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Research Article

Estimation of Metformin Hydrochloride in Bulk and Formulation by UV - Spectroscopic Area Under Curve Method

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ABSTRACT

The current work is carried out for estimation of Metformin Hydrochloride by using area under curve (AUC) method using UV-visible spectrophotometer. For this purpose the wavelength range 221-241 nm was selected. Distilled water was used as a solvent throughout the work. Linearity was observed in concentration range 5-25 µg/ml ($R^2 = 0.994$) for the method. The present method was found to be simple and linear which can be used for routine quality control analysis for spectrophotometric estimation of Metformin hydrochloride in bulk.

Keywords: Metformin Hydrochloride, Area under curve, Antidiabetic, λ_{max} .

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INTRODUCTION

Metformin hydrochloride is a hypoglycemic agent used in the treatment of non-insulin dependent diabetes mellitus. It acts as an antidiabetic agent by decreasing the uptake of glucose which enhance the glycemic control by increasing insuline sensitivity. Limitation associated with it is that, it does not show any response to dietary modification. It is basically a synthetic entity and chemically it is N,N-dimethylimido dicarbonimidic diamide hydrochloride (1,1-dimethyl biguanide hydrochloride). Generally used in combination with sulfonylureas, thiazolidinedione or other hypoglycemic agents or it can be used alone. ¹⁻³

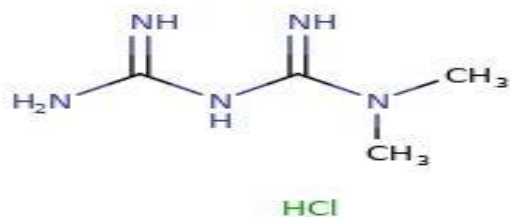


Figure 1: Chemical structure of Metformin HCL

MATERIAL AND METHOD

Chemicals:

Metformin hydrochloride was a gift sample from Flamingo Pharmaceutical, Taloja, Navi Mumbai, India. Metformin Hydrochloride Sustained Release Tablet 500 mg (Exermet 500) Cipla. All chemicals and reagents were of analytical (AR) grade.

Instrumentation:

A Shimadzu (Kyoto, Japan) UV-1800 double beam UV- Visible spectrophotometer attached with computer operated software UV probe 2.33 with spectral width of 2 nm, wavelength accuracy.

METHOD:

Area Under Curve Method:

The Area method is applicable where there is no sharp peak or when broad spectra are obtained. It involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelengths λ_1 and λ_2 . Area calculation processing item calculates the area bound by the curve and the horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observation so as to get the linearity between area curve and concentration. The above mentioned spectrums were

calculated to AUC. Thus, the calibration curve can be constructed by plotting concentration verses AUC. ⁴⁻⁸

Experimental Work:

1. To check the solubility of Metformin Hydrochloride:

10 mg of Metformin was weighed and solubility of this sample was checked in distilled water, Methanol, Ethanol. In this Metformin HCL freely soluble in distilled water, slightly soluble in alcohol. ⁴

2. To Identify the λ max of Metformin:

Accurately weigh 100 mg of pure drug and dissolve it in a small portion of distilled water and make up the final volume up to 100 ml using distilled water to give a standard stock solution of 1000 μ g/ml. From above solution withdraw 10ml solution and transfer it into a 100ml volumetric flask and make up final volume with distilled water to prepare 100 μ g/ml solution. Suitable dilutions made with distilled water to get working standard solutions of 5, 10, 15, 20, 25 μ g/ml.

3. Sample Preparation of Metformin:

Accurately weigh twenty tablets of metformin crush the tablets and measure the weight of powder equivalent to 100mg of drug. Then transfer it into a 100ml volumetric flask dissolve it into distilled water properly and make up the final volume with same distilled water to prepare 1000 μ g/ml solution. Then it filtered through whatman filter paper, pipette out 10ml filtrate transfer it into 100ml volumetric flask and make up the volume up to 100ml with distilled water to prepare 100 μ g/ml solution. Suitable dilutions made with distilled water to get working standards of 5, 10, 15, 20, 25 μ g/ml.

Analytical Method Validation: ⁵

1. Linearity:

Standard stock solution of Metformin, relevant amount of solution were pipette out into 25 ml volumetric flask and dilution were made with distilled water to be working standards of concentrations 5, 10, 15, 20, 25 μ g/ml. The difference in AUC of Metformin was measured area between 221.0-240.80 nm (Figure 6). The calibration curve of drug was plotted. The concentration range over which the drugs followed linearity was chosen as an analytical concentration range i.e 5-25 μ g/ml for Metformin.

2. Precision:

The precision of analytical procedure express closeness of agreement (degree of scattering) between a series of measurement obtained from multiple sampling of the same homogeneous sample under prescribed conditions. It may be considered at three levels: repeatability, intermediate precision and reproducibility. It is expressed as standard deviation or coefficient of variation.

3. Sensitivity:

The sensitivity of the method was determined in terms of limit of detection (LOD) and limit of quantitation (LOQ). The LOD and LOQ were calculated by using formula,

$$\text{LOD} = 3.3 \times \text{SD}/\text{slope}$$

$$\text{LOQ} = 10 \times \text{SD}/\text{slope}$$

Where, SD is the standard deviation of regression line.

RESULT AND DISCUSSION

The proposed UV- Spectroscopic, Area Under Curve method for determination of Metformin showed maximum absorbance at 233.00 nm (λ max). The result of UV- Spectroscopic analysis has been showed in Table.1 indicates that the representative calibration curve of the Metformin were plotted at 233.00 nm. A linear relationship was obtained for metformin in concentration range of 5-25 μ g/ml. Linear regression of absorbance on concentration gave the equation for Metformin,

$$\text{For Bulk, } y = 1.729x - 1.521$$

$$\text{Correlation coefficient (R}^2\text{)=0.992}$$

$$\text{For Formulation, } y = 1.356x - 1.024$$

$$\text{Correlation Coefficient (R}^2\text{)=0.994}$$

The area under curve of Bulk shown in Figure 5, and area under curve of formulation in figure 6.

Validation parameters results shown in Table.2 & 3. The overlay spectrum peak report shown in figure 7 and 8.

Table 1: Regression Analysis Data for Metformin by AUC Method

Parameter	AUC
Wavelength Range	221.0-240.80 nm
Concentration Range	5-25 μ g/ml
Slope (m)	1.3561
Intercept (c)	1.0245
Correlation Coefficient (R ²)	0.9941

Table 2: Summary of Data of Validation parameter

Sr. No.	Parameter	AUC Method
2	Linearity	5-25 μ g/ml
3	Regression Equation	y = 1.356x-1.0245
6	Correlation Co-efficient	R ² = 0.994
7	LOD (μ g/ml)	0.0070
8	LOQ (μ g/ml)	0.0213
9	Precision	
9.1	Interday Precision	0.337% RSD
9.2	Intraday Precision	0.671% RSD

Table 3: Result of Intraday and Interday Precision

Parameter	\pm S.D	RSD	% RSD
Interday	0.002898	0.00167	0.337
Intraday	0.00145	0.00334	0.671

Spectrum Peak Pick Report

15-04-2019 11:33:27

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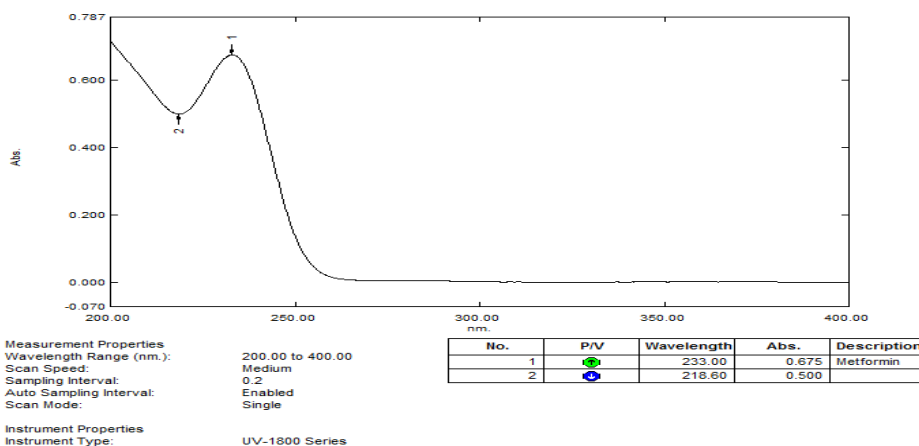


Figure 2: λ max of Metformin

Table 4: Calibration Curve of Pure Metformin (Bulk)

Concentration	Absorbance
5 ppm	0.325
10 ppm	0.720
15 ppm	1.073
20 ppm	1.469
25 ppm	1.782

Table 5: Calibration Curve of Metformin (formulation)

Concentration	Absorbance
5 ppm	0.385
10 ppm	0.669
15 ppm	0.968
20 ppm	1.262
25 ppm	1.549

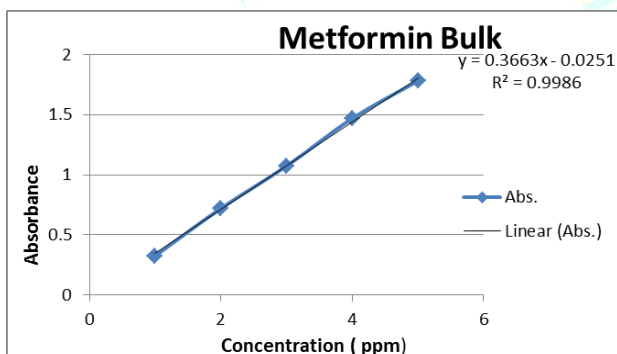


Figure 3: Calibration Curve of Metformin (Pure Drug)

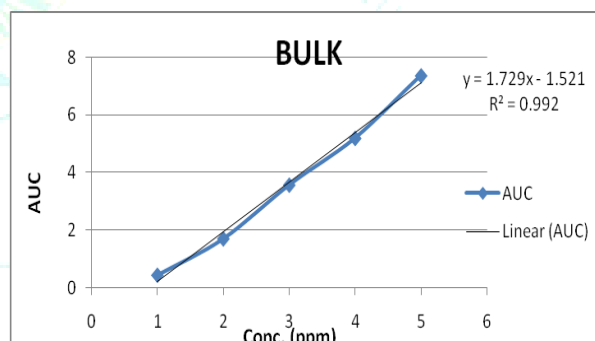


Figure 5: Calibration Curve of Metformin by AUC Method (Pure Drug)

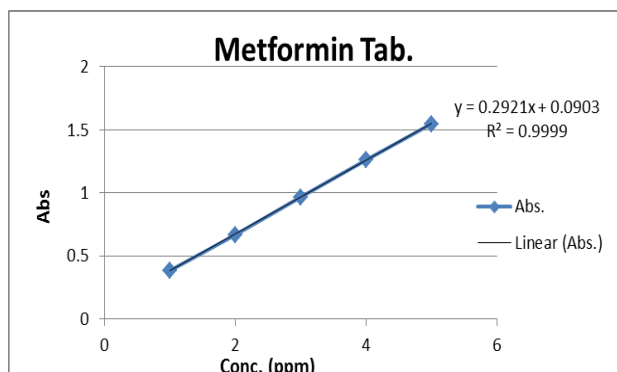


Figure 4: Calibration curve of Metformin (Formulation)

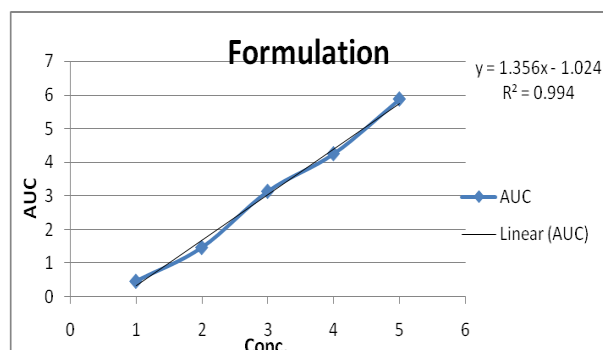
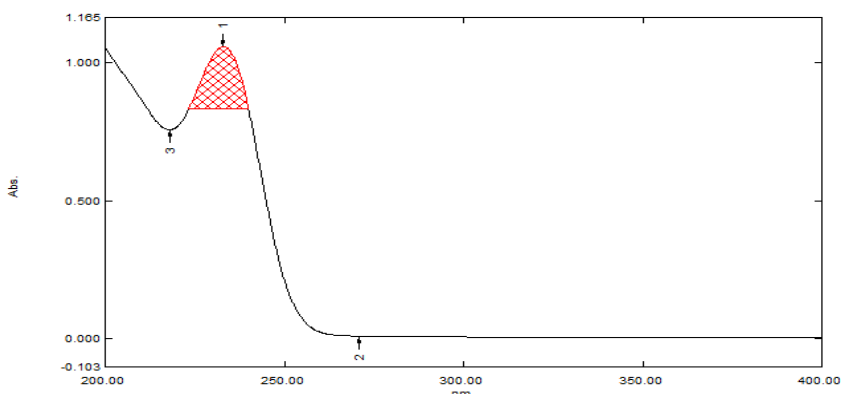


Figure 4: Calibration Curve of Metformin by AUC Method (Formulation)

Spectrum Peak Area Report

15-04-2019 12:01:52

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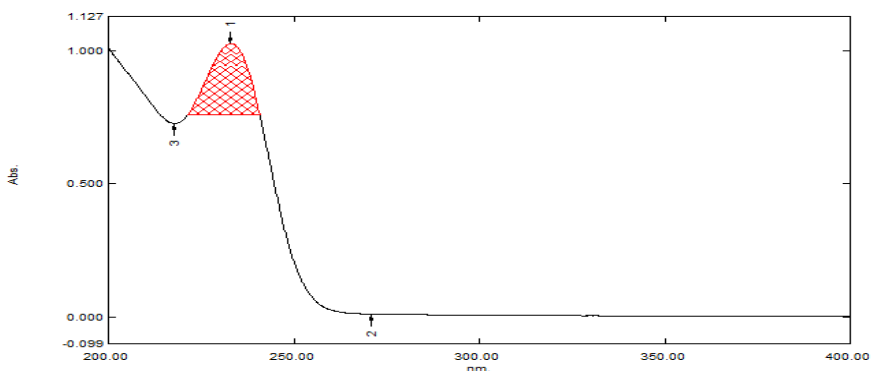


Region	Color	Start	End	Divisor	Area	Result	Description
1	Red cross-hatch	223.40	240.00	1.000	2.342	2.342	
2	Red cross-hatch						

Figure 5: Area between 223.40-240.00 nm selected for metformin (15 ppm) Bulk Spectrum Peak Area Report

15-04-2019 13:10:38

Data Set: File_190415_130904 - RawData



Region	Color	Start	End	Divisor	Area	Result	Description
1	Red cross-hatch	221.40	240.80	1.000	3.139	3.139	15 ppm
2	Red cross-hatch						

Figure 6: Area between 221.0-240.80 nm selected for Metformin (15 µg/ml) Formulation Overlay Spectrum Graph Report

15-04-2019 12:36:49

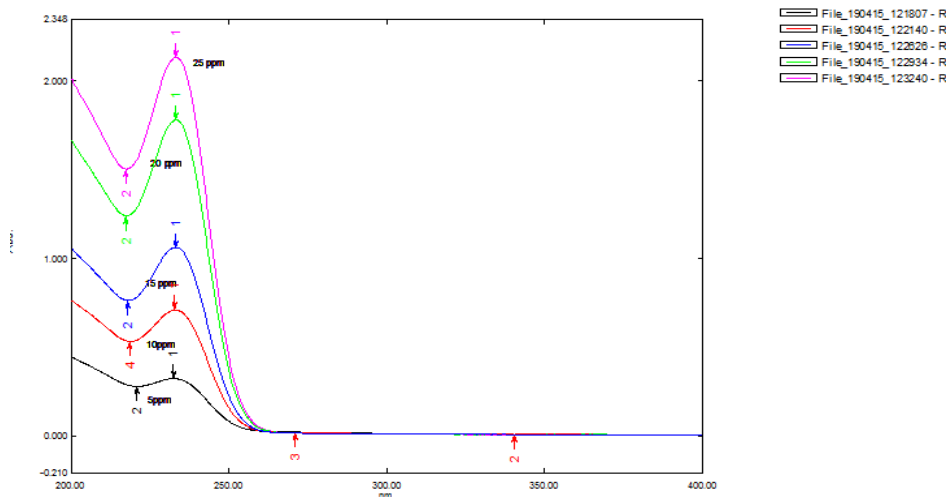


Figure 7: Overlay Spectrum of Metformin (Bulk)

Overlay Spectrum Graph Report

15-04-201 13:50:41

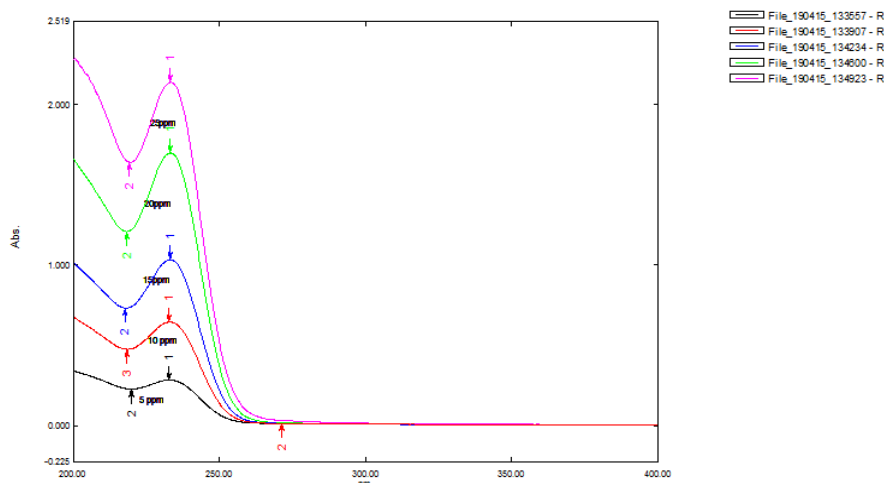


Figure 8: Overlay Spectrum of Metformin (Formulation)

CONCLUSION

The simple and economic UV spectrophotometric AUC methods have been developed and validated for the determination of Metformin Hydrochloride. The results of validation parameters show that the UV spectrophotometric method was found to be accurate, precise and sensitive. Because of cost-effective and minimal maintenance, the present UV-Spectrophotometric method can be preferred at small scale industries and successfully applied.

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