercept (0.0002) and correlation coefficient (0.9979). The regression equation (y=0.0005x-0.0002) was obtained, where 'y' is amplitude of the peak at 233.8 nm and 'x' is the concentration of the sample in µg/ml.

From calibration curve data, high value of the correlation coefficient (0.9979) was found and the value of the intercept on ordinate, which is close to Zero, shows very good linearity of the calibration graph and adherence of the method to Beer's law.

Precision: For Intraday and Interday precisions of the method, solutions of Metformin hydrochloride were prepared at three concentration levels 9.6, 12, 14.4 (µg/ml) each in triplicate. These solutions were analyzed respectively three times within one day and three consecutive days and the results are reported in terms of relative standard deviation(RSD).

Accuracy: The accuracy of the method was assessed, based on recovery study. The technique of standard addition was used to

assess accuracy of the method. For this purpose a concentration of 8 µg/ml was selected to prepare the sample matrix of the blank drug. Again 8 ml of sample was taken in three, 100 ml volumetric flasks. To these three flasks 6.4 ml, 8.0 ml and 9.6 ml of standard stock solution of API mixture of Metformin hydrochloride was added and volume was made up to 100 ml. The absorbances of the sample matrix and after standard addition were measured in triplicate. The results are reported in terms of % recovery.

RESULTS AND DISCUSSION

According to the International Conference on Harmonization, the main objective of the validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose, and the parameters that need to be selected are the responsibility of the analyst. the solubility of Metformin hydrochloride in distilled water, so it was used in this method. Metformin hydrochloride in distilled water shows absorption maxima at 233.8 nm in second order derivative spectrum. The response for Metformin hydrochloride was found to be linear in the concentration range of 4.0–20.0 µg/ml. The optical characteristics of the method and regression analysis of the calibration curve are shown in Table 3. The recovery of Metformin hydrochloride was found to be satisfactory. Excipients used in the specificity study did not interfere with response of the drug at its analytical wavelength. Also, no significant change in response of Metformin hydrochloride was observed after 8 hrs. Hence, the method is specific and robust for estimation of Metformin hydrochloride. The proposed spectrophotometric methods were applied to the determination of Metformin hydrochloride in its pharmaceutical formulations.

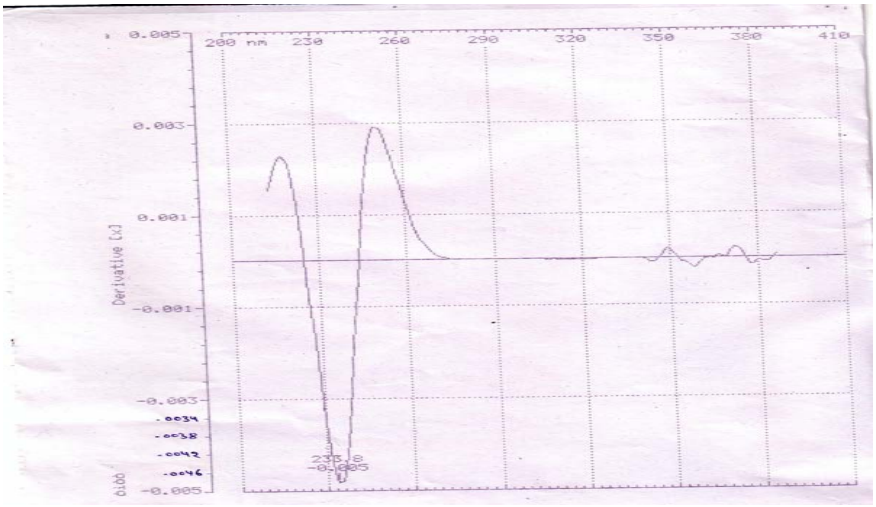

Fig. 1: It shows Second derivative UV spectrum

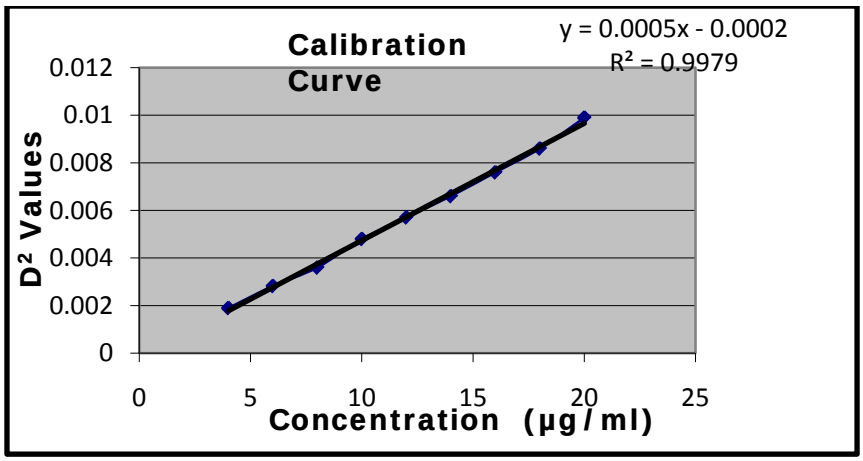

Fig. 2: It shows Calibration curve of Metformin hydrochloride at 233.8 nm

Table 1: Calibration curve data for Metformin hydrochloride

Conc. (µg/ml)	D² value (amplitude)
4	0.001900
6	0.002823
8	0.003600
10	0.004800
12	0.005706
14	0.006600
16	0.007600
18	0.008600
20	0.009900

Table 2: Assay result of Metformin hydrochloride in tablets

Label claim (mg/tab)	Amount found (mg/tab)	Standard deviation	% Mean recovery
500.0	495.83	1.94079	99.1666

Table 3: Optical characteristics and validation parameters of Metformin hydrochloride

Parameter		Values
Beers's law limit (µg/ml)		4.0-20
λ_{max} (nm)		233.8
Molar absorptivity (mole^{-1} cm^{-1})		794.88
Regression equation (Y=a + bc)		0.0005x-0.0002
Correlation coefficient (r^2)		0.9979
Slope (b)		0.0005
Intercept (a)		0.0002
Specificity		101.04537
Linearity		0.9979
Limit of detection (µg/ml)		0.008348413
Limit of quantitation (µg/ml)		0.025298221
Precision (RSD, %)	Repeatability	0.05436
	Intraday	0.068178
	Interday	2.339433
Accuracy (% recovery)		98.00-100.625
Percent mean recovery for Metformin hydrochloride tablets		99.1666

CONCLUSION

The method was validated and found to be sensitive, economic, accurate and precise. Hence, the method can be used successfully for routine analysis of pharmaceutical dosage form of Metformin hydrochloride.

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