ESTIMATION OF METFORMIN HYDROCHLORIDE AND GLIMEPIRIDE IN TABLET FORMULATIONS BY UV-VISIBLE SPECTROPHOTOMETRY

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ABSTRACT
In present research work attempt was made to estimate Metformin Hydrochloride and Glimepiride in combined Tablet formulations by UV-Visible spectrophotometric method. The dosage form contains 2 mg of Glimepiride and 500 mg of Metformin HCL and the ratio of both drugs in the dosage form is 1:250. Metformin HCL is freely soluble in water whereas Glimepiride is practically insoluble in water. So first both drugs are separated by solvent extraction method and then individually determined by UV absorbance method. Literature survey revealed that liquid chromatographic method and UV spectrophotometric method have been reported for estimation of Metformin HCL from combined dosage form. Also liquid chromatographic method and UV spectrophotometric method have been reported for estimation of Glimepiride from combined dosage form.

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INTRODUCTION
Modern medicines for human use are required to meet exacting standards which relate to their quality, safety and efficacy. The evaluation of safety and efficacy and their maintenance in practice is dependant upon the existence of adequate methods for quality control of the product. The standard of purity must therefore be strictly defined in such a way as to ensure that successive batches are consistent in composition, irrespective of whether they come from the same or different manufacturers. Diabetes is not a single disease but rather is a group of metabolic diseases characterized by hyperglycemia caused by inadequate insulin secretion with or without a simultaneous decrease in hormone action at its receptor. The World Health Organization estimates that 177 million people worldwide have diabetes. It is predicted that by 2011 there will be a 50% increase in this number. With the most significant increases in Africa, Asia and South America. Type I diabetes is caused by an absolute deficiency in insulin secretion. Type II diabetes for which 8 lacks new cases are diagnosed per year is a more complex disease. Major cause is hereditary. Type II diabetes is characterized by endorgan Insulin resistance and or a relative deficiency in insulin secretion. The pancreatic B cells in Type II diabetes undergo progressive deterioration over a fairly long time. Metformin HCl is a biguanide antidiabetic, is given by mouth in the treatment of Type II diabetes mellitus and is the drug of first choice in overweight patients. Initial dose is 500 mg two or three times daily with or after meals. The biguanides act in the liver by decreasing excessive glucose production, they also improve glucose utilization by restoring tissue sensitivity to insulin. Glimepiride II generation sulfonylurea class of drug is used in Type 2 diabetes mellitus, sulfonylureas act at the molecular level primarily as insulin secretagogues that is these compounds elicit insulin secretion from pancreatic β islet cells. Sulfonylureas act at the molecular level primarily as insulin secretagogues. That is these compounds elicit insulin secretion from pancreatic B islet cells. Glimepiride is sometimes classified as a third generation molecule. Metformin HCl is freely soluble in water whereas Glimepiride is practically insoluble in water. So first both drugs are separated by solvent extraction method and then individually determined by UV absorbance method. Literature survey revealed that liquid chromatographic method and UV spectrophotometric method have been reported for estimation of Metformin HCl from combined dosage form. Also liquid chromatographic method and UV spectrophotometric method have been reported for estimation of Glimepiride from combined dosage form.

EXPERIMENTAL METHOD
Instrument and Materials
UV-VISIBLE Double beam Spectrophotometer Shimadzu 1700 having spectral bandwidth 3nm and wavelength accuracy ±1nm ,with 1cm quartz cells was used. Gift samples of Metformin HCl and Glimepiride were procured from Cipla Ltd KurkumbhDist Pune and Glenmark Pharm, Nashik respectively. Distilled water available in lab used and Chloroform AR, KOH AR grade of Merck lab used. Combined Tablet of both drug purchased from local market. GLM ( Mfr By Systopic) Glyciphage G ( Mfr By Francoindian)

Method
Solutions of 10.0 mcg/ml of Metformin HCl in water and 10.0 mcg/ml of Glimepiride in 0.05 M KOH were prepared separately and were scanned in the spectrum mode from 400 to 200 nm and the λmax of both drug found at 233.2 (Fig 1) and 228.0 (Fig 2) respectively. Accurately weighed powder sample equivalent to 40 mg of Metformin HCl and dissolved in water into 100.0 ml volumetric flask and volume was made up to the 100.0 ml mark with water. The aliquots of stock solution were diluted to obtain various conc. From 8 to 40 mcg/ml and were scanned in the spectrum mode from 400 to 200 nm. It was found that Metformin HCl obeys
Beers law in the conc range 8 to 40 mcg/ml (Fig 3). Also accurately weighed powder sample equivalent to 10 mg of Glimepiride and dissolved in 0.05 M KOH into 100.0 ml volumetric flask and volume was made up to the mark i.e. 100.0 ml with 0.05 M KOH. The aliquots of stock solution were diluted to obtain various conc. From 5 to 30 mcg/ml and were scanned in the spectrum mode from 400 to 200 nm. It was found that Glimepiride obeys Beers law in the conc range 5 to 30 mcg/ml (Fig 4).

**SEPERATION BY EXTRACTION METHOD**

**Table 1: Result Analysis of Tablet Formulation**

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Tablet Sample</th>
<th>Label Claim (mg/Tab)</th>
<th>% Of Label Claim estimated</th>
<th>Standard Deviation</th>
<th>Coefficient of Variance %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MET</td>
<td>GLI</td>
<td>MET</td>
<td>GLI</td>
<td>MET</td>
</tr>
<tr>
<td>1</td>
<td>Batch I</td>
<td>500</td>
<td>2</td>
<td>100.322</td>
<td>98.864</td>
</tr>
<tr>
<td>2</td>
<td>Batch II</td>
<td>500</td>
<td>2</td>
<td>100.498</td>
<td>98.998</td>
</tr>
</tbody>
</table>

*Mean of Five Readings, MET – Metformin HCL, GLI - Glimepiride*

**Table 2: Result of Recovery Study of Tablet Formulation**

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Tablet Sample</th>
<th>Amount of Drug added (mcg/ml)</th>
<th>Total amount of Drug (mcg/ml)</th>
<th>% of Recovery estimated *</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MET</td>
<td>GLI</td>
<td>MET</td>
<td>GLI</td>
<td>MET</td>
</tr>
<tr>
<td>1</td>
<td>Batch I</td>
<td>4</td>
<td>5</td>
<td>29</td>
<td>15</td>
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<tr>
<td></td>
<td></td>
<td>8</td>
<td>10</td>
<td>33</td>
<td>20</td>
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<td></td>
<td></td>
<td>12</td>
<td>15</td>
<td>37</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>Batch II</td>
<td>4</td>
<td>5</td>
<td>29</td>
<td>15</td>
</tr>
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<tr>
<td></td>
<td></td>
<td>12</td>
<td>15</td>
<td>37</td>
<td>25</td>
</tr>
</tbody>
</table>

*Mean of Five Readings, MET – Metformin HCL, GLI - Glimepiride*
Powder of Metformin HCL and Glimepiride were weighed equivalent to quantity 40 mg and 10 mg respectively and transferred to clean and dry glass separating funnel with stopper. To this 50 ml water added and mixed well to dissolve. To this added 20 ml Chloroform to separate Glimepiride and flask was shaked well to intimately mix both the solvents. Flask was kept aside for the separation of both layer. After distinctly separation of layer, collected chloroform layer in the receiver by opening the cock of funnel. Same procedure of extraction repeated 2 times with 20 ml solvent chloroform each time and collected chloroform layer in same receiver. The receiver was heated on the waterbath to evaporate chloroform and residue was dissolved in 0.05 M KOH and transferred to 100.0 ml volumetric flask. Receiver was rinsed with 0.05 M KOH and transferred to flask so that Volume became 100.0 ml. Aliquots of this solution was diluted to 10.0 ml with 0.05 M KOH and absorbance was measured at 228.0 nm and conc of the solution was found by calibration graph method. Water layer containing Metformin HCL of funnel was transferred to 100.0 ml volumetric flask and volume was made up to the mark i.e. 100.0 ml with water. Aliquots of this solution was diluted to 100.0 ml with water and absorbance of this solution was measured at 233.2 nm. Concentration of the solution was found out by calibration graph method.

**PREPARATION AND ANALYSIS OF TABLET SAMPLE**

Twenty tablets were weighed and crushed to fine powder. Accurately weighed powder samples equivalent to 250 mg of metformin HCL and 1 mg of Glimepiride, and transferred to clean and dry glass separating funnel with stopper. To this 50 ml water added and mixed well to dissolve. To this added 20 ml Chloroform to separate Glimepiride and flask was shaked well to intimately mix both the solvents. Flask was kept aside for the separation of both layer. After distinctly separation of layer collected chloroform layer in the receiver by opening the cock of funnel. Same procedure of extraction repeated 2 times with 20 ml solvent chloroform each time and collected chloroform layer in same receiver. The receiver was heated on the waterbath to evaporate chloroform and residue was dissolved in 0.05 M KOH and transferred to 100.0 ml volumetric flask. Receiver
was rinsed with 0.05 M KOH and transferred to flask so that Volume became 100.0 ml. And absorbance was measured at 228.0 nm and conc of the solution was found by calibration graph method. Water layer containing Metformin HCL of funnel was transferred to 100.0 ml volumetric flask and volume was made up to the mark i.e. 100.0 ml with water. Aliquots of this solution was diluted to 100.0 ml with water and absorbance of this solution was measured at 233.2 nm. Concentration of the solution was found out by calibration graph method. (Table No 1)

To check the accuracy of the method and to study the interference of formulation additives, analytical recovery study were carried out by standard addition method. From that total amount of drug found the percentage recovery was calculated. (Table No 2)

RESULT AND DISCUSSION

The method is simple, easy and gives reproducible results. The recovery studies were carried out gave satisfactory results in the range of 99% to 102% which agrees with the standard values reported in literature for other methods.

REFERENCES

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