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METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF IRBESARTAN AND CHLORTHALIDONE IN BULK AND TABLET DOSAGE FORM BY UV SPECTROPHOTOMETRY

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Abstract: A simple, sensitive, rapid spectrophotometric method have been developed for simultaneous estimation of Irbesartan (IRB) and Chlorthalidone (CHL) in bulk and in tablet dosage form. The simultaneous equation based on measurement of absorbance at two wavelengths 270 nm and 223 nm λ_{max} of IRB and CHL respectively. Beer's law was obeyed in the concentration range of 30-150 µg/ml and 2.5-12.5 µg/ml for IRB and CHL. The method was validated as per ICH guidelines. Statistical analysis proved that the method were accurate, precise and reproducible for analysis of IRB and CHL in tablet dosage form. The wide linearity range, sensitivity, accuracy and simple procedure imply that the proposed technique demonstrated to be appropriate for routine analysis and quality control assay of tablet.

Index Terms **- Irbesartan, Chlorthalidone, Simultaneous equation method, Tablet dosage form**

I. INTRODUCTION

Irbesartan (IRBE), chemically known as (2-butyl-3-[[4-[2-(2H-tetrazol-5-yl) phenyl] phenyl] methyl]-1, 3-diazaspiro [4.4] non-1-en-4-one), is an anti-hypertensive drug (Angiotensin-II receptor antagonist) and prevents binding of Angiotensin-II to AT1 receptor. This is used for treatment of hypertension and diabetic nephropathy with an elevated serum creatinine and proteinuria (>300mg/day) in patients with type-2 diabetes & hypertension [1,2,3,4]. It is a long-acting thiazide like diuretic of the sulfamoylbenzamide class. Molecular formula is $C_{14}H_{11}ClN_2O_4S$. Molecular weight is 338.8 g/mol. IUPAC name is 2-chloro-5-(1-hydroxy-3-oxo-2,3- dihydro-1H-isoindol-1-yl) benzene-1-sulfonamide [5]. The developed method was validated as per ICH norms [6-7]. The literature reported few analysis methods for quantification of IRB and CHL alone and in combination with other antihypertensive drugs. However, no analytical method has been developed for simultaneous determination of IRB and CHL in bulk and tablet formulation by UV Spectrophotometry.

II. METHODS AND MATERIALS:

Instrumentation:

The instrument used in the present study was Shimadzu double beam UV/Visible spectrophotometer (Model UV-1700) with spectral band width of 1 nm. All weighing was done on electronic balance (Model Shimadzu AUX -220).

Reagents and Chemicals:

The pharmaceutical dosage form used in this study was a GRANRY-D tablet manufactured by AAR ESS REMEDIES PVT. LTD. (New Delhi, India) labeled to contain 150 mg of Irbesartan and 12.5 mg of Chlorthalidone. Methanol was used as solvent.

Preparation of standard stock solution:

Standard stock solution of IRB (1500 µg/ml) and CHL (125 µg/ml) were prepared by dissolving 150 mg of IRB and 12.5 mg of CHL in 10 ml of Methanol, separately to get a concentration of 15000 µg/ml of IRB and 1250 µg/ml of CHL. Further pipetted out 1 ml of IRB and CHL into 10 ml of volumetric flask, separately add methanol and made upto the mark with methanol.

Study of spectra and selection of wavelength:

For the selection of analytical wavelength, standard solution of 10 µg/ml IRB and CHL were prepared separately by appropriate dilution of standard stock solution with Methanol and scanned in the entire UV range to determine λ_{max} of these drugs. The λ_{max} of IRB and CHL were found to be 270 nm and 223 nm, respectively. A series of standard solutions were prepared having concentration range of 30-150 µg/ml for IRB and 2.5-12.5 µg/ml for CHL. The absorbance of resulting solutions was measured at 270 nm and 223 nm. The overlain UV absorbance spectrum of IRB and CHL is shown in Figure 1.

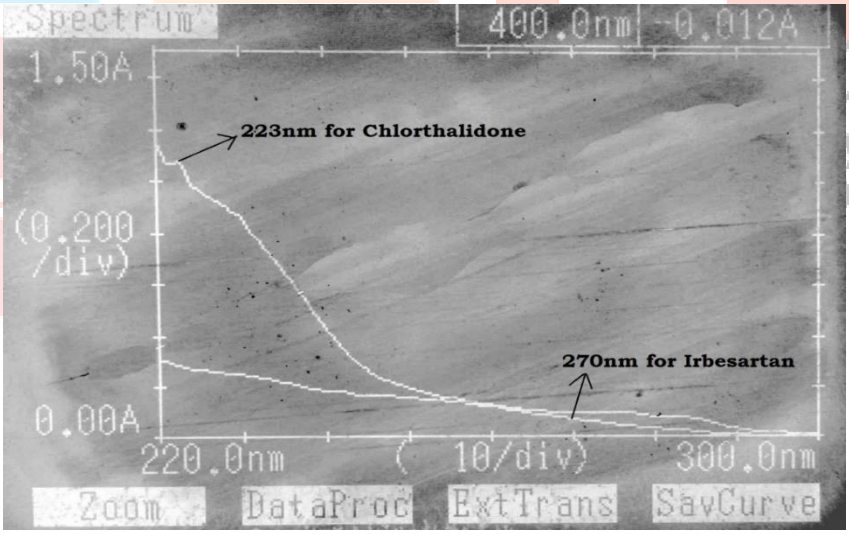

Figure 1: Zero order overlain spectra of 10µg/ ml of IRB and CHL respectively

Analysis of Marketed Tablet Formulation:

For the estimation of drugs in the commercial formulation, twenty tablets were weighed accurately. The average weight was calculated and then crushed to obtain fine powder. A quantity of tablet powder equivalent to about 150 mg of IRB was transferred into 10 ml volumetric flask; 8 ml Methanol was added and sonicated for 15 min, volume was then made up to the mark with Methanol. The resulting solution was mixed and filtered through Whatmann filter paper no 41 and filtrate was appropriately diluted to get approximate concentration of 60 µg/ml of IRB and 5 µg/ml of CHL, the concentration of IRB and CHL were determined by measuring absorbance of sample solution at 270 nm and 223 nm. Concentration of IRB and CHL in the diluted solution was obtained from calibration curves. Amount of IRB and CHL in mg/tab was then calculated,

by multiplying the concentration obtained with dilution factor. Results of tablet analysis was shown in Table No.1.

Validation:

The proposed methods were validated as per ICH guidelines.

Linearity:

Different aliquots (0.2-1.0 ml) of IRB from standard stock solution of IRB (1500 μg/ml) was transferred into series of 10ml volumetric flasks, separately and the volume was made up to the mark with methanol to get concentrations 30, 60, 90, 120 and 150µg/ml, Similarly, different aliquots (0.2-1.0 ml) of CHL from standard stock solution of CHL (125 μg/ml) was transferred into series of 10ml volumetric flasks, separately and the volume was made up to the mark with methanol to get concentrations 2.5, 5, 7.5, 10 and 12.5µg/ml, respectively. The absorbance of resulting solutions was measured at 270 nm and 223 nm, respectively.

Accuracy:

To the preanalysed sample solutions, a known amount of standard stock solution was added at different levels i.e. 50, 100 and 150 %. The solutions were reanalyzed by proposed method.

Precision:

The reproducibility of the methods was determined by analyzing tablets at different time intervals on same day in triplicates (Intra-day assay precision) and on three different days (Inter-day assay precision)

III. RESULT AND DISCUSSION:

The method discussed in the present work provide a convenient and reliable way for quantitative determination of IRB and CHL in combined dose tablet formulation. Wavelength of maximum absorbance for IRB (270 nm) and CHL (233 nm) were selected for analysis by simultaneous equation method. Percent label claim for IRB and CHL in tablet analysis was found to be 99.68 and 100.38 % as shown in Table 1. Percent recovery for IRB and CHL was found to be 100.06% and 100.38 % with standard deviation well below 2 indicating accuracy of the method as shown in Table 2. Intra-day and Inter-day precision studies were carried out by analyzing tablet formulation, three times on the same day and on three different days, respectively. Standard deviation and coefficient of variance for intra-day and inter-day precision studies was satisfactorily low indicating high degree of precision and reproducibility of this method.

Table 1. Results of Analysis of Tablets

Tablet Sample	Label claim (mg/tab)	% Label claim (n=6)	% RSD
Irbesartan	150 mg	99.68	0.6214
Chlorthalidone	12.5 mg	100.38	0.8462

Table 2. Results of Recovery Studies

Recovery level	Initial amount (μ g/ml)		Concentration of std drug added (μ g/ml)		% Recovery (n = 3)	
	IRB	CHL	IRB	CHL	IRB	CHL
50%	60	5	30	2.5	99.64	100.26
100%	60	5	60	5	100.12	100.28
150%	60	5	90	7.5	100.44	100.62
			Mean		100.06	100.38

IV. CONCLUSION:

The validated spectrophotometric method employed here proved to be simple, economical, rapid, precise and accurate. Thus, these can be used for routine simultaneous estimation of IRB and CHL in tablet dosage form instead of processing and analyzing each drug separately.

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