Development and Validation of Analytical Method for Quantitative Estimation of Miglitol and Metformin in Combined Dosage Form

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ABSTRACT

A simple, accurate, economical and reproducible UV spectrophotometric method for simultaneous estimation of Miglitol and Metformin in combined tablet dosage form has been developed. The developed method employs multi component spectroscopy using 300nm, 270nm, 240nm and 210nm as wavelengths for estimation. Miglitol and Metformin were found to be linear in the concentration range of 0.2–1.2 µg/ml and 2–12 µg/ml respectively. %Assay was found to be in the range of 99.27–99.92% and 99.29–99.97% for Miglitol and Metformin respectively. Results of analysis were validated statistically in accordance with ICH guidelines.

Keywords: Miglitol, Metformin, Multi Component Spectroscopy.

INTRODUCTION

Miglitol (MIG) is chemically (2R, 3R, 4R, 5S)-1-(2-hydroxyethyl)-2-(hydroxy methyl) piperidine-3, 4, 5-triol an oral anti-diabetic drug. It reversibly inhibits membrane-bound intestinal alpha-glucosidase hydrolyze enzyme which hydrolyzes oligosaccharides and disaccharides to glucose and other monosaccharides in the brush border of the small intestine. In diabetic patients, this enzyme inhibition results in delayed glucose absorption and lowering of postprandial hyperglycemia. Metformin (MET) is chemically N, N-dimethylimidodicarbonimidicdiamide. It is a biguanide class of oral anti-diabetic drugs. It improves hyperglycemia primarily through its suppression of hepatic glucose production and activates AMP-activated protein kinase. It also increases insulin sensitivity, fatty acid oxidation, peripheral glucose uptake and decreases absorption of glucose from the gastrointestinal tract. In literature, HPLC-UV-MS (Dai et al., 2010), Force degradation study (Chittora et al., 2009) and LC-MS (Xin et al., 2007) methods for estimation of MIG have been reported. Many analytical methods like Spectrophotometric method (Mubeen et al., 2010) available for estimation of MET individually and HPLC methods in combination with Glicazide (Dhable et al., 2010), Pioglitazone (Lakshmi et al., 2009, Sahoo et al., 2009), Repaglinide (Patel et al., 2007), Potentiometry, Spectrofluorimetry and UV-Visible Spectrophotometry, Stability indicating Capillary Electrophoresis (Hamdan et al., 2010) are available in the literature.
As there is no analytical method reported for quantitative estimation of MIG and MET in combination, the present study was aimed for the simultaneous estimation of Miglitol and Metformin by using multi component mode of analysis without prior separation in pharmaceutical dosage form.

**MATERIALS AND METHODS**

**Reagents and Materials**

Miglitol and Metformin in the form of gift samples were kindly supplied by Biocon and Micro Labs Ltd, Bangalore respectively. Double distilled water was used as solvent throughout the study. A combination of Miglitol (50 mg) and Metformin (500 mg) in tablet formulation was procured from local pharmacy (Mignar 50-MF Glenmark Ltd).

**Table 1:** Assay of Marketed Formulation (Mignar 50-MF).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Label claim per tablet (mg)</th>
<th>Mean Amount Found in tablet (mg)</th>
<th>Mean Amount found (%)</th>
<th>R.S.D. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG</td>
<td>50</td>
<td>49.88</td>
<td>99.76</td>
<td>0.83</td>
</tr>
<tr>
<td>MET</td>
<td>500</td>
<td>498.82</td>
<td>99.77</td>
<td>0.83</td>
</tr>
</tbody>
</table>

**Instrument**

A Shimadzu UV/Visible double beam spectrophotometer (Model 1700) with 1cm matched quartz cells was used in present study for multi component analysis.

**Method**

Five mixed standards of these two drugs were prepared so as to contain 2-10 µg/ml of MET and 0.2-1µg/ml of MIG in double distilled water. All mixed standard solutions were scanned over the range of 300nm to 200nm in multi component mode of spectrophotometer at medium scanning speed with measuring wavelength interval of 30nm. An overlain spectrum of mixed standard solutions is as shown in (Fig 2). The spectral data of these scans were stored in the instrument and used to determine the concentration of two drugs in the sample solution.

**Analysis of Commercial Formulation**

Twenty tablets were accurately weighed and crushed to fine powder. The tablet powder equivalent to 100mg of MET was accurately weighed, transferred to 100ml volumetric flask, dissolved in small quantity of double distilled water and finally made up to mark with double distilled water. This solution was filtered through Whatman filter paper No. 41. The filtrate was further diluted with double distilled water to get concentration of 6 µg/ml of MET and 0.6µg/ml of MIG.

The sample solution was scanned over the range of 300nm to 200nm in multi component mode immediately after scanning of mixed standard solutions and concentration of each component was estimated by analysis of spectral data of sample solution with respect to that of mixed standards by the instrument. The spectrum of sample solution is given in (Fig 3).

**Validation of Method**

Developed analytical method was validated in accordance with ICH guidelines (Q2A). Recovery studies were carried out by addition of pure drug to previously analyzed tablet sample at three different concentration levels (80%, 100% and 120%). The results of recovery studies are reported in Table 2. While precision of the method was determined by repeatability and intermediate precision (inter-day, intra-day) and expressed as %relative standard deviation (RSD). Intra-day precision was evaluated by analyzing concentration of MIG (0.6µg/ml) and MET (6µg/ml) of standard and sample solutions at three different time intervals under the same experimental conditions on the same day. Intermediate precision (inter-day precision) was determined by analyzing above mentioned concentrations of solutions on three consecutive days (Table 3).

**Table 2:** Results of Recovery Studies.

<table>
<thead>
<tr>
<th>LEVEL OF RECOVERY</th>
<th>Analyte</th>
<th>80% (±RSD)</th>
<th>100% (±RSD)</th>
<th>120% (±RSD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG</td>
<td>100.13 ±1.36</td>
<td>99.82 ±1.19</td>
<td>99.53 ±1.12</td>
<td></td>
</tr>
<tr>
<td>MET</td>
<td>100.12 ±0.31</td>
<td>99.81 ±0.54</td>
<td>99.53 ±0.65</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3:** Results of Precision Studies (Intra-Day Andinter-Day).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Concentrations of sample solution (µg/ml)</th>
<th>Intra-day precision</th>
<th>Inter-day precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG</td>
<td>0.6</td>
<td>1.182066</td>
<td>1.39</td>
</tr>
<tr>
<td>MET</td>
<td>6</td>
<td>1.178604</td>
<td>1.38</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

For selection of solvent, considering the common solubility of drugs, the stock solution was prepared in water while further dilutions were made in different solvents like methanol and glacial acetic acid. Results obtained were found to be satisfactory in water. Hence water was used as solvent throughout the experiment.

As the proposed method is specific to instrument having software for provision of such determination, selection of proper sampling wavelength and concentration of mixed standard are critical. Hence overlay spectra of analytes were studied carefully. Miglitol was found to be absorbing prominently at 200nm in the range of 300nm-200nm while Metformin absorbed at 232nm (λmax) hence, scanning range of 300nm to 200nm was selected for the multicomponent analysis.

The content of analytes in the marketed formulation was found to be 99.76% and 99.77% while recovery was found to be 99.5% and 100.1% for Miglitol and Metformin respectively. The values of relative standard deviations of inter-intraday studies were found to be less than 2%. The assay and validation results confirmed that the contents of MIG and MET estimated in the tablet dosage form were free from the interference of excipients.

CONCLUSION

The developed multi component spectroscopy method for simultaneous estimation of Miglitol and Metformin in combined tablet dosage form is simple, economical, accurate and reproducible and can be conveniently adopted for the routine quality control analysis from its pharmaceutical formulations and bulk drug.

REFERENCES


http://www.drugbank.com/Miglitol/ (access date Oct 28, 2010).


