DEVELOPMENT OF THE SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF PIOGLIAZONE AND METFORMIN


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ABSTRACT

The simple, accurate, precise, reproducible and economical procedure for simultaneous estimation of Pioglitazone (PGZ) and Metformin hydrochloride (MET) in tablet dosage form as well as in bulk drugs have been developed using double beam UV Spectrophotometer. The method based on solving of simultaneous equation using 250 nm (λmax of PGZ) and 218 nm (λmax of MET) as two analytical wavelengths for both drugs. The solution of both drugs was prepared using Methanol as a solvent. The proposed method is suitable for simultaneous determination of Pioglitazone and Metformin in pharmaceutical dosage form.

Key words: Pioglitazone, Metformine hydrochloride, λmax, Simultaneous estimation method.

INTRODUCTION

Analytical methods are required to characterize drug substances and drug products composition during all phases of pharmaceutical development. Development of methods to achieve the final goal of ensuring the quality of drug substances and drug products must be implemented in conjunction with an understanding of the chemical behaviour and physicochemical properties of the drug substance. This determination requires highly sophisticated methods and instruments like Spectrophotometer.[1]

Pioglitazone selectively stimulates the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-γ) and to a lesser extent PPAR-α. It modulates the transcription of the insulin-sensitive genes involved in the control of glucose and lipid metabolism in the muscle, adipose tissue, and the liver. As a result, pioglitazone reduces insulin resistance in the liver and peripheral tissues; increases the expense of insulin-
dependent glucose; decreases withdrawal of glucose from the liver; reduces quantity of glucose, insulin and glycated haemoglobin in the bloodstream.[2]

Metformin Hydrochloride (MET) is a biguanide class of antidiabetic drug, chemically is N,N-dimethylimidodicarbonimidic diamide hydrochloride 2-7. It is an oral anti-diabetic drug from the biguanide class. It is the first-line drug for the treatment of type 2 diabetes, particularly in overweight and obese people and those with normal kidney function and evidence suggests it may be the best choice for people with heart failure. It is also used in the treatment of polycystic ovary syndrome.[3]

MATERIALS AND METHOD[4-15]

**Instrument:** A Shimadzu UV-1700 UV/VIS Spectrophotometer was used with 1 cm matches quartz cell.

**Materials:** Gift samples of MET and PGZ were procured from Torrent Pharmaceutical LTD, Indrad, Dist. Mehsana (Gujarat) and Panacea biotech LTD, Baddi, Dist. Solan (H.P.) respectively. Tablets containing both drugs i.e. Metformine Hydrochloride and Pioglitazone were purchased from local pharmacy of commercial brand.

**Solvent used:** Methanol.

**Preparation of stock Solution:** PGZ (10mg) and MET(10mg) were accurately weighed and transferred to two separate 25 ml volumetric flask, dissolved in Methanol solvent to obtained stock solution of 400 μg/ml each. The stock solutions of both the drugs were further diluted separately with solvent i.e. Methanol to obtain the required range of 4-24μg/ml solution each and scanned in spectrum mode from 400-200nm. The overlain spectra of both the drug obtained (Fig No.1 and Fig No.2) to determine the λmax. PGZ has λmax 250nm while MET has λmax 218nm.

**Method (Simultaneous Equation Method):** From the stock solution, working standards solution of drugs was prepared by appropriate dilution and was scanned in the entire UV. Range Two wavelengths selected for the method are 250 nm and 218 nm that are absorption maxima of PGZ and MET respectively in Methanol. A series dilution was prepared of standard solutions PGZ and MET 4-24μg/ml and 4-24μg/ml respectively. The absorptivity coefficients of PGZ within concentration range of 4-24μg/ml and MET within concentration range of 2-14μg/ml were determined at 250 and 218nm by calibration curve. For the estimation of drugs in the commercial formulations, ten tablets
containing 15mg of PGZ and 500 mg of MET were weighed and average weight was calculated. The tablets were crushed and powdered in glass mortar. For the analysis of drugs, a standard addition method was used. An accurately weighed of pure PGZ was added to finely powdered sample to bring the concentration of PGZ in linearity range. With this addition, the ratio of MET to PGZ was brought to 1:2. Quantity of powder equivalent to 20mg of GLZ and 10 mg of MET was transferred to 100 ml volumetric flask, dissolved in sufficient quantity of methanol solvent, sonicated and volume was adjust up to mark with solvent to obtain a stock solution of 200 μg/ml of PGZ and 100 μg/ml of MET. This solution was then filtered through Whatmann filter paper # 41. Further dilutions were made from this stock solution to get required concentration. Absorbances of these solutions were measured at appropriate wavelengths, and values were substituted in the respective formula to obtain their respective concentrations. Results of tablet analysis are shown in Table No.1 The analysis procedure was repeated six times (n=6).

A set of two simultaneous equations as developed using these absorptivity coefficients as:

\[ C_x = \frac{(A_2 a_y - A_1 a_y)}{(a_x a_y - a_x a_y)} \] ..................................(1)

\[ C_y = \frac{(A_1 a_x - A_2 a_x)}{(a_x a_y - a_x a_y)} \] ..................................(2)

Where, \( C_x \) and \( C_y \) are concentrations of PGZ and MET respectively in μg/ml in sample solution. \( A_1 \) and \( A_2 \) are absorbances of the sample solution measured at 250 and 218nm respectively. The absorbances (\( A_1 \) and \( A_2 \)) of the sample solutions were recorded at 250nm and 218nm, respectively and concentration of both components were calculated using above mentioned equations (1 and 2) \(^{[4-16]}\).

**RESULTS AND DISCUSSION**

The methods discussed in the present work provide a convenient and accurate way for simultaneous analysis of PGZ and MET. In simultaneous equation method, wavelengths selected for analysis were 250nm for PGZ and 218nm for MET. This selection of wavelengths shown in Fig No. 1 This method linearity were observed in the concentration range of 4-24μg/ml and 4-24μg/ml for PGZ and MET respectively. Percent label claim for PGZ and MET in tablet analysis was found in the range of 95% to 105%. The results of proposed methods for estimation of PGZ and MET shown in following tables. The curves for solubility and linearity of PGZ and MET was shown in Fig No. 2
to Fig No.5 This method can be employed for routine analysis of these two drugs in combined tablet dosage form.

**TABLE 1: ABSORBANCE OF DRUG**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Absorbance at 218nm</th>
<th>Absorbance at 250nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. (Marketed Product)</td>
<td>0.738</td>
<td>0.500</td>
</tr>
<tr>
<td>2. (Pure drug)</td>
<td>0.791</td>
<td>0.511</td>
</tr>
</tbody>
</table>

**Figure 1**
Overlain spectra of Pioglitazone and Metformin Hydrochloride in Methanol.
Figure 2
Solubility of Pioglitazone in Methanol and DMS.

Figure 3
Solubility of Metformin Hydrochloride in Methanol and Water.
Figure 4
Linearity of Pioglitazone in Methanol.

Figure 5
Linearity of Metformin Hydrochloride in Methanol.
CONCLUSION

UV-Visible spectroscopic method for estimation of PGZ and MET in bulk and pharmaceutical dosage form was developed. The test solution was prepared using Methanol as a solvent. Prepared test solutions were scanned for determination of absorbance maxima. Absorbance of the test solutions were measured at 218nm and 250nm and plotted graphically to get calibration curves. Results revealed that the analytical method was accurate and highly precise.

REFERENCES

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