

Derivative Spectrophotometric Method for Estimation of Metformin Hydrochloride in Bulk Drug and Dosage Form

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ABSTRACT

A simple, precise and sensitive UV method has been developed for the estimation of Metformin HCl in bulk drug & Dosage form by Second order & Third order Derivative Spectrophotometric method at 235 nm & 228 nm respectively. Metformin HCl has exhibited maximum absorbance at 235 nm & 228 nm in solution & obeyed Beer's law in the concentration range of (2-20 mcg/ml) in Bulk drug and Dosage form. The proposed method was successfully applied for the determination of Metformin HCl in commercial tablet preparation. As per ICH guidelines the results of the analysis were validated statistically and were found to be satisfactory.

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

INTRODUCTION

Metformin HCl is chemically *N,N*-dimethylimidodicarbonimidic diamide. Metformin HCl is an oral antidiabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 diabetes, in particular. It is also used in the treatment of polycystic ovary syndrome.¹ It is aqueous soluble & shows absorbance at 235 nm & 228 nm wavelength by Second order & third order derivative spectrophotometric methods. The essential feature of derivative spectrophotometric assay is that the measured absorbance in solutions of the analyte in chemical forms which exhibit spectral characteristics & follows Beer's law²

EXPERIMENTAL METHODS

Chemicals and reagents

Metformin HCl [Bulk Drug] used were purchased from Research Lab fine Chem. Industries Mumbai, India., & tablet dosage form purchased from local market (GLYCIPHAGE, Franco india), Double distilled water was used throughout the analysis.

Instrumentation

A JASCO V-530 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements.

Selection of Common Solvent

Double Distilled Water was selected as a common solvent for developing spectral characteristics of drug.

Preparation of solution

Standard stock solution containing Metformin HCl was prepared by dissolving 100 mg in 100 ml of Distilled water and then diluted with Distilled water separately to get series of dilution ranging from 2- 20 mcg/ml and then absorbance recorded at 235 nm & 228 nm by second order & third order derivative spectrophotometric method respectively against reagent blank.

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 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. 45 μ Further suitable dilutions were made to obtain six replicates of 10 $\mu\text{g/ml}$ 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 1.

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 2-20 $\mu\text{g/ml}$. Regression analysis using the method of least square was made for slope (0.0007), intercept (0.000) and correlation coefficient (0.999). The regression equation ($y=0.0007x-0.000$) was obtained, where 'y' is amplitude of the peak at 235 nm and 'x' is the concentration of the sample in $\mu\text{g/ml}$. D^3 values versus concentration in the range of 2-20 $\mu\text{g/ml}$. Regression analysis using the method of least square was made for slope (0.000), intercept (0.000) and correlation coefficient (0.995). The regression equation ($y=0.000x-0.000$) was obtained, where 'y' is amplitude of the peak at 228 nm and 'x' is the concentration of the sample in $\mu\text{g/ml}$

From calibration curve data, high value of the correlation coefficient (0.999) &

(0.995) for second & third order derivative 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.

Accuracy

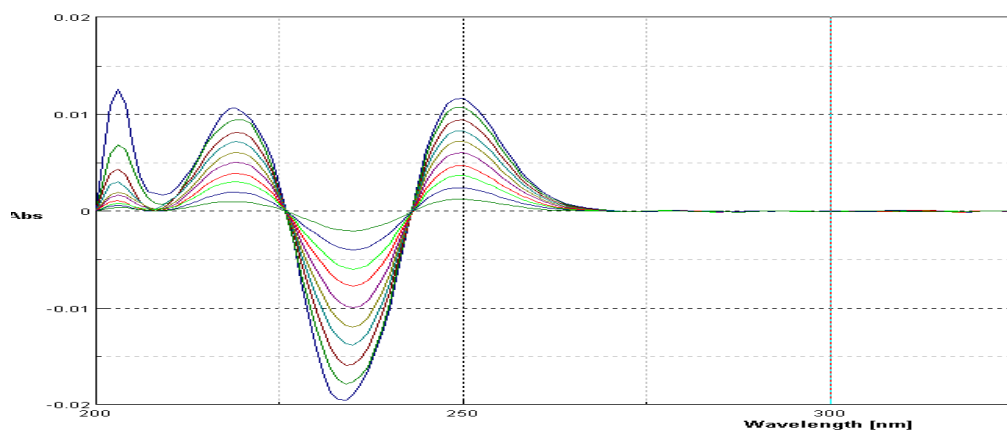
The accuracy of the method was assessed, based on recovery study. The technique of standard addition was used to assess accuracy of the method. For this purpose a concentration of 8 $\mu\text{g/ml}$ was selected to prepare the sample matrix of the blank drug.

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.

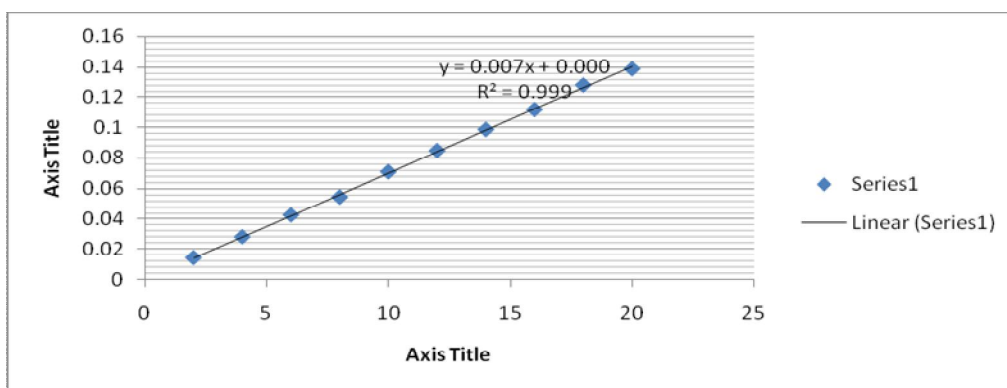
RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, percent relative standard deviation and % range of error were found to be within the limits and satisfactory. All of the analytical validation parameters for the proposed method were determined according to ICH guidelines. The method was found to provide high degree of precision and reproducibility. The recovery studies showed that the results were within the limit indicating no interference. The proposed method is simple, sensitive, accurate and precise and can be successfully employed for the routine analysis of the Metformin HCl in bulk drug.

a)Second order Derivative spectra (λ max 235 nm)



Graph 1: Linearity of Metformin HCl by Second Derivative Spectrophotometry



Graph 2: 3rd Order It shows Calibration curve of Metformin hydrochloride at 228 nm

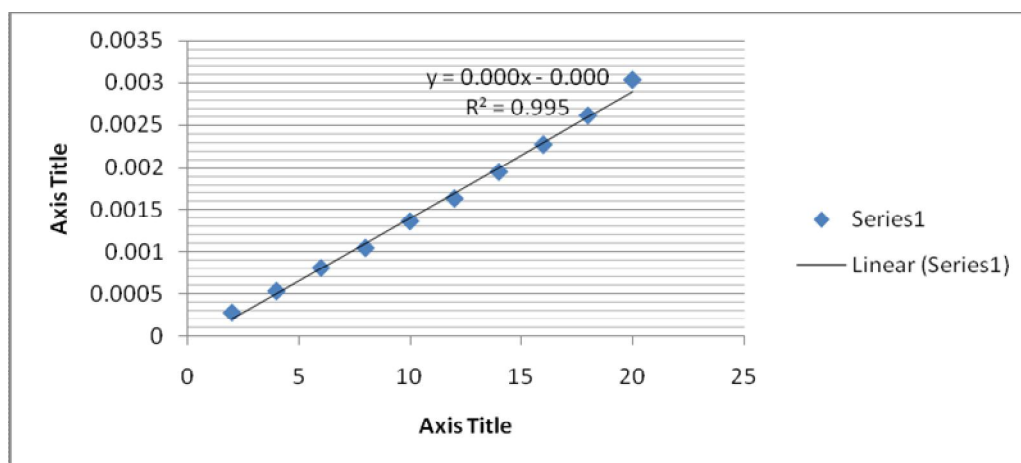


Table 1: Assay result of Metformin hydrochloride in tablets

Label claim (mg/tab)	Amount found (mg/tab)	Standard deviation	% Mean recovery
500	495.81	1.94079	99.1566

Table 2: Characteristics and validation parameters of Metformin hydrochloride

Parameters	Values	
	2 nd Order (235nm)	3 rd Order (228nm)
Beers's law limit ($\mu\text{g/ml}$)	2-20	2 – 20
λ_{max} (nm)	235	228
Molar absorptivity ($\text{mole}^{-1} \text{cm}^{-1}$)	794.88	
Regression equation ($Y=a + bc$)	$y=0.0007x- 0.000$	$y=0.000x-0.000$
Correlation coefficient (r^2)	0.999	0.995
Slope (b)	0.007	0.000
Intercept (a)	0.000	0.000
Specificity	101.04537	
Linearity	0.999	0.995
Limit of detection ($\mu\text{g/ml}$)	0.008348413	
Limit of quantitation ($\mu\text{g/ml}$)	0.025298221	
Accuracy (% recovery)	98.00-100.625	
Percent mean recovery for Metformin hydrochloride tablets	99.1566	

CONCLUSION

The proposed Second order & Third order Derivative spectrophotometric method is simple, accurate, precise and selective for the estimation of Metformin HCl in bulk drug & Dosage form . The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine analysis of Metformin HCl in bulk drug & Dosage form.

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