World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 5.008

ANTIBIOTIC DRUG QUALITY EVALUATION: DETERMINATION OF CEFADROXIL USED IN TREATMENT IN THE CASE OF RESISTANCE AT TASIKMALAYA CITY HEALTH CENTER, INDONESIA

Danni Ramdhani*, Wiwiek Indriyati and Muhammad Aiman

Department of Pharmaceutical Analysis and Medicinal Chemistry, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia 45363.

***Corresponding Author:** Danni Ramdhani
Department of Pharmaceutical Analysis and Medicinal Chemistry, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia 45363.

Article Received on 08/12/2018 **Article Revised on 29/12/2018** **Article Accepted on 20/01/2019**

ABSTRACT

Objective: Cefadroxil is one of the choices of antibiotics used in the management of Acute Respiratory Infection (ARIs) disease treatment. The good quality of antibiotics greatly determines the effectiveness and success in therapy. The level of an antibiotic is one of the quality parameters that must meet the requirements stated in the United State Pharmacopeia (USP). ***Methods:*** The cefadroxil antibiotic used in the treatment of ARIs was obtained from the health center of the City of Tasikmalaya. The determination of cefadroxil was carried out using HPLC instruments, using validation parameters linearity, precision, accuracy, limit of detection (LOD) and limit of quantification (LOQ). ***Results:*** The test results showed that the levels of levofloxacin antibiotics that are used to meet the requirements that exist in the United State Pharmacopeia grading 107.58 %, and the validation parameters that meet the requirements, correlation coefficient of 0.9999, recovery percent of 99.67 %, precision 0.06 %, LOD 0.5013 µg/mL and LOQ 1.519 µg/mL. ***Conclusions:*** The test results showed that the levels of cefadroxil antibiotics that are used to meet the requirements that exist in the United State Pharmacopeia (USP).

KEYWORDS: Acute respiratory infections, cefadroxil, resistance of antibiotics, validation parameters.

INTRODUCTION

Cefadroxil is one of the choices of antibiotics used in the management of ARIs disease treatment. ARIs in Indonesia are still a serious problem and cause 28% mortality in children. Inappropriate use of antibiotics will cause many bacteria to become resistant to antibiotics.[1]

The main bacteria that cause ARI include haemolyticus, Streptococcus, Staphylococcus, Pneumococcus, Haemophilus influenzae, Bordetella pertussis, Corynebacterium diphtheriae. The main bacteria that cause ARI include haemolyticus, Streptococcus, Staphylococcus, Pneumococcus, Haemophilus influenzae, Bordetella pertussis, Corynebacterium diphtheriae.[2] Treatment of respiratory diseases is usually administered with amoxicillin antibiotics, but cases of resistance have been reported to Streptococcus haemolyticus, Staphylococcus, and Corynebacterium diphtheriae.[3]

Cefadroxil is a broad spectrum antibiotic that acts against both Gram positive and Gram negative organisms, including Staphylococcus aureus, Proteus spp., Bacillus spp., Escherichia coli and more potent to Klebsiela spp. It is less sensitive to βlactamase produced by Staphylococcus aureus and Bacillus subtilis as compared to penicillins.[4]

This study aims to evaluate the quality of the antibiotic cefadroxil used in all health centers in the city of Tasikmalaya, whether it is in accordance with the requirements listed in the United State Pharmacopeia (USP).

MATERIALS AND METHODS

Materials tested were cefadroxil used in community health center in Tasikmalaya, monobasic potassium phosphate, potassium hydroxide, methanol, HCL p.a (PT. Merck Indonesia), aqua bidestilation (Ikapharmindo Putramas).

The tools used in this study is HPLC (Dionex Ultimate 3000) with Accalim Polar Advantage II column, UV detector, ultrasonic bath (NEY-1510), and glass tools commonly used in the Laboratory Analysis.

Method

The mobile phase consisted of methanol: phosphate buffer of pH 4.0at ratio of 10:90 and filtered before use through 0.45µ membrane filter and was pumped at a flow

rate of 1.5ml/min. The separation was carried out on a C18 column at a temperature maintained at 25ºC. The sample of 20µl was injected and analyzed under isocratic conditions. Chromatograms were recorded at λ = 260 nm.

Preparation of cefadroxil reference standard solution
Standard solution of cefadroxil monohydrate was prepared by dissolving 25mg of reference standard of cefadroxil in 25ml of mobile phase. The resulting concentration was 1mg/ml or 1000µg/ml. This solution was further diluted as required for calibration and linearity.[4]

Preparation of sample solutions from tablets
A total of 20 tablets of 200mg cefadroxil were carefully weighed, triturated with the help of mortar and pestle to get a fine powder and the amount of powder equivalent to 200mg of cefadroxil was transferred to a 200ml volumetric flask. It was dissolved in the buffer pH 4.0 by shaking for about 15min. The final concentration of sample solution was kept equivalent to 1mg/ml or 1000µg/ml.[4]

Validation procedure
Present study was conducted to obtain an innovative, simple, rapid and affordable method for the determination of cefadroxil. The HPLC method development and validation was performed according to the official specifications of Centre of Drug Evaluation and Research (CDER-1994), International Conference on Harmonization and United State Pharmacopeias. The method validation parameters included system suitability, linearity, specificity, accuracy, limit of detection, limit of quantification, precision.[5]

Accuracy
Accuracy was best determined by the standard addition method. Previously analyzed samples of Amoxicillin API were added with standard drug solutions and are analyzed by the proposed method. Recovery (%), RSD (%) and correlation coefficient, limit of detection (LOD), limit of quantification (LOQ) were calculated for each concentration. Accuracy is reported as percentage bias, which is calculated from the expression.[6]

$$\% \text{ Bias} = \frac{\text{Measured value - True value}}{\text{True value}} \times 100$$

Precision
System precision: Standard solution prepared as per test method and injected six times and the % RSD value was calculated. Method precision: Six preparations individually using single batch of Amoxicillin drug substance were prepared as per test method and injected each solution induplicate on the same day in to HPLC. % RSD value was calculated to determine intra-day precision.

Limit of Detection (LOD)
The Limit of Detection (LOD) of an analytical method may be defined as the concentration, which gives rise to an instrument signal that is significantly different from the blank. For spectroscopic techniques or other methods that rely upon a calibration curve for quantitative measurements, the IUPAC approach employs the standard deviation of the intercept (Sa), which may be related to LOD and the slope of the calibration curve.[5]

$$LOD = 3\ Sa / b$$

Limit of Quantitation (LOQ)
The LOQ is the concentration that can be quantitated reliably with a specified level of accuracy and precision. The LOQ represent the concentration of analyte that would yield a signal-to-noise ratio of 10.

$$LOQ = 10\ Sa / b$$

Where, Sa is the standard deviation of the peak area ratio of analyte to IS (6 injections) of the drugs and b is slope of the corresponding calibration curve.[6]

RESULTS AND DISCUSSIONS

Linearity Test
Linearity test is done with a series of standard solutions which consist of at least four different concentrations in the range of 50-150% of the content of the analyte in the sample. The concentration used in the assay was 10 ppm; 20 ppm; 40 ppm; 60 ppm; 80 ppm; and 100 ppm.

The calibration curve showed good linearity in the range of 0.6 - 3.4 µg/ml, for Cefadroxil (API) with correlation coefficient (r2) of 0.9993. The slope and intercept of the calibration graph was calculated by using linear regression analysis. The regression equation of the calibration curve was: y = 0.4234x + 0.2594; r2 = 0.9999. A correlation coefficient suggests that the developed HPLC method had an excellent linearity over the investigated range. Correlation coefficient meets the requirements is greater than 0.99 (5). The results for linearity are shown in Figure 1.

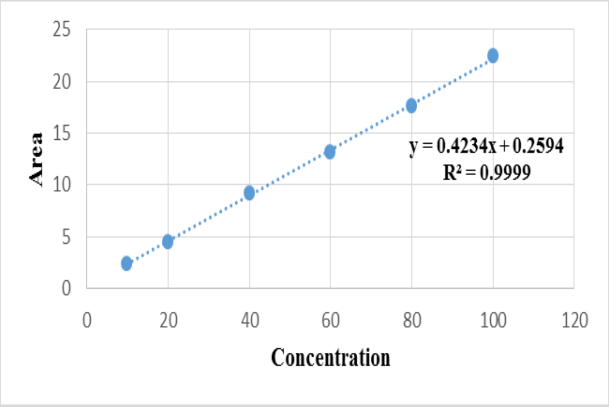

Figure 1: Calibration Curve for Cefadroxil.

Accuracy Test

Accuracy indicates the degree of closeness of the results of a series of measurements obtained from a homogeneous sample under specified conditions.[5] Accuracy expressed as a percent recovery (recovery) the analyte is added. Testing is done by six different of concentration are 10 ppm; 20 ppm; 40 ppm; 60 ppm; 80 ppm; and 100 ppm. The average value of recovery% is 99.67 %. This result is acceptable because it is still within the required range 80 - 110%.[8]

Precision Test

Precision is a measurement repeatability of analytical methods derived from multiple measurements on the same sample. Precision is measured as the standard deviation or relative standard deviation (coefficient of variation).[5] Precision test criteria can be distinguished as follows:

Table 1: Criteria of precision test.

% RSD	Criteria
< 1	very precise
1 – 2	Precise
2 – 5	Midle
> 5	Not pricise

System precision Aceptance criteria: RSD for area should not be more than 1%. The intra & inter day variation of the method was carried out and the high values of mean assay and low values of standard deviation and % RSD (% RSD < 2%). The RSD percentage of 0.64 % indicates that this method has a high degree of accuracy for sample testing.[5]

LOD and LOQ Test

The limit of detection is the smallest amount of analyte in a sample that can be detected which still provides significant response compared to the blank and the test parameters limits. Values obtained detection limit is 0.5013 µg/mL. Quantification limit is a parameter on the analysis of trace and is defined as the smallest quantity of analyte in the sample were still able to meet the criteria of a careful and thorough. Values obtained quantification limit was 1.519 µg/mL %).

Assays Cefadroxil

Determination of amoxicillin antibiotic sample level was done by HPLC method. Levels of antibiotic amoxicillin samples obtained from the calculation of 104.95 %. The results of amoxicillin level measurement meet the requirements listed in USP that is 90% -110%.[9]

CONCLUTION

Levels of antibiotic amoxicilllin used in Tasikmalaya City Health Center is 107.58 %. sResults are still within the range required by the USP 97% -120%.[9]

ACKNOWLEDGMENTS

The authors are deeply grateful to the subjects participating in this study. The author would like to thank Tasikmalaya City Health Office. The author also thanked Muhammad Aiman for its cooperation in this study.

REFERENCES

1. West Java Provincial Health Office. Profile of West Java Provincial Health Office. 2003. Bandung: West Java Provincial Health Office, 2003.
2. Ministry of Health RI., Guidelines for the Control of Acute Respiratory Disease. Jakarta: Ministry of Health RI, 2002.
3. Southwick, S.F. Infectious Diseases In 30 Days. USA: Mc Graw-Hill Companies Inc., 2003.
4. Parasrampuria J and Gupta VD, Quantitation of cefadroxil in pharmaceutical dosage forms using highperformance liquid chromatography. Drug Dev Ind Pharm, 1990; 16(8): 1435-1440.
5. ICH, Validation of analytical procedures. Methodology harmonized tripartiate guideline prepared within the international conference on harmonization of technical requirements for the registration of pharmaceuticals for human use. ICH-Q2B: Geneva, 1996.
6. Ermer, J., Method Validation in Pharmaceutical Analysis. Weinheim: Wiley-VCH Verlag GmbH & Co. KgaA, 2005.
7. McMaster, M.C, HPLC A Practical User's Guide, Edisi ke II, New Jersey: John Wiley and Sons Inc, 2007.
8. Harmita., Implementation Guidance Validation Method and Method Calculation. Pharmaceutical Science Magazine, December 2004; I(3): 117-135.
9. The United State Pharmacopeial Convention, *The United States Pharmacopoeia (USP)*. 37th Edition. United States: US Pharmacopeial Convention Inc, 2014; 79-82.