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EVALUATION OF CIPROFLOXACIN QUALITY IN ANTIBIOTIC RESISTANCE CASES OF ACUTE RESPIRATORY INFECTION (ARIS) IN TASIKMALAYA CITY HEALTH CENTER, INDONESIA

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ABSTRACT

Objective: ARIs is a disease of the upper and lower respiratory tract and is usually contagious and can cause various spectrums of disease. Monitoring of the quality of antibiotics is done to determine the effectiveness of the desired therapy. This study aims to determine the levels of ciprofloxacin antibiotics used in ARIs treatment. **Methods:** The ciprofloxacin drug sample used in this test was obtained from the health center of the city of Tasikmalaya. Testing the levels of ciprofloxacin antibiotics was carried out using HPLC systems, using validation parameters linearity, precision, accuracy, limit of detection (LOD) and limit of quantification (LOQ). **Results:** The test results obtained ciprofloxacin antibiotic levels 103.51%. These results indicate that the levels of ciprofloxacin antibiotics used meet the United State Pharmacopeia requirements. The test results showed that the levels of ciprofloxacin antibiotics that are used to meet the requirements that exist in the United State Pharmacopeia grading 103.51 %, and the validation parameters that meet the requirements, correlation coefficient of 0.9941, recovery percent of 93.19%, precision 0.0105%, LOD 6.97 µg/mL and LOQ 21.11 µg/mL. **Conclusions:** The test results showed that the levels of ciprofloxacin antibiotics that are used to meet the requirements that exist in the United State Pharmacopeia (USP).

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

INTRODUCTION

ARIs can be caused by viruses or bacteria that enter the human respiratory system. The cause consists of more than 300 types of bacteria, viruses and rickets. The bacteria that cause ARI include the genera Streptococcus, Staphylococcus, Pneumococcus, Hemophilus, Bordetella and Corynebacterium. The viruses that cause ARI include the Mikovirus, Adenovirus, Coronavirus, Pikornavirus, Mycoplasma, Herpesvirus and others.[1]

Based on the results of the basic health research in the province of West Java, the prevalence of ISPA in the city of Tasikmalaya occupies a position. ARI is a deadly infectious disease if not treated immediately. Therefore, prevention and control of ARI is one of the main priorities in health development in the Tasikmalaya region.[2]

Ciprofloxacin is one of the antibiotics recommended for treating ARIs, but several cases of resistance to this antibiotic have been reported. The use of antibiotics is rationally interpreted as giving antibiotics that are the right indication, the right patient, the right medicine, and being aware of antibiotic side effects.[3] In addition, the quality of antibiotics used also plays a role in the successful treatment of ARIs.

This study aims to determine the quality of ciprofloxacin antibiotics used in treating ARIs. Levels or concentrations of ciprofloxacin antibiotics play an important role in killing or inhibiting the growth of bacteria that cause ARIs.

MATERIALS AND METHODS

Materials tested were Ciprofloxacin used in community health center in Tasikmalaya, potassium dihydrogen phosphate, acetonitrile, glacial acetic acid was obtained (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 a mixture of 2% acetic acid aqueous solution and ACN (84:16, v/v). The flow rate was set at 1.0 mL/min and injection volume at 10 µL.[5]

Stock and working solutions: Stock solutions of ciprofloxacin were prepared at 5.18 mM in 2% acetic acid aqueous solution for pharmaceutical, respectively.[5]

Assay of Ciprofloxacin: Content uniformity determination of the tablet and injection was done as described in the following. Five ciprofloxacin tablets, two of each brand, were ground into powder and mixed well. The powder, containing approximately 50 mg ciprofloxacin, was measured. It was dissolved and diluted with mobile phase to a ciprofloxacin solution (approximately 8 µg/mL). The ciprofloxacin injection labeled concentration (2 mg/mL) was diluted by mobile phase to a ciprofloxacin solution (8 µg/mL). The previously mentioned ciprofloxacin solution (150 µL) was also mixed well with 154 µM IS solution 150 µL. The mixture solution (200 µL) was collected and analyzed by HPLC.[5]

Method Validation: The method was validated in accordance with ICH guidelines. The parameters assessed were linearity, accuracy, and precision, reproducibility, robustness and system suitability.[6]

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]

$$\% \text{ Bias} = \frac{(\text{measured value} - \text{true value})}{\text{true value}} \times 100$$

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.

$$LOD = 3\ Sa / b$$

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.

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. (Riyanto, 2014). 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 Ciprofloxacin (API) with correlation coefficient (r2) of 0.9941. The slope and intercept of the calibration graph was calculated by using linear regression analysis. The regression equation of the calibration curve was: y = 0.0005x + 0.0011. 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.[6] The results for linearity are shown in Figure 1.

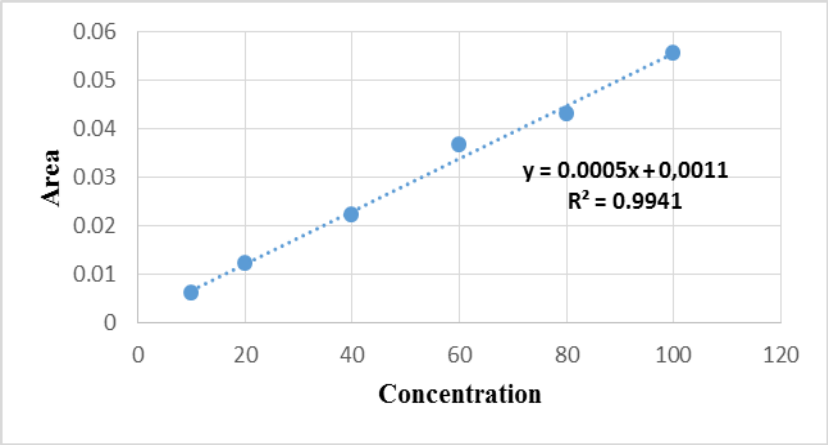

Figure. 1. Calibration Curve for Ciprofloxacin.

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 93.19 %. 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).(6) 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 0.01 % indicates that this method has a high degree of accuracy for sample testing.[6]

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 0.082 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 0.251 µg/mL.

Assays of Ciprofloxacin: Determination of ciprofloxacin antibiotic sample level was done by HPLC method. Levels of antibiotic ciprofloxacin 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 103.51%. Results are still within the range required by the USP 97% -120%.[9]

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