SIMULTANEOUS ESTIMATION OF IRBESARTAN AND HYDROCHLOROTHIAZIDE IN COMBINED PHARMACEUTICAL DOSAGE FORM BY UV SPECTROSCOPY

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Abstract

A simple, accurate, precise and economical procedure for simultaneous estimation of Irbesartan and Hydrochlorothiazide in combined tablet dosage form has been developed utilizing concept of standard addition. The method is based upon determination of irbesartan and hydrochlorothiazide at 215nm and 230nm in methanol. Different analytical parameters such as linearity, precision, and ruggedness were determined according to ICH guidelines. Irbesartan and hydrochlorothiazide at their respective wavelength shows linearity in the concentration range of 2-16 mcg/ml. The method was validated statistically. The results of analysis formulation given as percentage of label claim were found to be 106.6% and 101.6% for Irbesartan and Hydrochlorothiazide respectively. Therefore, the proposed method can be used for the routine analysis of both drugs in quality control laboratories.

Key words: Irbesartan, Hydrochlorothiazide, simultaneous estimation, methanol.

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INTRODUCTION: Irbesartan (IRB) is chemically 2-butyl-3-\{(4-[2-(2H-1,2,3,4-tetrazol-5-yl) phenyl]phenyl)methyl\}-1,3-diazaspiro[4.4] non-1-en-4-one is an orally active specific angiotensin II, AT1 receptor antagonist, and clinically effective drug in the treatment of hypertension. It is soluble methanol, ethanol, butanol, acetonitrile and 1N NaOH practically insoluble in water. Due to its hydrophobic nature IRB shows low dissolution profile in gastrointestinal fluid resulting poor absorption, distribution & consequently poor target organ delivery. Improvement of aqueous solubility in such cases shall lead to improved therapeutic efficacy of the drug. Hydrochlorothiazide (HCTZ), or 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulphonamide-1,1-dioxide, is a widely used thiazide diuretic. It increases urinary excretion of sodium and water by inhibiting sodium re absorption in the renal tubules. It is indicated for the treatment of edema, control of essential hypertension and management of diabetes insipid us. Usually in combination with other antihypertensive agents with different mechanisms of action. This is not only because blood pressure control is often inadequate using mono therapy but also because combination therapy can simplify dosing regimens, improve compliance, decrease side effects and reduce cost. For this combination derivative spectroscopic methods, one fluorimetric method and qualitative kinetic spectrophotometric methods are reported. There is however no work reported on combination of these drugs by simultaneous equation method. The significant feature of these combinations lies in the fact that hydrochlorothiazide is present in minute amount compared to Irbesartan which makes its analysis more complicated and tedious. Hence in the present communication we propose fast, simple and accurate spectrophotometric method, without tedious extraction procedure, was developed by applying standard addition method, for the simultaneous estimation of both the drugs in tablet dosage form by uv spectrophotometry.

MATERIALS AND METHODS

INSTRUMENT SPECIFICATIONS: UV Spectrophotometer, Shimadzu, model 1800

CHEMICALS AND REAGENTS: Methanol obtained from local market, manufacture pure irbesartan and hydrochlorothiazide were obtained as gift sample from Aurobindo Pharma limited, Hyderabad. The tablet dosage form XARB-H (claim: 150mg irbesartan and 12.5mg hydrochlorothiazide) was procured from local market.
PREPARATION OF STANDARD STOCK SOLUTIONS:
The 10 mg of standard Irbesarten and Hydrochlorichlorothiazice were weighed accurately and transferred into two different 100 ml volumetric flasks. Both the drugs were dissolved in methanol and diluted up to the mark by using the solvent methanol to obtain a final concentration of 100μg/ml. The resulting solution was used as a working standard solution. The aliquot portion of stock solutions of irbesartan and hydrochlorothiazide were diluted approximately with methanol to obtain concentration of 10 mcg/ml of each drugs. These solutions were scanned in the range of 200-400 nm in 1cm cell against blank. From the overlain spectra the wavelength selected for the estimation are 215 nm and 230 nm for irbesartan and hydrochlorothiazide respectively.

PREPARATION OF SAMPLE SOLUTIONS:
For the preparation of sample solution 20 tablets were taken and weighed, their mean weight was determined and finely powdered. An equivalent weight (12mg) of the tablet powder was weighed, it contains 12mg of irbesartan and 1 mg of hydrochlorothiazide. So 11mg of API of hydrochlorothiazide was added to make both drugs 12 mg(standard addition method).This powder was transferred into 10 ml volumetric flask, and dissolved in methanol. This solution was sonicated for 3 mins and filtered through whatman filter paper. From the filtrate 0.1 ml was taken and made up to 10 ml with methanol to give 12 mcg/ml of both drugs. This solution was scanned over the range of 200-400 nm, using two sampling wavelengths 215nm and 230nm determined the concentration of these drugs in tablet formulation.

VALIDATION OF THE METHOD:
1) LINEARITY: Standard stock solution of Irebesartan: 150 mg of Irebesartan was accurately weighed and transferred into a clean and dry 100 ml volumetric flask, dissolved with sufficient volume of methanol. The volume was then made up to 100 ml with methanol to obtain the concentration of 1000 μg/ml (1mg/ml). Working standard solution: 1 ml of the stock solution was further diluted up to 10 ml volumetric flask with methanol to get a concentration 100 μg/ml. Serial dilutions of concentration range 2-16 μg/ml were prepared from the working standard solution. These dilutions were scanned at the detection wavelength of 215 nm and 230 nm using methanol as blank. The regression equation, Y- intercept and correlation coefficient were calculated. The linearity was thus determined, and a concentration range was selected.
2) LIMIT OF DETECTION AND LIMIT OF QUANTITATION:
The LOD and LOQ were separately determined based on calibration curve. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines were used to calculate the LOD and LOQ.

I. Formula for LOD (µg/ml):
   \[ \text{LOD} = 3.3 \times \frac{SD}{S} \]
   Where,
   SD = The standard deviation of the response
   S = The slope of the calibration curve (mean)

II. Formula for LOQ (µg/ml):
   \[ \text{LOQ} = 10 \times \frac{SD}{S} \]
   Where,
   SD = The standard deviation of the response
   S = The slope of the calibration curve (mean)

3) ACCURACY:
The accuracy of the method was ascertained by carrying out recovery studies using standard addition method. The recovery studies are performed to determine if there was any positive or negative interference from excipients present in the formulation. The percentage recovery results revealed that the values were near to 100%, which indicates that the proposed method is accurate as the results are within the official limits. It also reveals that the commonly used excipients and additives in the formulation were not interfering with the proposed method. (Table no: 2)

PRECISION: The precision of analytical method is expressed as standard deviation or relative standard deviation of a series of measurements. It was ascertained by replicate estimation of drug by the proposed method. (Table no: 3)

RESULTS AND DISCUSSION:
Irbesartan and Hydrochlorothiazide showed maximum absorbance in Methanol at 215 and 230nm. The proposed method for simultaneous estimation of both the drugs was validated as per the ICH guidelines. The linearity was observed in the concentration range of 2-16 mcg/ml for both drugs with regression co-efficient of 0.999 and 0.999. Amount of drugs estimated by the proposed method was in good agreement with the label claim. The accuracy of the method was assessed by recovery experiments. The precision of the method was studied as repeatability,
intra-day and inter day variations; the %RSD less than 2 ,indicates proposed method is precise. Recovery was close to 100% for both the drugs.

**CONCLUSION**

The present study comprises a UV spectroscopic method of analysis for the simultaneous estimation of Irbesartan and hydrochlorothiazide in tablet dosage form. From the study of validation parameters, it was observed that the method is specific, accurate, precise, and reproducible. The proposed method could be applied to routine analysis in quality control laboratories.

**Table 1: Results of analysis of tablet formulation**

<table>
<thead>
<tr>
<th>BRAND</th>
<th>LABEL CLAIM(mg/tablet)</th>
<th>AMOUNT FOUND</th>
<th>%LABELCLAIM</th>
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</thead>
<tbody>
<tr>
<td>XARB-H</td>
<td>IRBESARTAN(150mg)</td>
<td>152.5mg</td>
<td>101%</td>
</tr>
<tr>
<td></td>
<td>Hydrochlorothiazide (12.5mg)</td>
<td>13.3mg</td>
<td>106%</td>
</tr>
</tbody>
</table>

**Table 2: Results of recovery studies**

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>LEVEL</th>
<th>CONCENTRATION</th>
<th>%RECOVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>50%</td>
<td>8mcg</td>
<td>112%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12mcg</td>
<td>102%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>4mcg</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6mcg</td>
<td>102%</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>50%</td>
<td>8mcg</td>
<td>110%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12mcg</td>
<td>102%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>4mcg</td>
<td>98%</td>
</tr>
<tr>
<td></td>
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<td>6mcg</td>
<td>96%</td>
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**Table No:3 Results of precision studies**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration(mcg/ml)</th>
<th>absorbance</th>
<th>%RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irbesartan</td>
<td>8</td>
<td>0.680</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>0.659</td>
<td>0.12%</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>0.679</td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>8</td>
<td>0.547</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>0.542</td>
<td>0.24%</td>
</tr>
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SELECTION OF WAVELENGTH

References:


