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A NON-AQUEOUS TITRIMETRY AND UV SPECTROPHOTOMETRIC STUDY OF METFORMIN HYDROCHLORIDE MARKETED TABLETS

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ABSTARCT

Metformin hydrochloride (MF.Hcl) is an anti-diabetic agent of biguanides class used for treating type-II diabetes. A number of generic tablets of MF. Hcl are available in global markets with diversified label claims nowadays. However, hardly any voluntary research organization takes the responsibility of checking the genuinely of the labels claimed by various manufacturers. The rationale of the present study was to quantify eight brands of MF. Hcl tablets marketed in India using non-aqueous titrimetry and UV-spectroscopic method and to ensure whether both the methods give similar results for all the brands as per their corresponding label claims such as uniformity of weight and percentage of purity. The result epitomizes that all the six brads out of eight had passed the assay specified in Indian Pharmacopoeia (IP), and the values obtained from uniformity of weight and weight variation tests were within the range as per the official standard. Nevertheless, the brands F2 and F3 had the highest and lowest percentage of purity respectively. However, the brand F5 failed the test. Thus, the study perhaps justified the fact that some volunteer organization should shoulder the responsibility of checking the pharmaceutical formulations available in the market to ensure that those are as per the prescribed standards of official monographs.

1. INTRODUCTION

The drug Metformin Hydrochloride is a biguanides moiety with a chemical name 1, 1- dimethylbiguanides, extremely it is used in the treatment of diabetes mellitus II. Metformin primarily by its suppressive action on production of hepatic glucose, improves hyperglycemia. Amruta B. Loni *etal*, (2012) developed a simultaneous UV Spectrophotometric method for estimation of sitagliptin phosphate and metformin hydrochloride in bulk and tablet dosage form. In the year of 2012 L.Adikari *etal* developed and validated an uv-visible spectroscopic method for analysis of metformin hydrochloride and glipizide in its bulk and pharmaceutical dosage form. Diversified brands of metformin hydrochloride are available in the market with common label claims. However, hardly any voluntary research organization takes the responsibility of checking the genuinely of the labels claimed by various manufacturers. The rationale of the present study was to quantify eight brands of MF. Hcl tablets marketed in India using non-aqueous titrimetry and UV-spectroscopic method and to ensure whether both the methods give similar results for all the brands as per their corresponding label claims such as percentage of purity.

2. MATRERIALS

Methanol, Ethanol, Aceto nitrile, Metformin hydro chloride, Formic acid, Acetic anhydride, 0.1 N perchloric acid, Crystal violet indicator, 0.1 N hcl, 0.1 N Naoh, Potassium hydrogen phthalate were procured from Siddhi chemicals, Visakhapatnam. The pure sample of metformin hydrochloride was a gift from Dr.Reddy's lab, Hyderabad. The tablets (different brands) from the market were utilized for the study. Rest of the chemicals was of pure and analytical grade.

3. METHODS

3.1. Solubility: First of all, the solubility of metformin hydrochloride was checked by using various solvents like hot water, distilled water, 0.1 N HCL, 0.1 N NaoH, methanol, ethanol, aceto nitrile. The result was conversed in the results and discussion section.

3.2. Titrimetric Method: Meformin hydrochloride was analyzed by non-aqueous titrimetry method using acetous perchloric acid as the titrant.

3.2.1. Preparation of 0.1N acetous perchloric acid and 0.1 N potassium hydrogen phthalate: 0.1N acetous perchloric acid and potassium phthalate were prepared and standardized as per the official procedure prescribed in the Indian Pharmacopoeia 2007(IP 2007).

3.2.2. Assay procedure: The assay was carried out by the standard procedure according to the IP 2007. Briefly, the average weights of 20 tablets of metformin hydrochloride of each marketed brand were taken. 60mg of accurately weighed pure metformin hydrochloride was shaken well with four ml of formic acid. 50ml of acetic anhydride was added to the solution and titrated against acetous perchloric acid using crystal violet as an indicator. Determination of blank was performed, and the value of blank was substrated from the volume consumed. Each ml of 0.1 N perchloric acid ≅ 8.28 mg of metformin hydrochloride. The percentage purity determined by titrimetric method by using the formula$\%\text{Purity} = \frac{\text{practical yield}}{\text{Theoretical yield}} \times 100$. Table number one epitomize the result of eight formulations being assayed by titrimetry.

3.3. Spectro photometric method:

3.3.1. Preparation of standard solution: A standard solution of metformin hydrochloride was prepared by dissolving 100 mg of the drug in 100ml of distilled water and further diluted with water to get a concentration of 100 µg/ml.

3.3.2. Sample preparation: Twenty tablets were weighed accurately and finely powdered. The powder equivalent to 100 mg of metformin hydrochloride from each brand was accurately weighed, dissolved in 100 ml of distilled water, filtered through whatmann filter paper no-41 and diluted further to get a concentration of 100 µg/ml. observe the absorbance of each brand using a double beam UV spectrophotometer(SHIMADZU UV 1800) .To a series of aliquots (S_1,S_2,S_3,S_4,S_5) 1 to 5 ml of the standard solution of metformin hydrochloride was made upto 25 ml with distilled water and the absorbance was measured at 233nm against blank. The absorbances of standard and sample solutions were measured and the amount of metformin hydrochloride present in tablet formulation was determined.

3.3.3. Determination of absorbances of standard and sample solutions with the solvent methanol: 25 mg of the standard metformin hydro chloride was taken and dissolved in 25 ml of methanol to get 1000µg/ml concentration. From this solution 2.5 ml of solution was taken and make up the volume up to 25 ml with methanol to get 100µg/ml concentration. The maximum wavelength and absorbance of this solution was determined by using double beam spectrophotometer. 25 mg of the powdered tablet formulation of metformin hydrochloride was taken and dissolved in 25 ml of methanol to get 1000µg/ml concentration, from this solution 2.5ml of solution was taken and made up the volume up to 25 ml by using methanol to get 100µg/ml concentration of solution. The wavelength and absorbance of the each tablet formulation solutions were measured by using double beam spectro photometer.

3.3.4. Determination of absorbance and wave lengths of standard and sample solutions with the solvent distilled water: 25mg of standard metformin hydrochloride was taken and dissolved in 25 ml of distilled water to get 1000µg/ml concentration. From this solution 2.5 ml of solution was pipetted and made up the volume up to 25 ml to get the concentration of 100µg/ml. The absorbance and wavelength were determined by using double beam spectro photometer.

3.3.5. Procedure for formulations (marketed Brands): Twenty tablets were powdered and 0.1 gram was taken, to it 70 ml of distilled water was added and shake for 15 minutes. The volume was made up to 100ml with the distilled water and filtered. The filterate was collected from which 10 ml pipette out and made up the volume up to 100 ml. again from the solution 10 ml was taken and made the volume up to 100 ml by using distilled water. Then the absorbance of each formulation was checked. The percentage purity was calculated by using following formula.

$$\text{percentage purity} = \frac{\frac{\text{absorbance}}{\text{E1\%1CM}} \times \text{standard dilution}}{\text{sample dilution}} \times \text{average weight}$$

3.3.6. Determination of uniformity of weight between formulations: The weight of each tablet present in the strip was taken and the average weight was calculated for all the brands of tablets. Finally the results were compared for variation.

4. RESULT AND DISCUSSION

4.1. Solubility study: The drug was soluble freely in hot water, distilled water, methanol and ethanol. However it was springly soluble in 0.1N Hcl and insoluble in acetonitrile and 0.1N NaoH.

4.2. Percentage of Purity: Assay of eight different marketed formulations were carried out by titrimetry. The following table elucidates an excellent result for formulation 08, 06, 07 and 04 having percentage purity 102.7, 101.4, 100.07 and 100.07 respectively.

Table 1: Percentage of Purity of standard and marketed tablets by titrimetry

Drug	Burette reading (final reading)	Practical yield	%purity
Standard	7.5ml	60 .858	101
Brand 1	8.0 ml	64.88	108
Brand 2	6.9 ml	55.98	93.3
Brand 3	7.2 ml	58.4	97.37
Brand 4	7.4 ml	60.04	100.07
Brand 5	7.3 ml	59.23	98.7
Brand 6	7.5 ml	60.8	101.4
Brand 7	7.4 ml	60.04	100.07
Brand 8	7.6 ml	61.66	102.7

In addition to the aforementioned method a series of spectro-photometric studies were also carried out to ascertain the accuracy and to support the results found in titrimetric method for all the brands. The subsequent table represents the percentage of purity by spectro photometry taking methanol and distilled water as solvent.

Table.2.Percentage of Purity of standard and marketed tablets by spectrophotometry

Drug	Methanol	Distilled water
Standard	99%	103%
Brand 1	68%	70%
Brand 2	81%	107%
Brand 3	80%	118%
Brand 4	50%	78%
Brand 5	43%	38%
Brand 6	48%	66%
Brand 7	51%	74%
Brand 8	61%	97%

5. SUMMARY AND CONCLUSION

The rationale of the study was to check the purity of formulations as per their level claims and to ascertain the accuracy and precision of the procedures. Diverse variables which affect the color formation in spectrophotometry were revised and optimized [6]. Various excipients used in the formulations did not interfered in the specrophotometric method. The results of formulation 08, 06, 07 and 04 in titrimetry demonstrate a striking purity as per the level claim. However in spectro photometry only brand 8 educe the purity as per the level claim. In an overall drug development process the analysis of pharmaceuticals is an integral and increasingly important part. Industrial and scientific advancement has produced a substantial number of synthetic drugs. Hence it is imperative to develop analytical methods to determine these drugs in the quality control manufacturing phase of the pharmaceutical formulations [7]. The universal accessibility of the instrumentation, the simplicity of procedures, speed, precision and accuracy of the technique still make spectrophotometric methods attractive. Hence the result obtained by spectroscopic method could be regarded as accurate precise and simple.

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