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Research Article

Determination of Simultaneous Irbesartan and Hydrochlorothiazide by Ultraviolet Spectrophotometry with Dual Wavelength Method

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A B S T R A C T

Objective: The present study was aimed to develop a spectrophotometric method by dual wavelength method in simultaneous analysis of irbesartan and hydrochlorothiazide on tablet preparations without separation. Irbesartan and hydrochlorothiazide are a group of anti-hypertensive drugs that are very effective and safe to use to reduce blood pressure and edema. These drugs often given in combination with these active ingredients can cause problems in quantitative analysis for the quality control of preparations.

Methods: The study was carried out experimentally with a spectrophotometric method, one of which was dual wavelength method and then tested its validity based on validation parameters, namely linearity, accuracy, precision, LOD and LOQ and intraday and interday. Then, this method of irbesartan and hydrochlorothiazide in tablet preparations.

Results: The results of the study were showed that the application of dual wavelength method on the concentration was carried out at λ 263.4 nm and 281 nm for irbesartan and at λ 243.4 nm and 247.6 nm for hydrochlorothiazide. The results obtained by irbesartan and hydrochlorothiazide on tablets were (108.04 ± 2.696) and (94.28 ± 4.48)% respectively, and with good precision and accuracy.

Conclusions: The ultraviolet spectrophotometry method is dual wavelength method successfully applied for the determination of the concentration of irbesartan and hydrochlorothiazide in tablets.

Keywords: Irbesartan, hydrochlorothiazide, tablets, ultraviolet spectrophotometry and dual wavelength method

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INTRODUCTION

The combination of Irbesartan (IRB) and Hydrochlorothiazide (HCT) is very effective and safe to use to reduce blood pressure and edema accompanied by complications and minimal side effects, namely hyperkalemia. Irbesartan has the chemical name 2-Butyl-3 - [[20- (1H-tetrazol-5-yl) [1, 10-biphenyl] -4-yl] methyl] 1, 3-diazaspiro [4.4] non-1- id -4-one and hydrochlorothiazide (HCT) chemical name 6-Chloro-3, 4-dihydro-2H-1, 2, 4-benzothiadiazine-7-sulfonamide 1,1 dioxide. Determination of IRB and HCT in one condition was determined by the spectrophotometric method, where the IRB had a maximum absorbance at 246 nm and 274 for HCT[1-2].

Spectrophotometry is a simple, fast and relatively easier method compared to other methods, dual wavelength method (DWM) is one of the spectrophotometric methods that can be used to analyze two drug mixtures simultaneously without having to do the separation, easily applied to routine analysis and without need derivatization first [3-4].Dual wavelength method, in this method two wavelengths are chosen (λ1, λ2) where drug A shows the same absorbance (or the difference between absorbance is zero) so drug B can be determined and vice versa for drug B[5]. This method can be an option in determining the level of the drug, it is necessary to do research with the aim to prove the Dual wavelength method can be used to

determine the levels of IRB and HCT in tablet dosage forms.

MATERIAL AND METHODS

Material

Pharmaceutical grades of IRB were from the National Agency of Drug and Food Control of Republic of Indonesia; HCT was from PT Kimia Farma. Tablet C (PT. Sanofi) contained 300mg IRB and 12.5mg HCT. All other chemicals and reagents used were for analytical grade.

Apparatus and conditions

UV-Visible Spectrophotometer (Shimadzu 1800) with a computer equipped with UV probe 2.43 software (UV-1800 Shimadzu), the absorption was recorded at a wavelength of 200-400nm using a 1 cm cuvette using UV-probe software. Analytical balance (sartorius), sonicator (Branson 1510) glass tools, mortal and other tool required in sample preparation.

Preparation of standard stock solution

The IRB and HCT (50 mg respectively) were moved into a 50mL volumetric flask and then were dissolved with 0.1 N NaOH and added it to the mark line. The standard stock concentration was 1000µg/mL (stock solution I). The 5 mL of parent solution was transferred into a 50mL volumetric flask and then was diluted with 0.1N NaOH by adding it to the mark line, and the concentration has become 100µg/mL.

Determination of Absorption Maximum Spectrum and Spectrum absorption ratio

The IRB (10mL) and HCT (8mL) were pipetted from (stock solution II) and transferred into a 25mL volumetric flask respectively. Next, the solution is diluted with 0.1 N NaOH, then homogeneous so that the concentration is 10 µg/mL for IRB, 8µg/mL for HCT and the mixture of the two drugs is the same with the same concentration. The absorption spectrum of the IRB ratio was in the range of 5-15µg/mL (series A) and 4-12µg/mL for HCT (series B) and the mixture of both the drugs (series C) in same concentration range were prepared for dual wavelength method.

Procedure Dual Wavelength Method

The spectrum of IRB show identical absorbance at 243.4 nm (λ_3) and 247.6nm (λ_4) therefore these two wavelengths were selected for the analysis of HCT. All the solutions of series A were scanned to ensure that the difference between λ_3 and λ_4 is zero. Similarly, the HCT solutions were scanned to determine the two wavelengths, where absorbance is the same. These two wavelengths were found to be 263.4 nm (λ_1) and 281 nm (λ_2) make were selected for the analysis of IRB. All the solutions of series B were scanned to ensure that difference between (λ_1) and (λ_2) is zero. Thereafter, the solution of series C were scanned to ensure that varying concentration of IRB and HCT are not affecting the absorbance at a selected wavelength. The difference in absorbance between (λ_1) and (λ_2) of series C solution used for the preparation of calibration curve for IRB. Similarly, difference in absorbance between λ_3 and λ_4 of mixed standard solutions was used for the preparation of calibration curve for HCT[6].

Validation test

Linearity

The solution standard for IRB and HCT for absorption spectrum were made from the selected wavelength points of 263.4 nm and 281 nm for IRB, while the HCT were used wavelength of 243.4 nm and 247.6 nm. The difference in absorbance values from series C was used to obtain a regression equation for each component at the selected wavelength[7-8].

Precision of the method

Reparability of the methods were studied by repeating the methods six times. To study intra-day precision, the method was repeated three times in a day. Similarly, the method was repeated on three different days to determine inter-day precision.

The determination of precision was based on the relative standard deviation (RSD) value 2%[7-8].

Recovery test

Recovery test was calculated by measured recovery percentage in three specific points which were: 80%, 100%, and 120%. In each of the specific points, the test was used 70% from the sample and 30% from the pure active substances (standard addition method) [7-8].

Preparation of sample solution

Twenty tablets were weighed and crushed homogeneous. Furthermore, weighed amount of powder equivalent to 300 mg of IRB and 12.5mg of HCT then the equivalence contained there is calculated and weighed up to six repetitions. Subsequently, the powder was incorporated into the flask 50mL and was diluted with 0.1N NaOH (with sonicator for 15 minutes). Thereafter, the solution was added with 0.1N NaOH to the mark line and was shaked until homogeneous. Afterwards, the solution was filtered, then was discarded approximately 10mL of the first filtrate. Next, 0.5mL of filtrate was putted into a 25 mL flask and was diluted with 0.1 N NaOH until the mark line to obtained solution for IRB and HCT concentration of 10µg/mL and 8µg/mL, respectively. Thereafter, the absorption of solution was measured at a wavelength of 200-400 nm.

RESULT AND DISCUSSION

Study of overlain spectra and selection of wavelength

In a study of overlain with the right concentration and in accordance with the law of lambert-beer. With the concentration of the measured solution, 10µg/mL and 8µg / m and the mixture of both in the same concentration, scanned each with a range of 200-400nm and the spectrum of overlain observed from the IRB and HCT is shown in figure 1

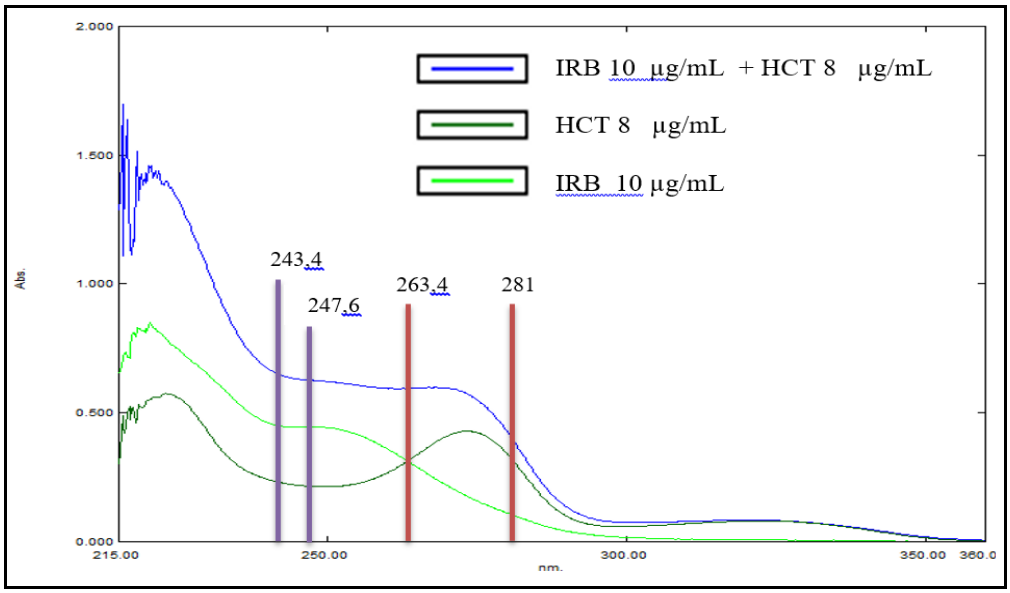

Figure :1 Overlain spectrum of IRB and HCT

Table: 1 Result of calibration readings for IRB and HCT

Concentration (ppm) IRB	The difference in absorbance from HCT at 263.4 and 281 nm	Concentration (ppm) HCT	The difference in absorbance from IRB at 243.4 and 247.6 nm
5	0.0934	4	0.0067
7,5	0.1483	6	0.0097
10	0.2003	8	0.0130
12.5	0.2545	10	0.0165
15	0.3079	12	0.0191

From the study of overlays, the two wavelength spectrums were chosen for 243.4 nm and 247.6 nm IRB where the difference in absorbance was 0 so that it could be used for HCT analysis, whereas for HCT 263.4 nm and 281 nm was used for IRB analysis. For the calibration curve, the ratio spectrum ranges from 5-15 µg / mL (series A) and 4-12 µg / mL for HCT (series B) and the mixture of both drugs (series C) in the same concentration range with a ratio of 5: 4. The result of calibration reading for IRB and HCT are shown in table 1.

Assay for the commercially available tablet dosage form is performed and the results are shown in table 2. The results of drug levels in the market indicate that the drug meets the requirements with values in the range for 270-330 mg IRB and 11.25-13.75 for HCT.

Method validation:

The developed method is validated for linearity, precision, and accuracy.

Linearity

The calibration curves of IRB and HCT were linear in the range of 5-15 µg/mL and 4-12 µg/mL respectively.

The regression equations of calibration curves were

Y_{irb} = 0.0207X - 0.0047, r = 0, 9994 for IRB and

Y_{hct}= 0.001606X – 0.000129, r = 0, 9995 for HCT

Precision

Relative standard deviations (% R.S.D.) for inter day were found to be 1.15 and 3.33 for IRB and HCT, respectively. The intraday precision showed % R.S.D 1.72 and 3.91 for IRB and HCT, respectively.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD for IRB and HCT was found to be 0.6374 µg/mL and 0.4931µg/mL respectively. The LOQ for IRB and HCT was found to be 1.9314µg/mL and 1.4943 µg/mL respectively. The validation results are shown in table 3.

Recovery

The percentage recoveries of drug from marketed formulation were determined by standard addition of pure drugs at three (80%, 100%, and 120%) known concentrations and excellent recoveries were obtained at each level. The percentage of recovery for IRBs is three levels, 80%, 100%, and 120% respectively 100.33, 101.14 and 100.29, while for HCT is 101.72, 99.64 and 99.64. The Recovery studies are shown in table 4

Table 2: Results of simultaneous estimation of AT and EZ in the marketed formulation by Dual Wavelength spectrophotometry method

Component	Claim on label (mg)	Content (mg)
IRB	**300**	324, 11 ± 8,09
HCT	**12.5**	11,78 ± 0,56

Table 3: Optical characteristics of the proposed methods and results of formulation analysis & precision study

No.	Parameter	IRB	HCT
1	Analytical weve lengths for determination (nm)	263.4 nm and 281 nm	243.4 and 247.5
2	Lamber beer (µg/mL)	5-15	4-12
3	Regression equation	Y_{irb} = 0.0207X - 0.0047	Y_{hct}= 0.001606X – 0.000129
4	Correlation coefficient	0,9994	0,9995
5	Accuracy (%)	100,59	100,34
6	Precision (RSD) (%)	0,87	45,70
7	Interday (% RSD)	1.15	3.33
8	Intraday (% RSD)	1.72	3.91
9	LOD (µg/mL)	0,64	0,49
10	LOQ (µg/mL)	1,93	1,49

Table 4: Recovery studies

No.	Drug	Concentration (%)	Mean % recovery
1	IRB	80 %	100.33
2	IRB	100%	101.14
3	IRB	120%	100.29
4	HCT	80 %	101.72
5	HCT	100%	99.64
6	HCT	120%	99.64

CONCLUSION

The proposed dual wavelength method gives accurate and precise results for determination of irbesartan and hydrochlorothiazide in marketed formulation (tablets) without prior separation and is easily applied for routine analysis. The most interesting feature of the dual wavelength method is its simplicity and rapidity. The validation method has been demonstrated by a variety of tests for linearity, accuracy and precision. The proposed methods were successfully applied to the determination of these drugs in commercial tablets.

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