Determination of Metformin. HCL in Pharmaceutical Formulations, Environmental Water Samples

Nief Rahman Ahmed*

Department of Environmental Technology, College of Environment, University of Mosul, Iraq

*Corresponding author: Nief Rahman Ahmed, Department of Environmental Technology, College of Environment, University of Mosul, Iraq

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ABSTRACT

A simple, accurate, precise, rapid, economical and sensitive ultraviolet spectrophotometric method has been developed for the estimation of metformin hydrochloride in pharmaceutical preparations and environmental wastewater samples, which shows maximum absorbance at 232nm in distilled water. Beer’s law was obeyed in the range of 2-16 μg/ml, with molar absorptivity of 1.28x10⁴ L.mol⁻¹.cm⁻¹, relative standard deviation of the method was less than 1.8%, and accuracy (average recovery %) was 100 ± 1.0. The method was successfully applied to the estimation of metformin hydrochloride in pharmaceutical formulations (tablets), environmental water samples and content uniformity testing. The proposed method was validated by sensitivity and precision which proves suitability for the routine analysis of metformin hydrochloride in true samples.

Keywords: Metformin Hydrochloride, Estimation; Pharmaceutical Preparations; Content Uniformity

Introduction

Metformin hydrochloride is an oral anti hyperglycemic agent used to lower blood glucose in patients suffering from diabetes of non-insulin dependent. Metformin hydrochloride (Glucophage) [1], chemically known as 1,1-Dimethyl biguanide hydrochloride with a molecular formula of C₄H₁₂Cl.N₅ (Figure 1). It is an oral ant diabetic drug that has been used in the treatment of non-insulin dependent diabetes which improves control of glycemia primarily by inhibiting hepatic gluconeogenesis and glucogenolysis[2] and seems to ameliorate hyperglycemia by improving peripheral sensitivity to insulin, reducing gastrointestinal glucose absorption and hepatic glucose production. Recently, metformin has also become available for the treatment of polycystic ovary syndrome and has been found to improve vascular function, prevent pancreatic cancer and revers fatty liver diseases [1-4].

Analytical procedures for the estimation of metformin hydrochloride include non-aqueous potentiometric titrimetric method [5], various spectrophotometric methods [6,7], HPLC [8,9]. Another different methods for the determination of metformin have been described, such as conduct metric titration, flow-injection chemiluminescence [10], capillary electrophoresis [11-13], ion-selective electrode [14], ion-selective electrode [15] and adsorptivecatalytic square-wave voltammetry [16]. However, all of these methods suffered from several disadvantages including tedious, time consuming, ultra-filtration and column-switching technique which required expensive or sophisticated instruments and not simple for routine analysis. The proposed method reports the development of a new...
UV method and can be applicable to routine analysis and content uniformity test of metformin hydrochloride in tablets and complies well with the validation requirements in the pharmaceutical industry[17].

**Experimental**

**Apparatus**

Shimadzu UV-1700 pharm aspect (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurement.

**Reagents**

All chemical used were of analytical or pharmaceutical grade and metformin hydrochloride standard material and pharmaceutical preparations (tablets) was provided from state company of drug industries and medical appliance (NDI) Nineveh – Iraq. Distilled water was used as a solvent.

**Metformin Hydrochloride Standard Solution 100ppm**

This solution was prepared by dissolving 10 mg of metformin hydrochloride in 100 ml of distilled water in calibrated flask.

**Estimation of Absorption Maxima**

The standard solution of metformin hydrochloride (10µg/ml) was scanned in the range of 200-350 nm which shows maxima located at 232nm (Figure 2). Therefore, 232nm wavelength was selected for the construction of calibration curve.

**Recommended Procedure**

Aliquots of standard solution of metformin hydrochloride (50-400µg) were transferred into a series of 25 ml calibrated flasks, calibration curve was prepared in the concentration range of 2-16 µg/ml. The absorbance was measured at 232nm against distilled water as a blank. The concentration of the sample solution can be determined by using the calibration curve.

**Procedures for Pharmaceutical Preparations (Tablets)**

To minimize a possible variation in the composition of the Tablets were provided from state company of drug industries and medical appliance (NDI) Nineveh - Iraq. Ten tablets were weighed and amount of tablet powder equivalent to 10 mg of metformin hydrochloride was weighed accurately and dissolved in about 80 ml Distilled water; mixed well for 20min and then filtered. The filtrate was made up to 100mL with Distilled water and aliquot of this solution was treated as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

**Procedure for Water Samples**

Distilled and tap water samples (100ml) were fortified with 10mg of metformin hydrochloride. The fortified water samples were analyzed as desired under general procedure.

**Results and Discussion**

UV-Visible spectrophotometry is still considered to be a convenient and low-cost method for the estimation of pharmaceuticals [18-20]. This method used for the estimation of metformin hydrochloride in pharmaceutical preparations and environmental wastewater samples was found to be sensitive, simple, accurate, and reproducible. Beer's law was obeyed in the concentration range of 2-16 µg/ml. Figure 3 with correlation coefficient of 0.998, intercept of 0.0258 and slope of 0.0773. The conditional molar absorptivity was found to be 1.28x104 l/mol.cm. The accuracy and precision of the method, a pure drug solution was analyzed at three different concentrations, each estimation being repeated six times. The relative error (%) and relative standard deviation values are summarized in Table 1. From Table 1 the values of standard deviation were satisfactory, and the recovery studies were close to 100%. The RSD% value is less than 1.8 indicative of accuracy of the method.

**Table 1: Accuracy and precision of the proposed method**

| Metformin hydrochloride taken (µg/ml) | Er (%) a | RSD (%) |
|--------------------------------------|----------|---------|
| 4                                    | 1        | 1.7     |
| 10                                   | 0.9      | 1.6     |
| 61                                   | 0.95     | 1.4     |

**Analytical Application**

The proposed method was satisfactorily applied to the estimation of metformin hydrochloride in its pharmaceutical
preparation'stablets. The results of the assay of the pharmaceutical preparations reveals that there is close agreement between the results obtained by the proposed method and the label claim. as cited in Tables 2 & 3.

**Table 2:** Determination of metformin hydrochloride in tablets formulations

| Pharmaceutical formulations | Label amount (mg) | Found by proposed method (mg)* | Recovery % |
|-----------------------------|------------------|-------------------------------|------------|
| Glucosam tablets (NDI-Iraq) | 500 mg/tab        | 499.85                        | 99.97      |
|                             | 850 mg/tab        | 851.25                        | 100.147    |
| METFORMAL (SPA-Italy)       | 500 mg/tab        | 499.4                         | 99.88      |

*mean value of ten determinations

**Table 3:** Determination of metformin hydrochloride in environmental water samples

| Water samples | Metformin hydrochloride (µg/ml) * | % Recovery (n=10) |
|---------------|-----------------------------------|-------------------|
|                | Found | Taken |                  |
| Tap water      | 4     | 3.98  | 99.5             |
|                | 10    | 10.02 | 100.2            |
|                | 16    | 15.88 | 99.25            |
| River water    | 4     | 3.99  | 99.75            |
|                | 10    | 9.95  | 99.5             |
|                | 16    | 16    | 100              |

*Mean of ten determination

**Application of the Proposed Method to Content Uniformity [21-23]**

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in Table 4 indicate that the proposed method can accurately and precisely quantify metformin hydrochloride in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.25 (0.64%) which fall within the content uniformity limits specified by the United State Pharmacopeia [22].

**Table 4:** Content uniformity testing of tablets using the Proposed method

| Parameter  | % of the label claim |
|------------|----------------------|
| Tablet No.1| 100.6                |
| Tablet No.2| 99.6                 |
| Tablet No.3| 100.5                |

**Conclusion**

The developed method is found to be highly sensitive, accurate, simple, precise and economical, and can be used for routine quality control analysis of metformin hydrochloride in pure form, pharmaceutical formulations and application to content uniformity testing.

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