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Original Article

# FORMULATION A CIPROFLOXACIN HYDROCHLORIDE EXTENDED-RELEASE TABLET WITH COMBINATION OF HYDROXYPROPYL METHYLCELLULOSE (HPMC) K100M AND HYDROXYPROPYL METHYLCELLULOSE (HPMC) K4M BY DIRECT COMPRESSION METHOD

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**ABSTRACT**

**Objective:** Ciprofloxacin hydrochloride tablets which are not extended-release will produce non-constant drug levels in the blood. This study aimed to overcome this problem by making ciprofloxacin hydrochloride extended-release tablets with a combination of hydroxypropyl methylcellulose (HPMC) K100M and hydroxypropyl methylcellulose (HPMC) K4M by a direct compression method.

**Methods:** The method in this study consisted of preformulation, formula design, manufacture of ciprofloxacin hydrochloride tablets, tablet print mass testing, IPC (In-Process Control) slow-release tablet mass print, IPC (In-Process Control) quality of slow-release tablet preparation, dissolution test, and statistical analysis. Preformulation was carried out aiming to determine the physical and chemical properties of active-excipient substances based on a certificate of analysis. This was done using a Fourier Transform Infrared (FT-IR) and UV-Vis spectrophotometer. Five kinds of ciprofloxacin hydrochloride tablet formulations were made using the direct pressing method with variations in the concentration of HPMC K100M and HPMC K4M. The ratio of percentage of HPMC K100M and HPMC K4M were F1 0,5%: 1%, F2 1%: 0,5%, F3 0,75%: 0,75%, F4 1%: 0%, F5 0%: 3%. Evaluation of tablet preparations (IPC control) included weight uniformity test, size uniformity test, hardness test, and friability test. The dissolution test was carried out for 2 h by hydrochloride acid 0,1 N pH 1.2 as (pH of gastric acid). Statistical analysis using Perfect Block Random Design (PBRD) method and further testing using the Newman-Keuls test was applied for the data obtained.

**Results:** The test results with FTIR showed that ciprofloxacin hydrochloride used compared to ciprofloxacin hydrochloride BPFI is equivalent and has a purity index of 0.992739. Determination of the level of the active ingredient ciprofloxacin hydrochloride was carried out by measuring the absorbance of a 5 ppm sample solution at a wavelength of 276 nm. The percentage of absorbance of the solution is then calculated and the result obtained is 98.87%. The range of levels that have been set is 98%-102%. These test results were under those listed on the certificate of analysis. The results of the IPC test in the form of weight uniformity test, size uniformity test, hardness test, friability test, and uniformity of ciprofloxacin hydrochloride levels in the preparation, showed all data obtained fulfilling the requirements set by USP 36 convention (2013). The result from dissolution tablet test on 30, 60, and 120 min showed the release of active substance on F1 56.00 %, 67.76 %, and 87.57 %. F2 were 53.42 %, 65.16 %, and 91.44 %. F3 were 59.18 %, 72.15 %, and 91.20 %. F4 were 50.51 %, 70.70 %, and 95.29 %. F5 were 53.75 %, 69.55 %, and 92.05 %. Statistical analysis was applied for the data obtained. Dissolution results illustrated the level of active substances dissolved in the dissolution medium for 2 h or in other words the dissolution test results indicated the number of active substances from tablets that were released and enter the digestive tract and came in contact with body fluids.

**Conclusion:** The dissolution test results as a basis of extended-release tablets showed all of the formulae met dissolution requirements of the United States Pharmacopeia (USP) 36 convention.

**Keywords:** Ciprofloxacin hydrochloride, Extended-release, Direct compression, In process control, Dissolution test


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## INTRODUCTION

The drug will affect if the drug level in the blood is between the minimum effective concentration (MEC) and below the minimum toxic concentration (MTC). Medicines given orally are usually given three times a day or even more than three times a day to get the concentration of drugs in the blood always between MEC and MTC so that the effectiveness of the drug takes place continuously. Conventional preparations can produce levels of active substances in the blood is not constant because it is generally absorbed quickly. Non-constant absorption causes the concentration of drugs in the blood to decrease. This has an impact on decreased drug effectiveness and bacterial resistance so that therapeutic goals are not achieved [1, 2].

Ciprofloxacin hydrochloride is a quinolone antibiotic. About 70% of ciprofloxacin hydrochloride is absorbed through the gastrointestinal tract. This drug has a fairly short half-life of 3-4 h. Ciprofloxacin has an average start of about 0.5-1 hour and the time to reach peak concentration is 1-2 h [3, 4].

The resistance of anaerobic bacteria to certain classes of antibiotics is increasing globally trending vary by geographic region and often vary between species [5]. The sensitivity of *pseudomonas aeruginosa* to ciprofloxacin has been reported [6, 7]. Besides, there are also cases of resistance to gram-positive bacteria against ciprofloxacin including *staphylococcus aureus* and *corynebacterium sp* [8, 9]. Budayanti conducted a sensitivity test on 47 *neisseria gonorrhea* isolates taken from 13 eye isolates, from 10 urethra isolates and 24 cervix isolates against several antibiotics that are often used for gonorrhea. It was found that *n. gonorrhoeae* resistance to ciprofloxacin was 42% [10]. Resistance can be prevented by controlling drug release so that drug concentration in the blood is maintained [2]. The extended-release form is designed so that the use of a single dose unit presents the release of several drugs immediately after use. This preparation can precisely produce the desired therapeutic effect gradually and continuously in releasing many drugs over an extended period [11]. Extended-release tablets can be made using matrix technology. Hydrophilic matrices can release 100% active ingredients [12]. When in contact with water, the hydrophilic matrix immediately forms a gel layer around the tablet [13]. Hydrophilic matrix types include hydroxypropyl methylcellulose (HPMC) [14]. The HPMC matrix needs to be combined with other types of HPMC to facilitate drug release.

This study reports the formulation of a ciprofloxacin hydrochloride extended-release tablet with a combination of HPMC K100M and

HPMC K4M by direct compression method with statistical analysis. It was recognized that other researchers have reported using different matrices and did not use direct compression [15, 16].

## MATERIALS AND METHODS

### Materials

Ciprofloxacin hydrochloride (Merck), hydroxypropyl methylcellulose K100M (Sigma-Aldrich), hydroxypropyl methylcellulose K4M (Sigma-Aldrich), avicel pH102 (Sigma-Aldrich), aerosil (Sigma-Aldrich). All chemicals used for the formulation were pharmaceutical grade. Equipments: Tablet printing machine (E. Korsch), mesh sifter no. 10, 16, 20, 40, and 60 (Retsch), analytical scales (Mettler Toledo), calipers (Mitutoyo), hardness tester (Erweka type tb-24), powder flow tester, friability tester, type dissolution tool 2 (paddle) (SOTAX AG), UV-Vis spectrophotometer (SPEC ORD 200), Fourier transform infrared spectra (FT-IR) (IRAffinity-1S Shimadzu), syringes, and glassware commonly used at the solida preparation and technology laboratory and research laboratory, Faculty of Pharmacy, Universitas Padjadjaran.

### Methods

The method in this study consisted of preformulation, formula design, ciprofloxacin hydrochloride tablet making, tablet print mass testing, IPC (In-Process Control) slow-release tablet mass print, IPC (In-Process Control) quality of slow-release tablet preparation, dissolution test, and statistical analysis.

### For preformulation

Preformulation was carried out aiming to determine the physical and chemical properties of active-excipient substances based on a certificate of analysis.

Two types of equipment namely Fourier Transform Infrared (FT-IR), the standard method of using FT-IR for determination of the functional groups of ciprofloxacin [17, 18] and UV-Vis. Spectrophotometer to determine the level of ciprofloxacin was applied. The following method was applied for the UV-Vis spectrophotometer: The initial procedure that was carried out before the determination of the content was to find the maximum wavelength of ciprofloxacin hydrochloride, obtained max. 276 nm. A standard curve for ciprofloxacin hydrochloride was made. The standard curve for ciprofloxacin hydrochloride was made to obtain a linear regression equation. The linear regression equation was used to determine the determination of levels of active substances in the tablet. The 40 ppm standard solution is diluted into 6 concentrations, namely 2 ppm, 3 ppm, 4 ppm, 5 ppm, 6 ppm, and 7 ppm. Each standard solution was then measured at the same wavelength. Determination of the level of the active ingredient ciprofloxacin hydrochloride was carried out by measuring the absorbance of a 5 ppm sample solution at a wavelength of 276 nm. The percentage of absorbance of the solution is then calculated and the result obtained is 98.87%. The range of levels that have been set is 98%-102%. These test results were per those listed on the certificate of analysis. Another researcher, however, had used HPLC to determine of ciprofloxacin in human plasma and its application in bioequivalence test [19].

### Design formula

Five ciprofloxacin hydrochloride tablet formulations were made using the direct pressing method with variations of HPMC K100M and HPMC K4M. Table 1 shows the designed formula for extended released ciprofloxacin hydrochloride.

**Table 1: Designed formula extended released ciprofloxacin hydrochloride tablet**

| Compounds (%) | Formula | | | | |
|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 |
| Ciprofloxacin hydrochloride | 44.769 | 44.769 | 44.769 | 44.769 | 44.769 |
| HPMC K100M | 0.50 | 1.00 | 0.75 | 1.00 | - |
| HPMC K4M | 1.00 | 0.50 | 0.75 | - | 3.00 |
| Avicel pH102 | 52.73 | 52.73 | 52.73 | 53.23 | 51.23 |
| Mg stearate | 0.77 | 0.77 | 0.77 | 0.77 | 0.77 |
| Aerosil | 0.23 | 0.23 | 0.23 | 0.23 | 0.23 |

### Manufacture of extended-release ciprofloxacin hydrochloride tablets

In this study, a formulation of ciprofloxacin hydrochloride extended-release tablets were formulated. The active ingredient used was ciprofloxacin hydrochloride. Ciprofloxacin hydrochloride was used as a urinary tract infection drug with a dose of 291 mg per day. Additional substances used are microcrystalline cellulose (avicel pH102) which functions as a filler-binder, mg stearate as a lubricant, and aerosil as a lubricant. The matrix used in this formula as hydroxypropyl methylcellulose (HPMC) K100M and K4M. Comparison of the concentration of HPMC K100M and HPMC K4M used were F1 0.50%: 1.00%, F2 1.00%: 0.50%, and F3 0.75%: 0.75%. In F4 a single HPMC K100M was used at 1.00%, while in F5 a single HPMC K4M is used at 3.00%. Details of the composition of each formula can be seen in table 1.

Ciprofloxacin hydrochloride tablets were prepared using the direct pressing method of 200 tablets for each formula. Formula tablets were prepared as many as 5 formulas with each containing an active substance (ciprofloxacin hydrochloride) of 291 mg as well as variations in the concentration of HPMC K100M and HPMC K4M. The manufacturing process was utilizing all the ingredients of the tablets that were sifted and weighed according to the amount in each formula. Then ciprofloxacin hydrochloride was mixed with HPMC K100M and/or HPMC K4M, microcrystalline cellulose (avicel), and aerosil for 15 min. After that, magnesium stearate is added to the mixture and stirred for 1 minute. Then the print mass of the tablet was tested. Then punch and die were prepared which could print tablets weighing 650 mg and do tablet printing.

The matrix used could help slow down the release of active substances. Avicel pH102 was used as a filler, binder, and shredder in the manufacture of tablets. The filler was used to increase the mass of the tablet that would be printed when printing the tablet. Binder was used to helping the binding process of the outer and inner phases. Also, avicel functions as a crushing agent which helps to destroy the tablet so that it could increase the solubility of drugs in body fluids. Allowed use of avicel was as much as 20%-90%. The amount of avicel used in each formula was approximately 52%. Magnesium stearate was used as a lubricant. Lubricants could help increase the flow strength of the granules at the time of pressing so that the granules could spread throughout the casting so that no blockage occurred. Besides, the function of magnesium stearate was to prevent the tablet from adhering to the die and punch surface. The level of magnesium stearate allowed as a sliding agent was 0.25%-5%. The amount of magnesium stearate used in each formula was 0.77%. Aerosil was used as glidan. Glidan was used to reduce friction between particles flowing from the hopper to the printing chamber (die), thereby improving the flow properties of the powder or granule to be compressed and would affect the uniformity of the weight of the tablet. The amount of glidan allowed was no more than 3.00% of the total formula. The total aerosil in each formula used for printing this tablet was 0.23% [20-23].

### In-process control (IPC) print mass

The evaluation of the print mass of the tablet included a flow velocity and rest angle test, and a compressibility test.

**In-process control (IPC) print tablet**

Evaluation of tablet preparations included weight uniformity test, size uniformity test, hardness test, and friability test.

**Dissolution test**

The dissolution test used a modification of Fahmy and Abu-Gharbiehmethod [24]. A total of 8.4 ml of 0.1N HCl (37% w/v) was diluted with water up to 1000 ml. Dissolution media were made to resemble a stomach with a pH of 1.2. The dissolution test was carried out based on the USP 36 convention using type II equipment (paddle) on 0.1 N HCl media as much as 900 ml at 37±0.5 °C for 2 h. A total of 6 tablets from each formula were put in a container. The first step was to take 5 ml of aliquots at the 30$^{th}$, 60$^{th}$ and 120$^{th}$ minutes. Then 5 ml of HCl was put back in each container to replace the aliquots taken. This process was carried out for 2 h. Then the amount of dissolved ciprofloxacin hydrochloride was determined by measuring dissolved ciprofloxacin hydrochloride using UV spectrophotometry at a wavelength of 276 nm. Calculation of the results of the dissolution test is carried out using the formula:

$$\%dissolution = (Conc.of\ substance.900.100\% \div Weight\ of\ active\ substance\ on\ etiquete$$

**Statistic analysis**

Statistical analysis for the dissolution test was carried out using the perfect random block design (PRBD) method and further testing was done with the Newman-Keuls test.

**RESULTS AND DISCUSSION**

**Preformulation**

Preformulation was carried out to ensure the active substance used as ciprofloxacin hydrochloride following the requirements.

**Test with fourier transform infrared (FT-IR)**

Fourier transform infrared test was performed to confirm the functional groups contained in ciprofloxacin hydrochloride by comparing to ciprofloxacin hydrochloride BPFI and to see the purity index of ciprofloxacin hydrochloride used (fig. 1)

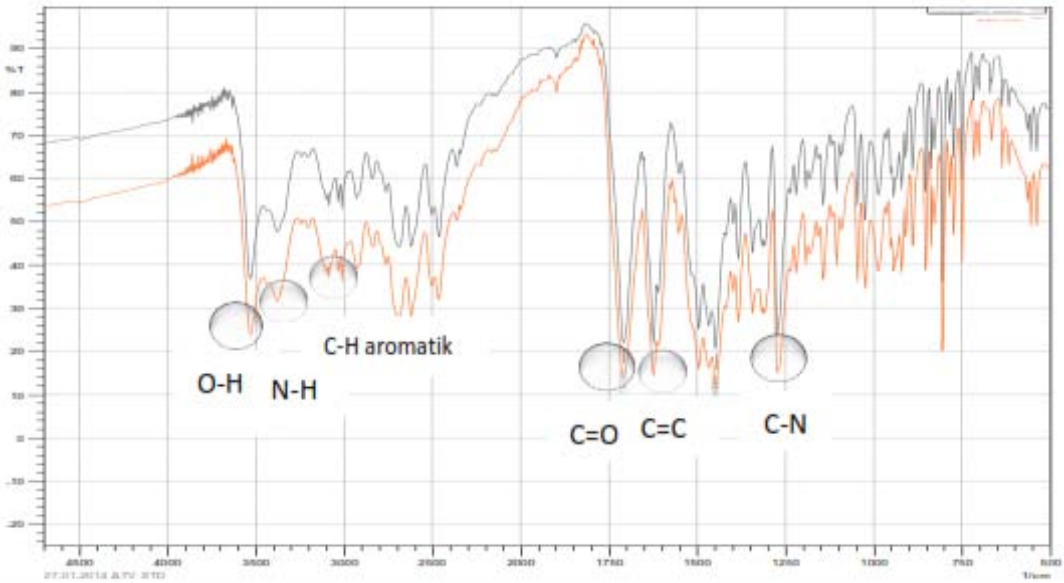


**Fig. 1: Results of FT-IR test for ciprofloxacin hydrochloride BPFI standard against ciprofloxacin hydrochloride sample, Note: Grayline = ciprofloxacin hydrochloride spectrum of the sample, Orange line = BPFI ciprofloxacin hydrochloride spectrum**

Data from the spectrum showed that the two substances tested were a similar compound. In the range 1600-1500 cm-1 there was a peak that indicated the presence of C-N bonds at a frequency of 1273.07 cm-1. In the range 1680-1620 cm-1 there was a peak indicating the functional group C = C with a frequency of 1624.13 cm-1. In the range 1725-1705 cm-1 there was a peak that indicated the presence of C = O bonds with a frequency of 1709 cm-1. In the range of 3150-2750 cm-1, there was a peak indicating an aromatic C-H functional group with a frequency of 3100.7 cm-1. In the range 3700-3000 cm-1 there was a peak which indicated that there was an N-H functional group with a frequency of 3378.47 cm-1. In the range 3700-3000 cm-1 there was a peak that indicated an O-H functional group with a frequency of 3529.88 cm-1 in the sample. The sample purity index value was 0.992739. These data quite similar to the FTIR result of Sahoo et. al results [25].

**Determination of the concentration of ciprofloxacin hydrochloride**

Determination of ciprofloxacin hydrochloride levels using a UV-Vis spectrophotometer has been carried out by researchers**.**

**In-process control (IPC) print mass**

This process was carried out after mixing the active substance and all additives. IPC on print mass was done before the tablet printing process. This test was carried out to determine the quality of print mass powder which could be used to evaluate if there was a problem in the printing process and also to determine the quality of the tablet. Print mass IPC included flow and angle of rest and compressibility tests. The print mass test results can be seen in table 2.

**Table 2: Print mass IPC results**

| Test | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Flow power (g/s) | 2.03±0.09 | 1.89±0.04 | 2.08±0.33 | 1.96±0.01 | 2.17±0.26 |
| Resting angle (°) | 34.95±1.07 | 35.33±0.85 | 35.75±1.21 | 33.95±1.40 | 36.00±0.43 |
| Compressibility (%) | 34.09±1.96 | 31.29±2.44 | 32.64±1.26 | 32.28±1.93 | 33.72±5.38 |

**Notes:** all data representing an average of 3 trials, given as mean±SD

Flow test and resting angle are performed to determine the flow capacity of the print mass because if the print mass is easy to flow, the resulting tablet will have a good uniformity of weight. The nature of the flow is said to be good if it has a range of values of 4-10 g/s, said to be difficult to flow in the range 1.6-4 g/s, and at values <1.6 g/s means it is very difficult to flow. A good resting angle value was in the range of 25-30 ° and the range of 30-40 ° including in the fairly good group [23]. Based on these results, it could be concluded that the resting angle of each formula was quite good.

The compressibility test was done by calculating the value of real tangibility and incompressible density through testing with a tap density device. The range of good compressibility was around 12-18 and in the range, 23-35 was poor [12]. The results obtained indicated that each formula had a poor compressibility value. Based on the test results it could be concluded that the process of compressing the print mass was difficult.

**In-process control (IPC) print tablet:** The printed tablet IPC results can be seen in table 3.

**Table 3: Results of IPC print tablets**

| Test | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Weight uniformity (g) | 0.65±0.00 | 0.64±0.00 | 0.65±0.00 | 0.65±0.00 | 0.64±0.00 |
| Diameter (mm) | 12.03±0.00 | 12.04±0.00 | 12.02±0.00 | 12.02±0.00 | 12.02±0.00 |
| Thick (mm) | 5.92±0.01 | 5.93±0.00 | 5.92±0.01 | 5.83±0.05 | 6.43±0.01 |
| Hardness (N) | 113.50±9.74 | 117.87±9.74 | 133.62±6.25 | 140.75±7.78 | 66.75±5.74 |
| Friability (%) | 0.24±0.00 | 0.09±0.00 | 0.36±0.00 | 0.25±0.00 | 0.06±0.00 |
| Content uniformity (%) | 92,72±0.01 | 90,90±0.00 | 102,80±0.01 | 92,93±0.00 | 100,94±0.05 |

Notes: all data representing an average of 3 trials, given as mean±SD

**Weight uniformity test**

This test was carried out on 20 tablets taken at random. According to Pharmacopoeia Indonesia Edition IV [26], uniformity of weights allowed for tablets of more than 300 mg was±5% of the weight of tablets. Based on these requirements, extended-release ciprofloxacin hydrochloride tablets ought to have weights ranging from 0.6175 g to 0.6825 g. The results obtained from this test were all tablets tested from each formula have a good weight uniformity because it did not deviate from the specified requirements.

**Size uniformity test**

In this test, the five formulas are measured in diameter and thickness. The size uniformity requirements were found in the Indonesian Pharmacopoeia IV Edition 1995, which was a diameter of no more than three times and no less than 4/3 of tablet thickness. Based on the data obtained, it could be concluded that the diameter and thickness of the tablets from each formula met the requirements set by Pharmacopoeia Indonesia Edition IV.

**Hardness test**

Hardness testing of tablets was done by using a hardness tester. The results of testing the hardness of tablets from each formula were 113.50±9.74, 117.87±9.74, 133.62±6.25, 140.75±7.78, and 66.75± 5.74. This value was greater than the ideal value of hardness, but hardness for an extended-release preparation was neither a requirement nor an official standard [27].

**Friability test**

The friability test was carried out by weighing as many as 10 tablets because the total unit weight of the tablet is 650 mg. After that, the tablet was included in the friability test equipment. The results of the friability testing of the five formulas showed good value or qualify because it was less than one percent, that was, 0.24%, 0.09%, 0.36%, 0.25%, and 0.06%. Good Friability indicated the tablet could withstand minor scratches or damage during storage [20].

**Uniformity test of ciprofloxacin hydrochloride content in the preparation**

This test was carried out to determine the uniformity of the active ingredient of ciprofloxacin hydrochloride in the extended-release tablet preparation. Uniformity testing of active substances was carried out on each tablet from each formula by weighing 10 tablets which were crushed one by one and re-weighed one by one. Then the absorbance is measured at a wavelength of 276 nm. The results of testing the uniformity of the active substance content are in formula 1 92.72%, formula 2 90.90%, formula 3 102.80%, formula 4 92.93%, and formula 5 100.94%. This value meets the USP 36 convention requirements, ie the levels of each tablet are in the range of 90%-110% of the levels listed on the label [28].

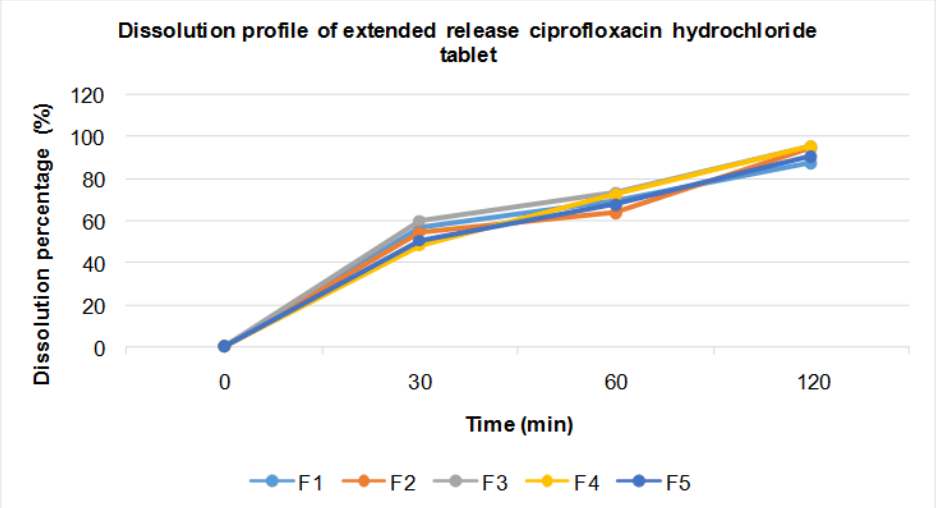


**Fig. 2: Dissolution profile of ciprofloxacin hydrochloride extended-release tablets**

**Dissolution test**

Dissolution testing was carried out using a dissolution test type II (paddle) for 2 h with dissolution media in the form of 0.1 N HCl pH 1.2. The use of hydrochloric acid media was to mimic gastric fluid. Before dissolution testing was carried out, a standard curve was made using pH 1.2 hydrochloric acid as a solvent and blank. Making this standard curve was done to calculate the dissolution level of the dissolved substance. The next step was dissolution testing. Six tablets were taken randomly and tested using a paddle-type dissolution test. The dissolution test was carried out for 2 h using a medium pH of 1.2. The dissolution results are measured. This absorbance was a data release of active substances from tablets to dissolution media. After that, the levels of each tablet were tested from each formula in the form of a percentage (fig. 2).

Dissolution test results of ciprofloxacin hydrochloride extended-release tablets obtained in the 30th minute ie in formula 1 showed the release of active substances by 56.00%, in formula 2 showed the release of active substances was 53.42%, in formula 3 showed the release of active substances was 59.18%, formula 4 shows the release of active substances by 50.51%, and in formula 5 shows the release of active substances by 53.75%. Based on USP 36 convention (table 4), at the 30$^{th}$ minute, tablets must release active substances by 40%-65% [28].

**Table 4: Requirements for dissolution of ciprofloxacin hydrochloride extended-release**

| Time (min) | Dissolution amount (%) |
|---|---|
| 30 | 40-65 |
| 60 | Not less than 60 |
| 120 | Not less than 80 |

From the data that has been obtained, each formula met the requirements for the release of active substances. It was found that dissolution results at the 60th minute, each formula showed a good release of active substances. This could be seen from the data from each formula that met the requirements of the USP 36 convention where the level of release of active substances at the 30th minute was not less than 60%. Dissolution data in the 60$^{th}$ minute, for example, formula 1, 2,3,4, and 5 showed the release of active substances respectively at 67.76%, 65,16%, 72.15%, 70.70%, and 69.55%. The percentage of levels of release of active substances at the 120$^{th}$ minute according to USP 36 convention was no less than 80%. Based on the overall dissolution data that had been obtained, an increase in the content of the HPMC matrix could slow the release of active substances because when it came in contact with water or gastrointestinal fluid hydration and stretching chains would occur so that it could form a thick gel layer. Drug release can occur through diffusion and or erosion from the matrix [29].

In formula 1, a combination of a matrix with a greater K4M HPMC content than the K100M HPMC content resulted in a greater release of active substances than formula 2. This Formula 2 contains less HPMC K4M compared to HPMC K100M. From these data, it could be concluded that the HPMC K4M produced a higher release of active substances than the HPMC K100M. The viscosity of HPMC K100M was higher than HPMC K4M so it had a slow hydration ability [29]. HPMC K4M has a lower viscosity than HPMC K100M which helps release the active substance in the early minutes. The dissolution test is an *in vitro* test that is used as a parameter to determine the solubility of active substances in the body. The dissolution test shows the release of active substances from the tablet when it enters the digestive tract and comes in contact with body fluids [30, 31]. Based on this description, the dissolution results of extended-release ciprofloxacin hydrochloride tablets depicted the levels of active substances dissolved in the dissolution medium for 2 h.

**Statistic analysis**

Statistical analysis for the dissolution test used the PRBD method [32, 33], in which time as a block and HPMC concentration were treated, with the following hypothesis:

H0 = there was no significant dissolution difference between all formulas

H1 = there was a significant dissolution difference between all formulas

Because $F_{arithmetic} < F_{table}$, then accept H0 and the test results were not significant. It could be concluded that there was no significant difference in dissolution between all formulas with a confidence level of 95%. If further testing is done using the Newman-Keuls test [34], it can be seen whether there is a difference between each treatment. From the Newman-Keuls range test the following values were obtained:

F3 vs F5 = 74.1814-71.7857 = 2.33957<3.9096

F3 vs F4 = 74.1814-72.1746 = 2.0068<3.9096

F3 vs F2 = 74.1814-70.0106 = 4.1708<4.7668

F3 vs F1 = 74.1814-70.44465 = 3.7349<3.9096

F4 vs F5 = 72.1746-71.7857 = 0.3889<3.9096

F4 vs F2 = 72.1746-70.0106 = 2.164<3.9096

F4 vs F1 = 72.1746-70.44465 = 1.7281<3.9096

F5 vs F2 = 71.7857-70.0106 = 1.7751<3.9096

F5 vs F1 = 71.7857-70.4465 = 1.3392<3.9096

F1 vs F2 = 70.4465-70.0106 = 0.4359<3.9096

Based on these results, there was no significant difference in the dissolution test results of each formula.

**CONCLUSION**

From the results of the study, it could be concluded that the formula for the preparation of ciprofloxacin hydrochloride extended-release tablets met USP 36 convention requirements. Tablet formulations were carried out using a combination of HPMC K100M and HPMC K4M concentrations as a polymer matrix. Tablet dissolution test results showed that the preparation of formula 1 with a combination of concentration of HPMC K100M and HPMC K4M 1.5% (1:2), formula 2 with a combination of HPMC K100M concentration and HPMC K4M 1.5% (2:1), formula 3 with the combination of HPMC K100M concentration and HPMC K4M 1.5% (1:1), formula 4 with HPMC K100M concentration of 1%, and formula 5 with HPMC K4M concentration of 3% met the dissolution requirements at USP 36 convention.

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**AUTHORS CONTRIBUTIONS**

All the authors have contributed equally.

**CONFLICT OF INTERESTS**

There is no conflict of interest between authors

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