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Research Article

SPECTROPHOTOMETRIC VALIDATION METHOD OF DEXCHLORPHENIRAMINE MALEAT AND BETAMETHASONE

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ABSTRACT

This paper have a purpose to determine the condition of analysis of betamethasone and dexchlorpheniramine maleat on tablet using ultraviolet spectrophotometry and high perfomance liquid chromatography (HPLC) methods. The spectrophotometry method used phosphate buffer pH 7,2 as the solvent, whereas the HPLC method used HPLC, LC-10AT VP, Shimadzu;μ BondapakTM C18 10μm 125Å, 4,6 x 150 mm coloumn Waters (Irlandia); methanol buffer (45:55) pH 7,2 as mobile phase; ultraviolet detection 240 nm; flow rate 1 mL/menit. Result showed that the correlation coefficient of spectrophotometry were 0,9998 and 0,9997 for dexchlorpheniramine maleat dan betamethasone at wavelength 239 and 262. The LOD for spectrophotometry were 2,261 ppm for dexchlorpheniramine maleat at λ 239 ; 0,707 ppm for dexchlorpheniramine maleat at λ 262 ; 0,088 ppm for betamethasone at λ 239 ; dan 0,127 for betamethasone at λ 262, the LOQ were 7,536 ppm for dexchlorpheniramine maleat at λ 239 ; 2,357 ppm for dexchlorpheniramine maleat at λ 262 ; 0,295 for betamethasone at λ 239 ; dan 0,425 for betamethasone at λ 262. The recovery percentation of the spectrophotometry methods for dexchlorpheniramine maleat and betamethasone were 101,32% and 100,77%. The recovery percentation of the HPLC methods for dexchlorpheniramine maleat and betamethasone were 107,6% and 100,8%. Coefficient of variance of the spectrophotometry methods methods for dexchlorpheniramine maleat and betamethasone were 1,413 % and 0,466 %, coeffisien of variance of the robustness test of the spectrophotometry methods for dexchlorpheniramine maleat and betamethasone were 0,834 % and 1,140 %. Based on this research has been found that the the analysis method of spectrophotometry was eligible for the validation parameter value. These data may be applied in Pharmaceutical industries.

Keywords: Dexchlorpheniramine maleat, Betamethasone, Spectrophotometry, Validation Method.

INTRODUCTION

To get the effective usefulness and the complement, a supply of medicine is occasionally made in the form of the mixture. Meaning that, in one supply of medicine is gotten more than one active substance. One of the examples of the supply of medicine that has the shape of the mixture is the tablet betamethason and dexchlorpheniramine maleat (Daru, 2013). This tablet has the effect antiinflammation and light analgetic. This effect is received from the work betamethason in hindered fosfolipase that resulted in the barrier towards the synthesis prostaglandin and leukotrien. Dexchlorpheniramine maleat works hinder the receptor histamin H1 so as to give the hindered effect to the reaction of the allergy (de Ruiter, 2001; Tjay and Rahardja, 2003).

Beside the difficulty in determining the formulation, the problem in the production of the mixed product often emerged when determining the analysis method of the valid and effective supply. Daru (2013) mentioned the diffulties in analyzing the betamethason and dexchlorpheniramine maleat in pharmaceutical industry. One of the methods for the analysis of the effective mixture and popular at this time is the HPLC method and spectrophotometry. HPLC is the analysis method that is accompanied by the separation of the mixed compound that had the achievement and sensitivity

that was high. Generally, HPLC is used for the separation of several organic compounds, inorganic and the biological compound; the Impurities analysis; the determination of neutral molecules, ionic and zwitter ion; as well as the separation of fine compounds (trace elements), in a large number, and the scale of the process of the industry. HPLC is the not destructive method and could be used is good for the qualitative analysis and the quantitative analysis.

Betamethasone has the aromatic ring that contains carbonil that is the cluster chromophore that give the absorption against the rays of UV whereas dexchlorpheniramine maleat contained the ring benzen and piridin that also is the cluster chromophore (Farmakope Indonesia, 1994). With the existence of these clusters chromophore, then the compound betamethasone and dexchlorpheniramine maleat could be analysed by using the method spectroscopy UV-Vis and HPLC with the UV Detector.

In the analysis used the HPLC method often was encountered by the problem take the form of unrealistic results of the analysis. This was often caused by the method inaccuracy and instrument that was used. By that, the influence of the other compound in the mixture also had the big contribution in the analysis mistake. A synthetic medicine company had the problem in the determination of the analysis method that was exact for the product of the mixed tablet betamethasone and dexchlorophenіramine maleat. The problem that emerged was the level of dexchlorpheniramine maleat always was on 140 %. This was really unrealistic because tolerance for the deviation for the analysis used the HPLC method only 3 %. In other words, the level of dexchlorpheniramine maleat that was obtained necessarily might not exceed 103 %.

Unrealistic results of the analysis of using the HPLC method could be caused by various matters, among them the mistake and the determination mistake of the method of the instrument choosen. The instrument held the important role towards the analysis. The difference of the use of the instrument will give results of the different analysis. The method election also was the determining factor in the success of the analysis. This method included the condition regulation for the analysis as well as the standard election. The biggest challenge in carrying out the analysis used HPLC and spectroscopy UV was the appropriate standard election. Vignaduzzo SE and Kaufman TS (2013), however found that HPLC in good validation results in their reseach on determination of bromohexine, chlorpeniramine, paracetamol, and pseudoephedrine in their combined cole medicine formulations. Actually, Hood DJ and Cheung HY (2003) has analyzed codeine phosphate, ephedrine HCl and chlorpheniramine maleate in cough-cold syrup formulation by HPLC. Hugest DE (1998) used reversed-phase, pairedion and competing-base high-performance liquid chromatography in simultaneous determination of phenylephrine hydrochloride, chlorpheniramine maleate and sodium benzoate. Marin et al (2002) validated of a HPLC quantification of acetaminophen, phenylephrine and chlorpheniramine in pharmaceutical formulations: capsules and sachets.

Donato et al (2012) used HPLC coupled to electrospray ionization tandem mass spectrometry to simultaneous determine dextromethorphan, dextrorphan and doxylamine in human plasma.

Unlike in the HPLC area, not so many publications spectrophotometrically on betamethasone and dexachlorpheniramine maleat. Viana et al (2005) has published derivative ultraviolet spectrophotometric determination of dexchlorpheniramine maleate in tablets in presence of coloring agents. Weldesenbet (2008) in his thesis studied Chemometrics-Assisted UV-Spectrophotometric determination of betamethasone and dexchlorpheniramine maleate in laboratory prepared mixtures and combined tablet forms was based on this background, we were interested researching the cause of the occurrence of this mistake at the same time looking for the optimum condition for the analysis method of the tablet betamethasone and dexchlorpheniramine maleat.

Experimental

Instruments

The instrument used in this study were: UV spectrophotometer, UV-1700 Pharmaspec, Shimadzu, KCKT, LC-10AT VP, Shimadzu, column: µ bondapakTM C18 10 µm 125 ´, µm paper whatman 0:45, 0:45 µm filter syring, ultrasonic, analytical balance, pumpkin measuring, Volume pipettes.

The determination of the condition for the analysis with spectrophotometry

a. The production of the spectrum of the absorption dexchlorpheniramine maleat

Weighed totalling 60 mg dexchlorpheniramine maleat. Put in the gourd measured 10 of mL. Add methanol. Ultrasonic for 15 minutes. Add methanol until the sign of the limit, shook homogeneous. Then pipet totalling 1 mL and was diluted in the gourd 25 mL so as to be received the solution with the concentration 96 ppm. The spectrum of the absorption was received by means of plotting absorbances the solution against wavelengths. Then was determined the maximum wavelength.

b. The production of the spectrum of the absorption betamethasone

Weighed totalling 37.5 mg betamethason. Put in the gourd measured 50 of mL. Add methanol. Ultrasonic for 15 minutes. Add methanol until the sign of the limit, shook homogeneous. Then pipet totalling 200 µL and was diluted in the gourd 25 mL so as to be received the solution with the concentration 12 ppm. The spectrum of the absorption was received by means of plotting absorbance the solution against wavelength. Then was determined the maximum wavelength.

c. The search for the dexchlorpheniramine maleat and betamethasone absorbances of each respectively

By means of like in the production of the spectrum of the absorption, was made by seven concentration variations dexchloropheniramine maleat and betamethason, respectively of 33.68; 38.48; 43.12; 48.24; 53.04; 57.60; 62,48 ppm to dexchloropheniramine maleat and 4.240; 4.800; 5.400; 6.000; 6.608; 7.216; 7,808 ppm to betamethasone. Absorbance the solution was measured by each one totalling one time in long the wave 239 and 262. The absorbency dexchloropheniramine maleat and betamethasone in the wavelengths 239 and 262 were counted with the formula.

d. The linearity test

By Means Of like in the production of the spectrum of the absorption, was made by seven concentration variations dexchloropheniramine maleat and betamethasone, respectively of 33.68; 38.48; 43.12; 48.24; 53.04; 57.60; 62,48 ppm to dexchloropheniramine maleat and 4.240; 4.800; 5.400; 6.000; 6.608; 7.216; 7,808 ppm to betamethasone. Absorbance the solution was measured by each one totalling one time in the wavelengths 239 and 262, then was counted the correlation coefficient r in the equality of linear regression of $Y = ax + b$.

e. The accuracy test

Was made by nine concentration variations dexchloropheniramine maleat and betamethasone of 38.48; 38.64; 38.72; 48.32; 48.48; 48.32; 58.00; 58.32; 58,08 ppm to dexchloropheniramine maleat and 4.896; 4.864; 4.832; 6.048; 6.016; 6.048; 7.216; 7.104; 7,200 ppm to betamethasone. Absorbance the solution was measured by each one totalling one time, then was counted by their mean recovery.

f. Precision Test

Made seven variations dexchloropheniramine maleat concentration and betamethasone in ppm. Absorbance solution measured each one-time, and then calculated the value of its VC.

g. Robustness

Seven solvents used for precision tests stored for 24 hours, then the solution was measured absorbance each a one-time, and then calculated the value of its VC.

h. Detection (LOD) and Quantity limit (LOQ)

Based on the standard deviation ratio (SB) of the absorption and the slope (a) The standard curve linearity test data, LOD and LOQ can be calculated mathematically by the equation:

Detection Limit (Xd)

Quantity Limit (Xk)

Determination of the analysis conditions HPLC

a. Mobile Phase

Solution of potassium dihydrogen phosphate, 0.02 M, Solution of sodium hydroxide 0.2 M, Phosphate buffer pH 7.2, Moblile phase of methanol-buffer (45:55)

b. Instrument Preparation

HPLC column washed with methanol elution way that was filtered first. Elution process conducted for ± 1 hour. Then the column washed with aqua bidestillata (pro HPLC) for ± 30 minutes. After a washing step, the column was conditioned with methanol and phosphate buffer (45:55) for ± 20 minutes, conducted base line.

c. Test preparation solution

Standard solution dexchloropheniramine maleate, Standard solution betamethasone, other solutions.was done by creating a concentration of 50 ppm, where the active substance and excipients were weighed according to the concentration of substances that would be made.

RESULTS AND DISCUSSION

1. UV-Vis Spectrophotomety

Spectrum making

The method used in making spectra of analysis of dexchloropheniramine maleate and betamethasone tablet was simultaneous spectrum analyisis in which each components was measured and analysis in two different maximum wavelengths.

Determination of analysis conditions

After spectrum making was done, analysis conditions was then set up. One of the conditions factor was solvent. Due to the fact that dexchloropheniramine maleate and betamethasone had different polarities, in which the dexchloropheniramine maleate as a salt easily solved in water whereas betamethasone unsolved. Methanol was then chosen as a solvent..As betamethason difficult to fully solve in methanol, an ultrasonic was apllied for 15 minutes. As far as posible to fulfill Lambert-Beer law, range absorbances had to be in the range of 0.2 – 0.8 and for this purpose, a concentration of 48 ppm and 6 ppm of respectively dexchloropheniramine maleate and betamethasone were used.

After preparation was done, measurement was carried out. It was found that absorbance of simple was always higher then simple standard. It was thought that exipient may contribute to this result. To correct this, a correlation factor was made by using 7 measurements for the same concentration, but absorbance of exipient was negatif indicating that absorbance of metanol higher than exipient. This also indicated that there was other factors influenced the high measurement.

To prove this hypothetic that there was unsoluble material influences to this high absorbances, all samples were then filtered and measured. But the result still unaccepted. We conclude that metanol was not the right solvent for this analysis purposes due to its evaporation characteristic and other unknow factors.

Further steps was taken by changing the solvent with buffer phosphate pH. 7.2. There were three reasons : (a) To lower basecorr or zero point of solvent absorbance in order to avoid negative absorbance of exipient. (b) To stabilize the active components of dexchloropheniramine maleate and betamethasone. (c) To avoid evaporation of solvent during filtration and centrifugation. This buffer was applied to active component, mixture, as well as exipient. The result showed that absorbance of test sample was higher then sample standard but the diffrence accepted to correction factor of exipient. This prove that buffer phosphat pH. 7.2 suited for this study.

Validation of Analysis Method

Validation of analysis method was carried out in order to prove that chosen analysis method would fulfill the user needs including consistency and quantity required. Validation proceduce included linearity, accuracy, precision, roburtsness, as well as detection and qantification limits.

Linearity test proved its llinerity between absorbance vs concentration showed by correlation coefficient of standard curve. Standard curve was made by concentrations range of 33.68 – 62.48 ppm and 4.24 – 7.808 ppm of dexcholorpheniramine maleate and betamethasone, respectively, and measured each λ 239 dan λ 262. Correlation coefficient was found 0,9998 for dexcholoropheniramine maleate at λ 239, and 0,9997 at λ 262, whereas 0,9998 for betamethasone at λ 239 and 0,9997 at λ 262 (see data on attachment I). Attachment IV showed complete calculation of detection limit and quantity limit using standard curve equations for both dichloropheniramine maleate and betamethasone.

Accuracy test was determined with recovery test (UPK) by comparing directly to standard. It was used 9 concentarions of standard samples in which three first variations had closed concentrations (about 38 ppm for dexchloropheniramine maleat and 4, 8 ppm for betamethason), also the second three variation concentrations (about 48 ppm for dexchloropheniramine maleate and 6 ppm for betamethasone), and last three groups concentrations (about 58 ppm for dexchloropheniramine maleate and 7,2 ppm for betamethasone).

Precison test was made by measuring 7 same and close concentrations, i.e about 48 ppm for dexchloropheniramine maleate and 6 ppm for betamethasone. Based on these reults, it was found good degree of recovery with the variation below 2 %.

Robustness test carried out by measuring 7 standard concentrations for Precision test which had been stored for 24 hours. This test to see how strong was the analysis method

against storage. From 7 concentrations, the recovery gave variation coefficeint below 2 %.

From the validity test the following results were obtained.

1. Linearity Test

1. Dexchloropheniramine maleat (D.M.)at λ = 239 nm

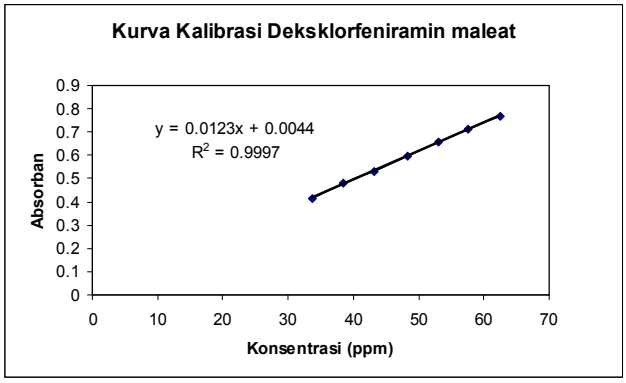

Fig.1. D.M. standard curve at λ = 239

2. Dexchloropheniramine maleat at λ = 262 nm

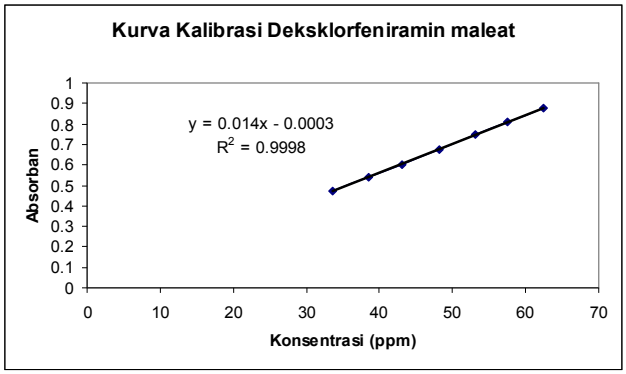

Fig.2. D.M. standard curve at λ = 262 nm

3. Betamethason at λ = 239 nm

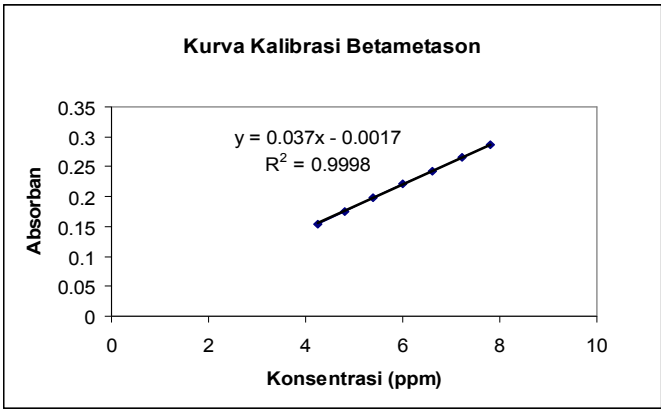

Fig.3 Betamethason standard curve at λ = 239 nm

4. Betamethason at λ = 262 nm

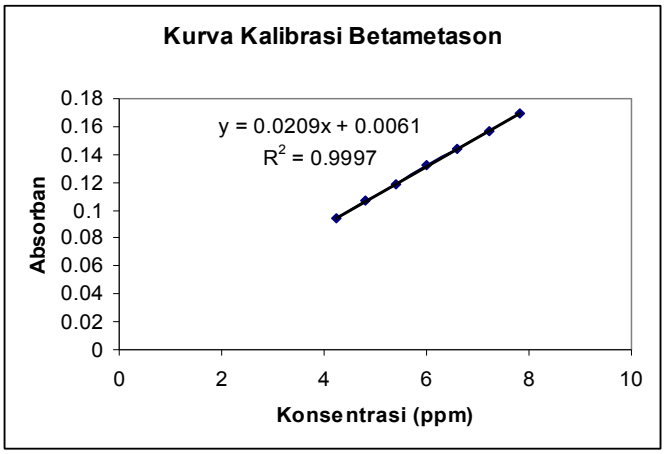

Fig.4 Betametason standard curve at λ = 262 nm

Kurva kalibrasi = calibration curve,

konsentrasi = concentrations

2. Accuracy Test

Table .1 Results of Accuracy Test

No	Concentration(st) (ppm)		Absorbance (239)	Absorbance (262)	Concent. (S) (ppm)		% UPK	
	Dex.	Beta.			Dex.	Beta.	Dex.	Beta.
1	38,48	4,896	0,658	0,639	39,16	4,963	101,82	101,36
2	38,64	4,864	0,663	0,652	39,43	4,936	102,04	101,48
3	38,72	4,832	0,666	0,655	38,91	4,921	100,49	101,84
4	48,32	6,048	0,828	0,815	48,44	6,202	100,25	102,54
5	48,48	6,016	0,816	0,808	49,33	6,108	101,75	101,52
6	48,32	6,048	0,813	0,804	49,22	6.064	101,86	100,26
7	58,00	7,216	0,977	0,963	58,27	7,221	100,46	100,06
8	58,32	7,104	0,976	0,960	59,04	7,070	101,23	99,52
9	58,08	7,200	0,979	0,963	59,23	7,084	101,98	98,39
Total							911,88	906,97
Mean							101,32	100,77

3. Precision Test

Table L.10 Results of Precission Test

No	Concentration(st) (ppm)		Absorbance (239)	Absorbance (262)	Concent. (test) (ppm)		% UPK	
	Dex.	Beta.			Dex.	Beta.	Dex.	Beta.
1	48,08	6,000	0,823	0,810	48,53	6,09	100,93	101,50
2	47,92	6,016	0,831	0,813	48,93	6,13	102,04	102,24
3	48,08	6,032	0,826	0,810	48,46	6,14	100,79	101,79
4	47,92	6,000	0,829	0,813	48,65	6,16	101,52	102,66
5	47,92	6,000	0,824	0,810	47,27	6,16	98,66	102,66
6	48,00	6,032	0,818	0,807	47,32	6,14	98,58	101,79
7	48,32	6,016	0,822	0,812	47,63	6,17	99,17	102,55
Total							701,69	715,19
Mean							100,24	102,17
Standard deviation							1.417	0.477
Variance Coefficient							1,413 %	0,466 %

4. Robutsness Test

Table L.11 Results of *Robustnes Tests*

No	Concentration(st) (ppm)		Absorbance (239)	Absorbance (262)	Concent. (test)) (ppm)		% UPK	
	deks	Beta			deks	beta	deks	beta
1	48,08	6,000	0,824	0,812	48,02	6,041	99,88	100,64
2	47,92	6,016	0,829	0,817	48,45	6,080	101,10	101,09
3	48,08	6,032	0,827	0,810	47,65	6,111	99,11	101,38
4	47,92	6,000	0,825	0,814	48,12	6,061	100,42	101,15
5	47,92	6,000	0,822	0,810	47,48	6,090	99,09	101,64
6	48,00	6,032	0,819	0,810	48,18	5,931	100,39	98,31
7	48,32	6,016	0,824	0,814	48,84	6,013	101,09	99,95
Total							701,08	704,16
Mean							100,15	100,59
Standard Deviation							0.836	1.147
Variance Coefficient							0,834 %	1,140 %

5. LOD dan LOQ

1. Dexchloropheniramine maleat at λ 239 nm

Table L.12 Calculation results of calculated LOD and LOQ tests

No	Concentration (ppm)	Absorb. (y_i)	Absorb. ($\hat{y}_i$)	$(y_i - \hat{y}_i)^2$
1	33,68	0,416	0,409	0,000049
2	38,48	0,478	0,468	0,000100
3	43,12	0,532	0,526	0,000036
4	48,24	0,595	0,589	0,000036
5	53,04	0,659	0,648	0,000121
6	57,60	0,710	0,704	0,000036
7	62,48	0,769	0,764	0,000025
Σ				**0.000403**

$Y = 0.0123x + 0.0044$

$a = 0,0123$

$$S_{y/x} = \left[\frac{0,000403}{7-2}\right]^{\frac{1}{2}} = 0,00927$$

$$X_d = \frac{3 \times 0,00927}{0,0123} = 2,261 \text{ ppm}$$

$$X_k = \frac{10 \times 0,00927}{0,0123} = 7,536 \text{ ppm}$$

2. Dexchloropheniramine maleat at λ 262 nm

Table L.13 Results of Calculted LOD dan LOQ test

No	Concentration (ppm)	Absorb. (y_i)	Absorb. ($\hat{y}_i$)	$(y_i - \hat{y}_i)^2$
1	33,68	0,472	0,471	0,000001
2	38,48	0,542	0,539	0,000009
3	43,12	0,603	0,604	0,000001
4	48,24	0,675	0,675	0,000000
5	53,04	0,748	0,742	0,000036
6	57,60	0,808	0,806	0,000004
7	62,48	0,876	0,874	0,000004
Σ				0,000055

$Y = 0.014x - 0.0003$ $\quad a = 0.014$ $\quad S_{y/x} = \left[\frac{0,000055}{7-2}\right]^{\frac{1}{2}} = 0,0033$ $\quad X_d = \frac{3 \times 0,0033}{0,014} = 0,707 \text{ ppm}$

$$X_k = \frac{10 \times 0,0033}{0,014} = 2,357 \text{ ppm}$$

3. Betamethason at λ 239 nm

Table L.14 Results of Calculated LOD dan LOQ test

No	Concentration (ppm)	Absorb. (y_i)	Absorb. ($\hat{y}_i$)	$(y_i - \hat{y}_i)^2$
1	4,240	0,154	0,155	0,000001
2	4,800	0,176	0,175	0,000001
3	5,400	0,198	0,199	0,000001
4	6,000	0,221	0,220	0,000001
5	6,608	0,243	0,242	0,000001
6	7,216	0,265	0,265	0,000000
7	7,808	0,286	0,287	0,000001
Σ				0,000006

Y = 0.037x - 0.0017 a = 0.037

$$S_{y/x} = \left[\frac{0,000006}{7-2}\right]^{\frac{1}{2}} = 0,00109$$

$$X_d = \frac{3 \times 0,00109}{0,037} = 0,088 \text{ ppm}$$

$$X_k = \frac{10 \times 0,00109}{0,037} = 0,295 \text{ ppm}$$

4. Betamethason at λ 262 nm

Table L.15 Results of Calculted LOD dan LOQ test

No	Concentration (ppm)	Absorb. (y_i)	Absorb. ($\hat{y}_i$)	$(y_i - \hat{y}_i)^2$
1	4,240	0,094	0,095	0,000001
2	4,800	0,107	0,106	0,000001
3	5,400	0,119	0,119	0,000000
4	6,000	0,132	0,131	0,000001
5	6,608	0,144	0,144	0,000000
6	7,216	0,157	0,156	0,000001
7	7,808	0,169	0,169	0,000000
Σ				0,000004

Y = 0.0209x + 0.0061

a = 0,0209

$$S_{y/x} = \left[\frac{0,000004}{7-2}\right]^{\frac{1}{2}} = 0,00089$$

$$X_d = \frac{3 \times 0,00089}{0,0209} = 0,127 \text{ ppm}$$

$$X_k = \frac{10 \times 0,00089}{0,0209} = 0,425 \text{ ppm}$$

6. Absorbtivity

For dexchloropheniramine maleat at λ = 239 nm, found as a means : 0,012358 and at λ = 262 nm, found as a means : 0,014032436, wherea for Betamethason at λ = 239 nm, found as a mean : 0,036642974 and at λ = 262 nm, found as a mean : 0.021955989

2. High Performance Liquid Chromatography

Preparation Conditions

In the analysis using instruments HPLC, determined some working parameters such as mobile phase, static phase, injection volume, detector, flow rate, and solvent. The parameters used as reference in this research is Indonesian Pharmacopoeia IV edition in 1995. In this literature the selected parameters are parameters for betamethasone. The column used was bondapak C18 column. Selected mobile phase was a mixture of water - acetonitrile in the ratio 63: 37. However, previous research had found the ratio of water: acetonitrile 80: 20 for the tablet mixture dexchloropheniramine maleate and betamethasone. Flow rate used 1 mL / min and the solvent for methanol sample. HPLC analysis performed by UV spectrometer by setting detector at λ 240.

At the beginning of the study, conducted orientation using parameters such as the above work. The result, obtained by the two peak (peak) chromatogram good enough. However dexchloropheniramine maleate area test higher than the standard area up to 140%. Allegations that came up was the top chromatogram is the peak dexchloropheniramine maleate other substances. To prove it, made modifications mobile phase compositions. With the mobile phase of water: acetonitrile ratio of 60: 40 obtained three peaks on the chromatogram of 2 minutes, 2.5 and 4.5 minutes. Peak at 2.5 min was much smaller than the other two peaks that summed up as the top polluter. To find a substance that has a peak, each injected substance and solvent. Obtained results proved that the peak was the property of the solvent. So that the allegations that emerged was the peak of the solvent affect the peak dexchloropheniramine maleate. So the search phase compositions that can separate the motion of the peak chromatogram dexchloropheniramine maleate and solvent. Mobile phase composition obtained was water: acetonitrile 50: 50.

But the test area remained too high and the precision obtained area was not good. There was the possibility of the solvent methanol was still exert influence. So to eliminate the influence of the solvent methanol, on further analysis, the solvent used was changed into a mobile phase. The result area to be more stable but the value remains too high. In the next step was a change in the wavelength of the first detector 240 becomes 254. But do not give any significant change. So the remaining possibility was to mobile phase. On further analysis, the mobile phase that was used was methanol - phosphate buffer pH 7.2 the ratio 70: 30 and the solvent methanol. Mobile phase was chosen because the mobile phase containing solvent used was methanol which was expected to reduce the influence of the solvent. Optimun mobile phase compositions found in the methanol: phosphate buffer pH 7.2 the ratio 55: 45. However, the test area produced dexchloropheniramine maleate still higher but only about 106%. So that the above conditions was the most optimum conditions found in this study. Percent recovery test was obtained for 106% dexchloropheniramine maleate and 102% for betamethasone.

CONCLUSIONS

The recovery percentation of the spectrophotometry methods for dexchlorpheniramine maleat and betamethasone were 101,32% and 100,77%. The recovery percentation of the HPLC methods for dexchlorpheniramine maleat and betamethasone were 107,6% and 100,8%. Coefficient of variance of the spectrophotometry methods for dexchlorpheniramine maleat and betamethasone were 1,413 % and 0,466 %, coeffisien of variance of the robustness test of the the HPLC methods for dexchlorpheniramine maleat and betamethasone were 0,834 % and 1,140 %, respectively. Based on this research has been found that the analysis method of spectrophotometry was eligible for the validation parameter value. These data may be applied to Pharmaceutical industries.

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