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Estimation and validation of metformin by UV spectroscopy

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ABSTRACT

A simple highly sensitive spectrophotometric method was developed for the quantification of Metformin hydrochloride (*N, N*-dimethylimidodicarbonimidic diamide). U.V.Spectrophotometric estimation of Metformin hydrochloride in bulk and in formulation using 0.1M Sodium hydroxide (NaOH) solution as solvent. The absorption maxima was measured at 233nm. The linearity was found in the concentration range 5-25mcg/ml. The proposed method can be utilized as a stability indicating assay. Under the described conditions the proposed method is linear over the concentration range of 5-25mcg/ml and the coefficient of determination were >0.999 with a relative standard deviation of 0.702105%. The average recovery of the target compound is 98.62% with a limit of quantification (LOQ) of 158.13mcg/ml and the limit of detection (LOD) 52.183mcg/ml.

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KEYWORDS

Metformin hydrochloride;
NaOH.

INTRODUCTION

The quality control of active pharmaceutical ingredients (APIs) in the formulation is always a thrust area for the pharmaceutical industries. So the development of reproducible, sensitive, simple and extremely inexpensive methods for the determination of APIs in the formulation is always challenging. Metformin (*N, N*-dimethylimidodicarbonimidic diamide) is an oral anti-diabetic drug. It is the first-line drug of choice for the treatment of type 2 diabetes, particularly in overweight and obese people and those with normal kidney function^[1-3].

Evidence is also mounting for its efficacy in gestational diabetes, although safety concerns still preclude its widespread use in this setting. It is also used in the treatment of polycystic ovary syndrome and has been investigated for other diseases where insulin resistance

may be an important factor. When prescribed appropriately, metformin causes few adverse effects the most common is gastrointestinal upset and, unlike many other anti-diabetic drugs, does not cause hypoglycemia if used alone. Lactic acidosis (a buildup of lactate in the blood) can be a serious concern in overdose and when it is prescribed to people with contraindications, but otherwise, there is no significant risk. Metformin helps reduce LDL cholesterol and triglyceride levels and is not associated with weight gain, and is the only anti-diabetic drug that has been conclusively shown to prevent the cardiovascular complications of diabetes. As of 2009, metformin is one of only two oral anti-diabetics in the World Health Organization Model List of Essential Medicines (the other being glibenclamide)^[4]. First synthesized and found to reduce blood sugar in the 1920s, metformin was forgotten for the next two decades as research shifted to insulin and other anti-dia-

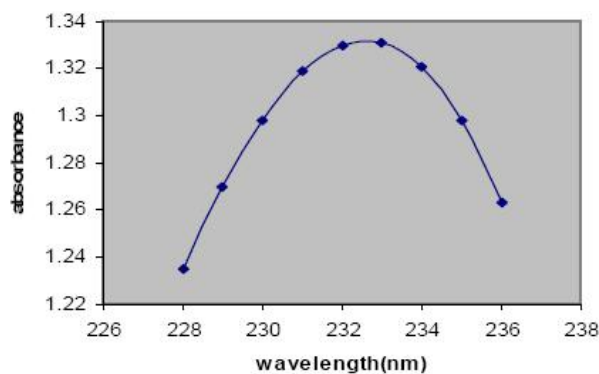


Figure 1 : Metformin HCL: 15mcg/ml in 0.1M NaOH solution

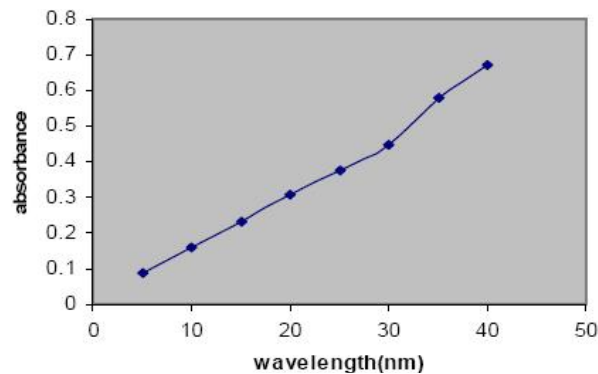


Figure 2 : Metformin: 5.0-40.0mcg/ml in 0.1M NaOH solution

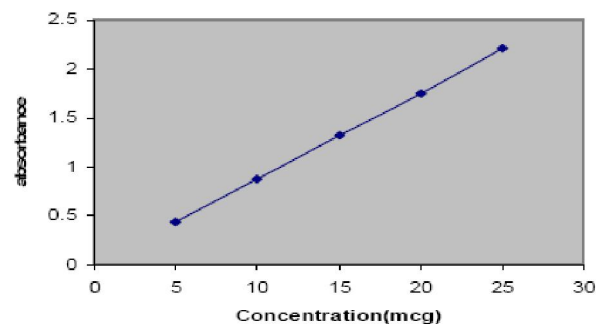


Figure 3 : Metformin: 5.0-25.0mcg/ml in 0.1M NaOH solution

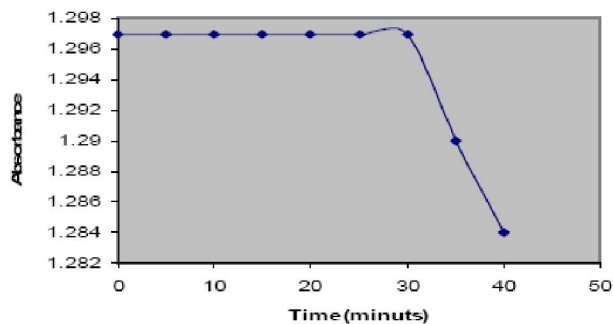


Figure 4 : Metformin: 200.0mcg/ml in 0.1M NaOH solution

betic drugs. Interest in metformin was rekindled in the late 1940s after several reports that it could reduce blood sugar levels in people, and in 1957, French physician Jean Sterne published the first clinical trial of metformin as a treatment for diabetes. It was introduced to the United Kingdom in 1958, Canada in 1972, and the United States in 1995. Metformin is now believed to be the most widely prescribed anti-diabetic drug in the world; in the United States alone, more than 40 million prescriptions were filled in 2008 for its generic formulations^[5,6]. Numbers of analytical methods have been reported for measuring metformin in biological fluids and tissue extracts. These methods involved UV techniques^[7-9].

Aim of this work was to develop a sensitive and simple spectrophotometric method for the quantification of metformin is finding new dimensions of clinical importance. To support its investigation an appropriate analytical method (sensitive, selective, reproducible and simple) for quantification of metformin is essential. For the drugs that obey the Beer Lambert's law, spectrophotometric methods of analysis of single component in solution are usually rapid, sensitive and economical.

EXPERIMENTAL

Apparatus

A model Shimadzu UV-1601 double beam spectrophotometer with a fixed slit width of 2nm using a pair of 1cm matched quartz cells was used for spectrophotometric analysis.

Materials

All the chemicals were of analytical reagent grade, and the solvents were of spectroscopic grades. A Metformin hydrochloride (*N, N*-dimethylimidodicarbonimidic diamide) (Wintac Limited, Bangalore, Karnataka State, India), Distilled water and 0.1M NaOH solution.

Spectrophotometric method

Preparation of standard metformin hydrochloride

An accurately weighed 100.0mg of pure drug Metformin hydrochloride was taken in clean, dry 100ml volumetric flask and dissolved in small volume of 0.1M sodium hydroxide solution (10.0-20.0ml). The solution is diluted to 100.0ml with 0.1M sodium hydroxide solution, resulting in 1000.0 mcg/ml of drug concentra-

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TABLE 1

| Si. No. | Parameters | Results |
|---------|---|----------------------|
| 1 | Absorption maxima (nm) | 233 |
| 2 | Beer's law limits (mcg/ml) | 5-25 |
| 3 | Molar extinction coefficient ($\text{mole}^{-1} \text{cm}^{-1}$) | 8.7×10^{-2} |
| 4 | Sandall's sensitivity (mcg/cm ² /0.001 absorbance units) | 11×10^{-2} |
| | Regression equation (y) | 0.9998 |
| 5 | Slope (b) | 0.0444 |
| | Intercept (a) | 0.014 |
| 6 | Coefficient of variance | 5.3020625 |
| 7 | Standard deviation | 0.702105 |
| 8 | Limit of detection (mcg/ml) | 52.183 |
| 9 | Limit of quantitation (mcg/ml) | 158.13 |
| 10 | % Recovery | 98.62 |

tion. Now pipette out 10ml of this solution and diluted to 100 ml with 0.1 N Sodium hydroxide solution, resulting in 100 $\mu\text{g/ml}$ of the drug concentration.

Determination of absorption maxima of metformin hydrochloride in 0.1M NaOH solution

1.5ml aliquot of Metformin hydrochloride solution of 100mcg/ml in 0.1M sodium hydroxide was pipetted into 10ml volumetric flask and volume was made up to the mark with 0.1M sodium hydroxide solution. The final concentration of drug was 15mcg/ml. The solution was then scanned in UV range between 200 to 400nm to get absorption maxima using 0.1M sodium hydroxide solution as blank. On scanning the absorption maxima of Metformin hydrochloride 15mcg/ml in 0.1M sodium hydroxide was found out to be 233 nm and represented graphically in figure 1.

Determination of concentration range of metformin hydrochloride

Aliquots of 0.5ml, 1.0ml, 1.5ml, 2.0ml, 2.5ml, 3.0ml, & 4.0ml of 100 $\mu\text{g/ml}$ of Metformin Hydrochloride were pipetted into each of eight 10ml volumetric flask the volume were made up to 10ml with 0.1M Sodium Hydroxide solution was measured at 233nm against 0.1M Sodium Hydroxide solution as a blank. The abs. Vs conc. curve was found to be linear in the concentration range 0.5-25mcg/ml of Metformin hydrochloride in 0.1M sodium hydroxide solution and represented graphically at figure 2.

Preparation of standard curve of metformin hydrochloride

Aliquots of 0.5, 1.0, 2.0, 2.5ml of 100 $\mu\text{g/ml}$ solution of Metformin Hydrochloride was pipetted into each of five 10 ml of volumetric flask. The volume was made up to 10.0ml with 0.1M sodium hydroxide solution. The absorbance of the solution was measured at 233.0nm against 0.1M sodium hydroxide solution as blank. The calibration curve shows that Beer's law was obeyed in the concentration range 5.0-25.0mcg/ml of Metformin hydrochloride in 0.1M sodium hydroxide solution and represented graphically in figure 3.

Optical characteristics

The optical characteristics of the proposed method have been calculated. The values are given in TABLE 1.

Validation parameters

Recovery studies

Aliquots of 2.0ml of sample drug Metformin Hydrochloride solution of 100.0mcg/ml were pipetted into each of four 10 ml volumetric flasks. To the first three volumetric flasks 0.5ml, 0.1ml and 1.5ml of standard drug solution of 100.0mcg/ml was added respectively. The volume was made up to 10.0 ml with 0.1M sodium hydroxide solution and the absorbance was measured at 233.0 nm against reagent blank. The percentage recovery by the proposed method was ranging from 100.27 to 96.96% indicating no interference of excipients present in the formulation.

Precision

Repeatability

100.0mg of Metformin hydrochloride was weighed in three replicates and transferred into three clean and dry 100ml volumetric flasks. The compound was first dissolved in small volume (10.0-20.0ml) of 0.1M sodium hydroxide solution and volume was made up to 100.0 ml with 0.1M sodium hydroxide solution. 0.20ml aliquots of the above stock solution were pipetted into three different 10.0ml volumetric flasks and volume was made up to 10.0ml with 0.1M sodium hydroxide solution. The absorbance of each of these solutions was recorded at 233.0 nm against reagent blank. The average percentage recovery by the proposed method was ranging from 99.88 and standard deviation 0.0848 %

indicating good repeatability.

Intermediate precision

100.0mg of Metformin hydrochloride was weighed in three replicates and transferred into three clean and dry 100ml volumetric flasks. The compound was first dissolved in small volume of 0.1M sodium hydroxide solution and volume was made up to 100.0ml with 0.1M sodium hydroxide solution. 0.15 ml aliquots of each of the stock solution were pipetted into three different 10.0ml volumetric flasks and volume was made up to 10.0ml with 0.1M sodium hydroxide. The absorbance of each of test solutions was recorded at 215.0nm against reagent blank. The average percentage recovery by the proposed method was ranging from 99.89 and standard deviation 0.438 % indicating good repeatability.

Stability

An aliquot of 1.5ml standard Metformin hydrochloride solution of 100.0mcg/ml was pipetted into 10ml volumetric flask. The volume was made up to 10ml with 0.1M sodium hydroxide solution. The absorbance was measured at 233.0nm against reagent blank at different time intervals. The results are represents in figure 4. The absorbance of Metformin hydrochloride solution 200mcg/ml in 0.1M NaOH was found to be stable for 30.0 minutes after which the absorbance decreases.

RESULT AND DISCUSSIONS

U.V. Spectrophotometric estimation of Metformin in bulk formulation using 0.1M Sodium hydroxide (NaOH) solution as solvent the absorption maxima was measured at 233.0 nm. The linearity was found in the concentration range 05-25mcg/ml. The Sandell's sensitivity was found to be $0.01135 \text{mcg/cm}^2 \text{0.001 absorbance units}$ and Molar absorptivity $0.08748 \text{mol}^{-1} \text{cm}^{-1}$, Regression, Slope and Intercept was found to be 0.9998, 0.0444 and 0.014. Coefficient of variance was found to be 5.3020625. The Standard deviation of 0.702105. LOD and LOQ was found to be 52.183mcg/ml and 158.13 (mcg/ml), indicated accuracy and reproducibility of the method. The method was extended for the determination in bulk drug formulation. It was observed that the results obtained were

comparable to that of Lable claim. The recovery studies of the standard drug when performed in the preanalysed formulation gave percentage recovery of 100.27 to 96.96 % indicating practically no interference of formulation excipients with the proposed method.

CONCLUSION

It was found that no spectrophotometric methods were available for the estimation of Metformin hydrochloride in bulk and in formulations.

The new method developed was New Simple, Accurate, Sensitivity, Economical and Reproducible which could provide satisfactory results. The methods can be used for routine analysis of Metformin hydrochloride in bulk and in formulation. The methods are practical and valuable.

The described method has many advantages: it does not need expensive apparatus; it is simple and quick; its linear range is relatively wide, it has good selectivity. Furthermore, the proposed method may be successfully used to determine Metformin in bulk and in pharmaceutical formulations. Accordingly, the method is practical and valuable.

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