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Development and Validation of Analysis Methods of Captopril in Tablets with Methods of Area under Curves and Absorbance by Ultraviolet-Visible Spectrophotometry

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Abstract

Development and validation of analytical methods of captopril tablets have been carried out by absorbance method and area under the curve method by UV-Vis spectrophotometry. This study used absorbance calculation principle and area under the curve obtained from measurement of analytical solution using UV-Vis spectrophotometer and distilled water as solvent with several reagents. This reagent is used to oxidize captopril compounds having thiol (-SH) groups in their structure. Captopril linearity was obtained in the concentration range 20 - 60 µg/mL. Correlation coefficient value with absorbance method and area under the curve method are 0.9998 and 0.9994 respectively. The results showed that the sample rate obtained by absorbance method and area under the curve method were 104.55 % ± 0.433 and 92.22 % ± 0.351 for patent tablets; 93.42 % ± 1.306 and 91.09 % ± 0.093 for generic tablets. The average per cent of recovery obtained by absorbance method and area under the curve method were 95.62 % ± 14.444 and 101.55% ± 15.989 for patent tablets; 95.33 % ± 14.278 and 100.96 % ± 15.655 for generic tablets.

Keywords: Captopril, validation, absorbance, area under the curve, UV-Vis spectrophotometry.

1. Introduction

The two primary groups of angiotensin antagonists are the angiotensin-converting enzyme (ACE) inhibitors and the angiotensin II receptor blockers (ARBs). ACE inhibitors (e.g., captopril), which inhibit the enzyme variously known as angiotensin-converting enzyme, kinase II, and peptidyl dipeptidase, cause a reduction in blood levels of angiotensin II and aldosterone and an increase in endogenous vasodilators of the kinin family. ACE inhibitors have a low incidence of serious adverse effects (except in pregnancy) when given in normal dosage and produce minimal compensatory responses. The ACE inhibitors are useful in heart failure and diabetes as well as in hypertension (Trevor *et al.* 2015).

Captopril has molecular formula $C_9H_{15}NO_3S$ and molecular weight 217.28 g/mol. Chemically, captopril is 1-[(2S)-3-Mercapto-2-methylpropionyl]-L-proline [62571-86-2] as presented in Figure1. The chemical properties for captopril are powdered crystal; white or almost white; typical odours such as sulphides; melting at 104 - 110 ºC; easily soluble in water, methanol, ethanol, and chloroform. (Kementerian Kesehatan, 2014)

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Figure 1: Chemical stucture of captopril

Determination of captopril levels in bulk can be performed by titrimetric method (Mohamed *et al.*, 1983; Kementerian Kesehatan, 2014), kinetic spectrophotometric method (Rahman *et al.* 2006). A flow injection spectrophotometric method for the determination of captopril involving measurement of the absorbance of the captopril complex with palladium (II) in a 0.12 M HCl medium at 400 nm is presented. The calibration graph was linear over the range $2 \times 10^{-5} - 6 \times 10^{-4}$ M. The sampling frequency was 90 h^{-1} with sample injections of 70 µL. The proposed method was applied to the determination of captopril in pharmaceutical samples (Albero *et al.* 1993). The determination of captopril levels in pharmaceutical preparations has been carried out by various methods such as titrimetric method (Mohamed *et al.*, 1983; Ribeiro *et al.*, 2003), high performance liquid chromatography (Kementerian Kesehatan, 2014) and kinetic spectrophotometric method (Rahman *et al.* 2006). A reverse-phase high performance liquid chromatography (RP–HPLC) method with ultra-violet (UV) detection for a routine control of hydrochlorothiazide and captopril in tablets has been developed (Ivanovic *et al.*, 2004). The method of identification of captopril in medicines by thin layer chromatography has been developed. It has established that the most optimal Rf observed using mobile phases: Chloroform R-propanol R (9:1). The detection limits of captopril in this system are 0.4 mcg (Liliya, *et al*. 2016).

Two indirect methods are described for the micro determination of captopril using hexacyanoferrate (III) as reagent. The reaction used for titrimetric proceeds at room temperature and will be complete in 10 minute with a stoichiometry of 1:1 with respect to the oxidant and captopril. The reaction product used for spectrophotometric determination shows the absorption maximum at 510 nm. The Beer's law is obeyed over the concentration range 0.25-12.00 mg mL^{-1}, the molar absorptivity and Sandell sensitivity for the system being 9.14×10^3 L $mol^{-1}cm^{-1}$ and 23.78 ng cm^{-2}, respectively. The limit of detection and quantification are found to be 0.08 and 0.26 mg mL^{-1}, respectively. Both procedures have been applied to the determination of captopril in tablets. The results have been statistically compared with those obtained by the official (BP) method (Chandru & Sharada, 2007).

A simple, accurate and sensitive indirect spectrophotometric method for the determination of captopril in pharmaceutical preparation (tablets) and environmental water samples has been developed. The method is based on the oxidation of captopril by a known excess of potassium iodate (KIO_3) in sulphuric acid medium to form iodide ion which reacts with excess iodate to liberate iodine which then reacts with starch to form a stable blue coloured Iodine-starch complex which shows maximum absorbance at 606 nm. Beer's law was obeyed in the concentration range (2-28 ppm). The molar absorptivity and Sandell's sensitivity of the coloured complex are 1.716×10^4 l/mol.cm and 12.66 ng / cm^2, respectively. The analytical parameters were optimized and the method was successfully applied to the determination of captopril in pure form, its tablets form and environmental water samples (Ahmed, 2013).

Among the various methods used in the determination of drug levels, UV-Vis spectrophotometry is still very popular. In our previous research we have developed several analytical methods using the absorption method and the area measurement method under the curve with ultraviolet-visible spectrophotometry (Rivai *et al.*, 2018; Asra *et al*., 2016; Chandra *et al*., 2017; Chandra *et al.*, 2016; Rivai *et al*., 2017a,b,c). In this research, the best condition for captopril analysis was done, and then developed the method for determination of captopril concentration by UV-Vis spectrophotometry. The method developed was the method of absorbance and method of area under the curve.

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2. Materials and Methods

2.1 Tools and materials

The tool used in this research is UV-Vis spectrophotometer (Shimadzu UV-1800), analytical balance (Precisa XB 220 A), sonicator (Branson 1800), filter paper (Whatman No. 41), funnel (Pyrex), measuring cylinder (Pyrex), pipettes (Pyrex), measuring flask (Pyrex), Erlenmeyer (Pyrex), dropper drops, spatula, parchment paper, mortars, stamfer, suction ball, and aluminium foil. The materials used in this study were standard pure captopril (Sigma-Aldrich, Lot SLBM6819V, ED November 2018); captopril tablets Farmoten® 25 mg (PT Pratapa Nirmala), generic tablet Captopril 25 mg (PT Kimia Farma), distilled water (PT Brataco), starch (PT Brataco), potassium iodate (PT Brataco), and sulphuric acid (PT Merck).

2.2 Procedures

2.2.1 Preparation of solutions and reagents

2.2.1.1 Standard solution of captopril (1000 ppm)

This solution is prepared by dissolving 100 mg captopril in 100 mL of distilled water in a measuring flask (Ahmed, 2013).

2.2.1.2 Standard solution of captopril (100 ppm)

This solution is prepared by diluting 10 mL of a 1000 ppm mains solution in 100 mL of distilled water in a measuring flask (Ahmed, 2013).

2.2.1.3 Iodate potassium reagent 0.1% (4.6×10^{-3} M)

This reagent is prepared by dissolving 100 mg of potassium iodate in 100 mL of distilled water in a measuring flask (Ahmed, 2013).

2.2.1.4 Sulphuric acid reagent 1 N

The reagent is prepared by diluting 2.8 mL of concentrated sulphuric acid 36 N in 100 mL of distilled water in a measuring flask (Ahmed, 2013).

2.2.1.5 Starch solution 1%

The reagent was prepared by dissolving 1 gram of starch in 20 mL of hot distilled water, then adding distilled water to 100 mL in a measuring flask (Ahmed, 2013).

2.2.2 Maximum wavelength determination

A total of 10 mL of standard solution of captopril 100 ppm was taken with pipette and fed into a 25 mL measuring flask, then reacted with 1 mL of 1 N sulphuric acid solution, added 3 mL 1% starch solution and 1 mL of 0.1% potassium iodate solution, then added distilled water until the boundary marks. The spectra were measured at 400 - 800 nm against the prepared blend reagents in the same manner but did not contain captopril (Ahmed, 2013).

2.2.3 Preparation of the calibration curve

Captopril standard solution series was prepared with concentrations of 20, 30, 40, 50, and 60 µg / mL. The trick is to take 100 ppm captopril solution of 5, 7.5, 10, 12.5 and 15 mL with measuring pipette, put into a 25 mL measuring flask. Then 1 mL of 1 N sulphuric acid solution, and 3 ml of 1% starch solution, and 1 mL of 0.1% potassium iodate solution were added to each measuring flask, diluted with distilled water up to the boundary marker. The absorption and area under the curve were measured by a UV-Vis spectrophotometer at a maximum wavelength of 600.5 nm. Then find the linear regression equation of captopril (Ahmed, 2013).

2.2.4 Determination of captopril levels in tablets

A total of 20 captopril tablets were weighed, then crushed until smooth and weighed the equivalent of 50 mg of pure captopril. The powder is dissolved with distilled water until the limit marks up to 50 mL to obtain 1000 µg / mL concentration. The solution was filtered using a filter paper. This solution was taken with a pipette of 1

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mL, then reacted with 1 mL of 1 N sulphuric acid solution, and 3 ml of 1% starch solution, and 1 mL of 0.1% potassium iodate solution, and then added distilled water until the limit mark up to 25 mL. This solution was sonicated for about 10 minutes. Then the absorbance and area under the curve were measured at a wavelength of 600.5 nm with a UV-Vis spectrophotometer. The experiment was repeated 3 replications. Captopril levels in tablets were determined by linear regression equation (Ahmed, 2013).

2.2.5 Validation of Analysis Methods

2.2.5.1 Linearity Test

Linearity test is done from measurement data of calibration curve, then analysed with linear regression so that obtained correlation coefficient (r) which shows its linearity. The good linearity value is $0.999 \leq r \leq 1$ (Rohman, 2016).

2.2.5.2 Limit of detection (LOD) and limit of quantitation (LOQ)

The limits of the detection and limits of quantization are determined by the regression of the standard curve obtained. The value of LOD = 3.3 (SD / S) and LOQ = 10 (SD / S). The standard deviation (SD) response is determined based on the standard deviation of the linear regression value of y = a + bx (Rohman, 2016).

2.2.5.3 Accuracy test

The accuracy test is carried out by the retrieval test by the "spiking" method by adding a standard amount of captopril solution into a test solution which is known from the added standard solution concentration of 80%, 100%, and 120%. Each is done 3 repetitions. Then the computed raw material recovery values were added to the test solution expressed by per cent recovery. Validate methods are eligible if the recovery show values in the range 80% to 120% (Rohman, 2016).

2.2.5.4 Precision test

The precision test was performed at the repeatability level by measuring the standard captopril solution concentration at 40 µg / mL, 50 µg / mL, and 60 µg / mL at 3 different times of the day (intraday) with 6 repetitions each. Measurement of standard captopril solution with the same concentration on 3 consecutive days (interday) was done by repeating each of 6 times. The relative standard deviation (RSD) values are between 1 and 2% (Rohman, 2016).

2.2.6 Data analysis

2.2.6.1 Determination of Content

Captopril levels in tablets were determined by linear regression equation y = a + bx.

$$a = \frac{\Sigma y - b\Sigma x}{n} \qquad b = \frac{n\sum xy - \sum x.\sum y}{n\sum x^2 - (\sum x)^2}$$

Notes:

y = absorbance or area under the curve

x = concentration (µg / mL)

a = intercept (the intersection point on the y-axis)

b = slope (slope)

2.2.6.2 Linearity of the standard curve

The purpose of linearity is to know how well the calibration curve connects between response (y) and concentration (x). Linearity is determined based on the correlation coefficient value (r) of the regression equation y = a + bx.

2.2.6.3 Limit of detection (LOD) and limit of quantitation (LOQ)

The purpose of determining the detection limit is to know the smallest amount of analyte that can still be detected but not necessarily measurable and the purpose of determining the quantitative limit is to know the smallest amount of analyte that can still be accurately measured (Rohman, 2016).

2.2.6.4 Accuracy

The purpose of determining accuracy is to know that the analytical method has a degree of proximity to the analysis results with the actual levels of analytes. Accuracy is measured as the number of recovered analytes.

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$$\% \text{ recovery} = \frac{CF-CA}{C*A} \text{ x } 100\ \%$$

Notes:
CF = total concentration of the sample obtained from the measurement
CA = actual sample concentration
C*A = concentration of analyte added
Validation methods are eligible if per cent recovery shows a range of 80% to 120% (Rohman, 2016).
2.2.6.5 Precision
The purpose of the precision test is to know the proximity of the analysis if done by the same analyst with different time. Precision is expressed by a percentage of relative standard deviation (RSD) or per cent coefficient of variation.

$$RSD = \frac{SD}{\bar{x}} x100\%$$

Relative standard deviation (RSD) is valid if the RSD value is between 1 - 2% (Rohman, 2016).

3. Results and Discussion

3.1 Determination of maximum wavelength captopril

In this study, the solvent used to determine the maximum wavelength is distilled water. In addition, three kinds of reagents are used, including 1 N sulphuric acid solution, 1% starch solution, and 0.1% potassium iodate solution. This reagent when reacted with standard pure composite captopril solution will result in a strong blue colour. This reagent is used to detect visible absorption within a maximum wavelength range of 400 to 800 nm by using a UV-Vis spectrophotometer. The obtained results show maximum absorption wavelength at 600.50 nm with an absorbance of 0.536. This wavelength is close to that obtained by Ahmed (2013) (Figure 2).

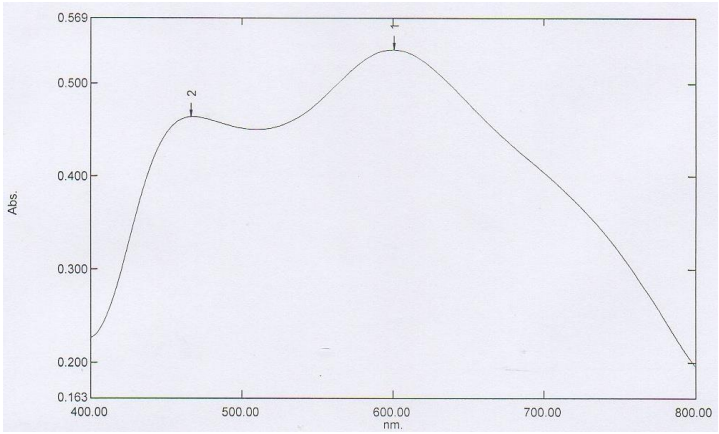

Figure 2: The pure captopril absorption spectrum (concentration 40 µg / mL) in distilled water with the addition of 1 ml of 1 N sulfuric acid and 3 mL of 1% starch solution, and 1 mL of a 0.1% potassium iodate solution

Based on the results of a study conducted by testing a comparable standard pure captopril solution in distilled water by the addition of 1 ml of 1 N sulphuric acid solution and 3 ml of 1% starch solution, and 1 mL of 0.1% potassium iodate solution showed that the mixture was well soluble in distilled water form a strong blue solution. The blue colour solution is caused by the captopril having a thiol group (-SH) in the structure. Captopril reduces potassium iodate to potassium iodide, and then is oxidized to disulphide. Potassium iodide is immediately reacted with excess potassium iodate to produce iodine form which is then reacted with starch to form blue iodine-blue compound (Ahmed, 2013). The study shows that the absorption wavelength of 600,50 nm with the absorbance of 0.536 in accordance with the Indonesian Pharmacopoeia and absorbance has a value in the range between 0.2 to 0.8 (Rohman, 2016).

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3.2 Preparation of the calibration curve

In preparing the calibration curve the standard solution of captopril was prepared by making series of standard solutions at concentrations of 20, 30, 40, 50, and 60 µg / mL using a distilled water solvent, and reacted with 1 ml of 1 N sulphuric acid solution and 3 mL of solution 1% starch, and 1 mL of 0.1% potassium iodate solution. The solutions were measured the absorbance and area under the curve at maximum wavelength by using a UV-Vis spectrophotometer.

The data of standard captopril calibration curve with absorbance method is shown in Table 1 and with area under the curve method is showed in Table 2. On the measurement obtained absorbance 0.322, 0.428, 0.53, 0.627 and 0.726 with linear regression equation is y = 0.0101x + 0.124 and correlation coefficient (r) 0.9998 (Figure 3). On the measurement of the area under the curve obtained the area of 7.469, 9.569, 11.499, 13.489 and 15.192, respectively, with the linear regression equation y = 0.1937x + 3.6972 and the correlation coefficient (r) 0.9994 (Figure 4).

Table 1: Data on the calibration curve of standard captopril in distilled water by the addition of 1 mL of 1 N sulphuric acid solution, and 3 mL of 1% starch solution, and 1 mL of 0.1% potassium iodate solution with absorbance method

Concentration of captopril (µg/mL)	Absorbance
20	0.322
30	0.428
40	0.531
50	0.627
60	0.726

Table 2: Data on the calibration curve of standard captopril in distilled water by the addition of 1 ml of 1 N sulphuric acid solution, and 3 mL of 1% starch solution and 1 mL of 0.1% potassium iodate solution by method of area under the curve

Concentration of captopril (µg/mL)	Area under the curve
20	7.469
30	9.569
40	11.499
50	13.489
60	15.192

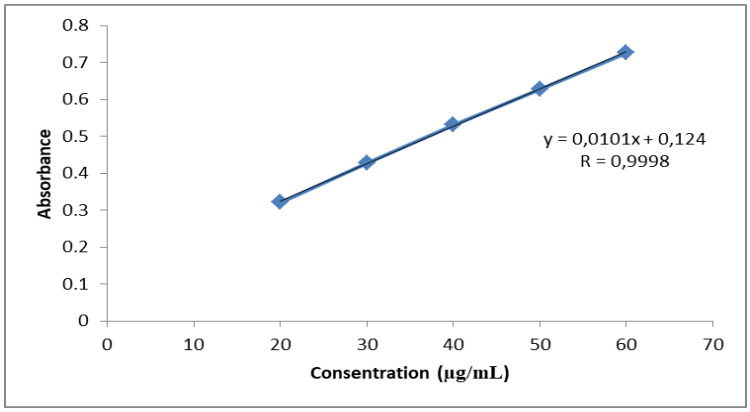

Figure 3: Standard captopril calibration curve in distilled water by addition of 1 ml of 1 N sulfuric acid solution, and 3 ml of 1% starch solution, and 1 mL of 0.1% potassium iodate solution by absorbance method

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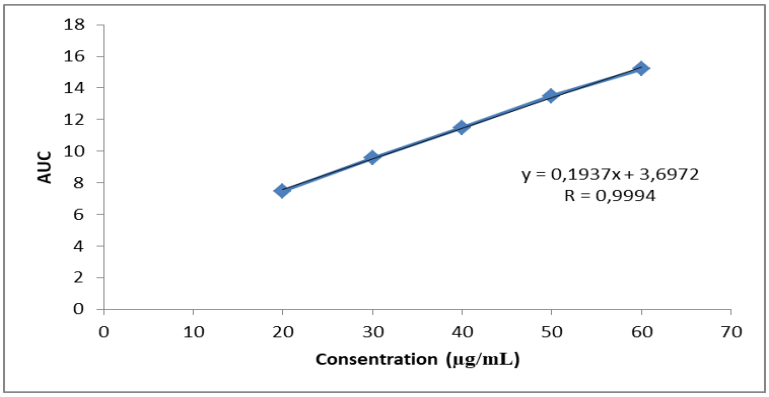

Figure 4: Standard captopril calibration curve in distilled water with addition of 1 ml of 1 N sulfuric acid solution, and 3 ml of 1% starch solution, and 1 mL of 0.1% potassium iodate solution by method of area under the curve

3.3 Determination of captopril concentration in tablets

The results of the determination of captopril content in the patent tablet of Farmoten® 25 mg (PT Pratapa Nirmala) showed 104.55% with standard deviation 0.433% (Table 3), whereas with area under the curve method showed the level of 92.22% with standard deviation 0.351% (Table 4). Meanwhile, in the determination of captopril content in generic tablets of Captopril 25 mg (PT Kimia Farma) was obtained 93.42% with standard deviation 1.306% with absorbance method (Table 5), whereas with method of the area under the curve obtained 91.09 % with standard deviation 0.093% (Table 6). So captopril levels in both patent and generic tablets have met the requirements in accordance with Pharmacopoeia Indonesia edition V that is 90% to 110% (Kementerian Kesehatan, 2014).

Table 3: Captopril levels in patent tablets with absorbance method

No.	Absorbance	Concentration (µg/mL)	Amount (mg) in the sample solution	Level (%) in tablets
1	0.549	42.02	52.525	105.05
2	0.546	41.72	52.150	104.30
3	0.546	41.72	52.150	104.30
Average			52.275	104.55
SD				0.433

Table 4: Captopril levels in patent tablets with area under the curve method

No.	Area under the curve	Concentration (µg/mL)	Amount (mg) in the sample solution	Level (%) in tablets
1	10.868	37.02	46.275	92.55
2	10.845	36.90	46.125	92.25
3	10.813	36.74	45.925	91.85
Average			46.108	92.22
SD				0.351

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Table 5: Captopril levels in generic tablets with absorbance method

No.	Absorbance	Concentration (µg/mL)	Amount (mg) in the sample solution	Level (%) in tablets
1	0,508	37.96	47.450	94.90
2	0,500	37.17	46.463	92.93
3	0,498	36,.97	46.213	92.43
Average			46.709	93.42
SD				1.306

Table 6: Captopril levels in generic tablets with area under the curve methods

No.	Area under the curve	Concentration (µg/mL)	Amount (mg) in the sample solution	Level (%) in tablets
1	10.759	36.46	45.575	91.15
2	10.757	36.45	45.563	91.13
3	10.746	36.39	45.488	90.98
Average			45.542	91.09
SD				0.093

3.4 Validation of Analysis Method

3.4.1 Linearity

From the result of preparation of calibration curve connecting concentration with absorbance and concentration with area under the curve is determined its linearity. The purpose of linearity is to know how well the calibration curve connects between response (y) and concentration (x). Linearity with absorbance method obtained correlation coefficient (r) is 0.9998 and linearity with the method area under the curve obtained correlation coefficient (r) is 0.9994. But from the two correlation coefficients, the correlation coefficient between concentration and absorbance method has a value that is more in line with the literature which states the acceptance criterion is the correlation coefficient value (r) close to 1 ($0.999 \leq r \leq 1$) (Rohman, 2016).

3.4.2 Limit of detection and limit of quantitation

Determination of detection limits and quantitation limits are parameters of sensitivity. The purpose of determining the detection limit is to know the smallest amount of analyte that can still be detected, but not necessarily can be measured. While the purpose of determining the limit of quantitation is to determine the smallest amount of analyte that can still be measured accurately (Rohman, 2016). The limits of the detection and limits of the quantities obtained from the absorbance method are 1.16336 µg / mL and 3.52532 µg / mL, respectively. While the limits of the detection and limits of the quantities obtained from the wide area methods under the curve were 2.08691 µg / mL and 6.32397 µg / mL, respectively.

3.4.3 Accuracy

Accuracy testing is to know that the analytical method has a degree of proximity to the analysis results with the actual levels of analytes. This test uses addition method by adding a number of analyte with a certain concentration on the sample being examined. Per cent recovery is determined by determining what percentage of the analyte you have added can be found. The percentage of added analyte is 80%, 100%, and 120%. From result of captopril recovery test in patent tablet with absorbance method obtained per cent recovery that is 112.19%, 88.95% and 85.71%, respectively; average 95.62% and standard deviation 14.444%. The wide area method under the curve shows a recovery per cent of 118.47%, 99.49% and 86.69%, respectively; averaging 101.55% and standard deviation of 15.989%. Meanwhile, from captopril recovery test results in generic tablets with absorbance method obtained per cent recovery of 111.77%, 86.03% and 88.19%, respectively; average 95.33% and standard deviation 14.278%. The area wide method under the curve shows a recovery percentage of 117.22%, 99.67% and 85.99%, respectively; average 100.96% and standard deviation 15.655%. Both

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methods are within the allowed range of between 80% and 120% (Rohman, 2016). Thus, based on the results of research that has been obtained shows that the tablets patent and tablet generic captopril have met the accuracy test.

3.4.4 Precision

The determination of intraday precision of captopril was performed at morning, noon and afternoon with three different concentrations. Patent captopril tablet sample with absorbance method at 40 µg / mL concentration showed RSD of 0.25%, 0.14% and 0.25%, respectively. Concentrations of 50 µg / mL showed RSD of 0.55%, 0.56% and 0.59%, respectively. Concentrations of 60 µg / mL showed RSD by 0.41%, 0.25% and 0.17%, respectively. Methods of area under the curve at a concentration of 40 µg / mL showed RSD of 0.46%, 0.07% and 0.08%, respectively. The concentration of 50 µg / mL showed RSD of 0.03%, 0.18% and 0.03%, respectively. Concentrations of 60 µg / mL showed RSD by 0.04%, 0.02% and 0.67%, respectively. Meanwhile, samples of generic captopril tablets with absorbance method at concentrations of 40 µg / mL showed RSD of 0.25%, 0.48% and 0.38%, respectively. The concentration of 50 µg / mL showed RSD by 0.20%, 0.19% and 0.50%, respectively. Concentrations of 60 µg / mL showed RSD of 0.16%, 0.25% and 0.26%, respectively. Methods of area under the curve at a concentration of 40 µg / mL showed RSD 0.08%; 0.46% and 0.07%. The concentration of 50 µg / mL obtained RSD is 0.03%; 0.18% and 0.03%. The concentration of 60 µg / mL obtained RSD is 0.67%; 0.04% and 0.02%

The determination of captopril interday precision was performed for 3 days with three different concentrations. In patent tablet captopril samples with absorbance method, the first, second, and third day at concentrations of 40 µg / mL showed RSD of 0.38%, 0.25% and 0.25%, respectively. Concentrations of 50 µg / mL on the first, second, and third day showed RSD of 0.31%, 0.59% and 0.56%, respectively. Concentrations of 60 µg / mL on the first, second, and third day showed RSD by 0.26%, 0.16% and 0.25%, respectively. Methods of the area under the curve on the first, second, and third day at concentrations of 40 µg / mL showed RSD of 0.24%, 0.07% and 0.09%, respectively. The concentration of 50 µg / mL on the first, second, and third day showed RSD by 0.03%, 0.18% and 0.67%, respectively. The 60 µg / mL concentrations on the first, second, and third day showed RSD of 0.67%, 0.04% and 0.04%, respectively. Meanwhile, samples of generic captopril tablets with absorbance method, day one, second, and third with concentration of 40 µg / mL showed RSD of 0.48%, 0.38% and 0.25%, respectively. The concentration of 50 µg / mL on the first, second, and third day showed RSD of 0.50%, 0.20% and 0.19%, respectively. Concentrations of 60 µg / mL on the first, second, and third day showed RSD of 0.17%, 0.26% and 0.25%, respectively. Methods of area under the curve on the first, second, and third day at concentrations of 40 µg / mL showed RSD by 0.07%, 0.09% and 0.24%, respectively. The concentration of 50 µg / mL on the first, second, and third day showed RSD by 0.03%, 0.03% and 0.18%, respectively. Concentrations of 60 µg / mL on the first, second, and third day showed RSD by 0.04%, 0.67% and 0.04%, respectively.

Precision testing is to know the proximity of the analysis results when done by the same analyst with different time. The results of the research obtained RSD less than 5% then it can be said that this method has a good value of repetition. The precision criterion is given if the method provides a relative standard deviation or a 2% or less variation coefficient. However, this criterion is very flexible depending on the concentration of the analyte examined, the number of samples, and the laboratory conditions. At a 1% or more analytical level, the relative standard deviation between laboratories is about 2.5% and at one per thousand is 5%. At the analytical level of one per million (ppm), RSD is 16% and at the part-per-billion (ppb), the RSD is 32%. In a very critical method it is generally accepted that RSD should be more than 2% (Rohman, 2016). Based on a series of measurements obtained from repeated sampling of the same homogeneous sample, the results of a study of patent and generic tablets of captopril have met the precision test requirements.

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4. Conclusion

Based on the research that has been done can be concluded as follows:

1. The absorbance method and the area under the curve indicate that both methods are valid methods for captopril analysis in tablets.
2. The absorbance method and the area under the curve by the validated spectrophotometry can be used for the determination of captopril content in tablets, i.e. 104.55% for patent tablets and 94.98% for generic tablets with absorbance method; 92.22% for patent tablet and 91.15% for generic tablet with method of area under the curve.
3. Captopril levels in patent tablets and generic tablets studied meet the requirements of Pharmacopoeia Indonesia edition V 2014 with captopril tablet levels listed between 90 to 110%.

Conflict of Interests

The authors declare that no conflict of interest is associated with this work.

References

[1] Ahmed, N. R. (2013). Indirect spectrophotometric determination of captopril in pharmaceutical tablets and spiked environmental samples. *Iraqi National Journal of Chemistry*, *49*, 1-11.
[2] Albero, M. I., Sánchez-Petreño, C., Garcia, M. S., & Ródenas, V. (1993). Determination of captopril in pharmaceutical samples by flow injection analysis. *Journal of pharmaceutical and biomedical analysis*, *11*(10), 887-891.
[3] Asra. R., Rivai, H., & Riani, V.L. (2016). Pengembangan dan Validasi Metode Analisis Tablet Furosemid dengan Metode Absorbansi dan Luas Daerah di Bawah Kurva secara Spektrofotometri Ultraviolet. *Jurnal Farmasi Higea*, *8*(2), 110-121.
[4] Chandra, B., Rivai, H., & Apriansyah, E. (2017). Pengembangan dan Validasi Metode Analisis Propranolol Hidroklorida Tablet dengan Metode Absorbansi dan Luas Daerah di Bawah Kurva secara Spektrofotometri Ultraviolet. *Jurnal Farmasi Higea*, *9*(1), 20-29.
[5] Chandra, B., Rivai, H., & Marianis, M. (2016). Pengembangan dan Validasi Metode Analisis Ranitidin Hidroklorida Tablet dengan Metode Absorbansi dan Luas Daerah di Bawah Kurva secara Spektrofotometri Ultraviolet. *Jurnal Farmasi Higea*, *8*(2), 96-109.
[6] Chandru, H., & Sharada, A. C. (2007). Simple and rapid methods for the analysis of captopril in dosage forms. *Journal of Chemistry*, *4*(2), 216-221.
[7] Ivanovic, D., Medenica, M., Malenovic, A., & Jancic, B. (2004). Validation of the RP–HPLC method for analysis of hydrochlorothiazide and captopril in tablets. *Accreditation and quality assurance*, *9*(1-2), 76-81.
[8] Kementerian Kesehatan, R. I. (2014). Farmakope Indonesia Edisi V. Jakarta: Kementerian Kesehatan Republik Indonesia, 601-603.
[9] Liliya, L., Dmytro, K., Olena, S., Ihor, B., & Tamara, K., (2016). Development of Methodology for Identification of Captopril in Medicines. *Asian Journal of Pharmaceutics*, *10*(3), 168-171.
[10] Mohamed, M. E., Aboul-enein, H. Y., & Gad-kariem, E. A. (1983). Potentiometric and visual titrimetric methods for analysis of captopril and its pharmaceutical forms. *Analytical Letters*, *16*(1), 45-55.
[11] Rahman, N., Anwar, N., Kashif, M., & Hoda, N. (2006). A sensitive kinetic spectrophotometric method for the determination of captopril in bulk and dosage forms. *Acta pharmaceutica*, *56*(3), 347-357.
[12] Ribeiro, P. D. S., Santini, A. O., Pezza, H. R., & Pezza, L. (2003). Potentiometric determination of captopril in pharmaceutical formulations. *Eclética Química*, *28*(1), 39-44.
[13] Rivai, H., Hasanah, R., & Azizah, Z. (2018). Development and Validation of Omeprazole Analysis Methods in Capsules with Absorbance Methods and Areas under Curves Methods with UV-Vis Spectrophotometry. *International Journal of Pharmaceutical Sciences and Medicine (IJPSM)*. *3*(3), 21-32.
[14] Rivai, H., Astuty, W., & Asra, R. (2017a). Pengembangan dan Validasi Metode Analisis Betametason dalam Tablet dengan Metode Absorbansi dan Luas Daerah di Bawah Kurva Secara Spektrofotometri Ultraviolet. *Jurnal Sains dan Teknologi Farmasi*, *19*(Supl1), s52-s57.
[15] Rivai, H., Larasaky, M., & Azizah, Z. (2017b). Pengembangan dan Validasi Metode Analisis Klorfeniramin Maleat Dalam Tablet dengan Metode Absorbansi dan Luas Daerah di Bawah Kurva Secara Spektrofotometri Ultraviolet. *Jurnal Sains dan Teknologi Farmasi*, *19*(Supl1), s58-s63.
[16] Rivai, H., Pratama, N., & Asra, R. (2017c). Development and Validation of Bisacodyl Analysis Method in Tablet with Absorbance Method and Area under Curves Method in Ultraviolet Spectrophotometry. *International Journal of Pharmaceutical Sciences and Medicine (IJPSM)*, *2*(12), 1-8.
[17] Rohman, A. (2016). Validasi dan Penjaminan Mutu Metode Analisis Kimia, Cetakan Kedua, Yogyakarta: Gadjah Mada University Press.
[18] Trevor, A.J., Katzung, B.G., & Kruidering-Hall, M. (2015), Katzung & Trevor's Pharmacology Examination & Board Review, 11th Edition, New York: Lange McGraw-Hill Education, 97.

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