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Original Article

BEYOND-USE DATE DETERMINATION OF CETIRIZINE HYDROCHLORIDE SYRUP PREPARATION

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ABSTRACT

Objective: To determine Beyond Use Date (BUD) of cetirizine hydrochloride syrup preparation by analyzing cetirizine concentrations using High-Performance Liquid Chromatography (HPLC) with an Ultraviolet (UV) detector.

Methods: The analysis was carried out using mobile phase acetonitrile-phosphate buffer pH 3 (50:50 v/v), flow rate 1 ml/min with isocratic elution, and detected using a UV detector at 232 nm. The BUD was determined by measuring the cetirizine level in the syrup sample since the primary packaging was opened (day 0) for 5 w of storage.

Results: The analytical method was selective and specific. The linearity results show a correlation coefficient (r) of 0.9998 in the 4-32 g/ml concentration range. The limit of detection (LOD) and limit of quantification (LOQ) values were 0.5 µg/ml and 1.7 µg/ml, respectively. The method satisfies accuracy, precision, robustness, and ruggedness criteria. The data showed a decrease in cetirizine concentration level in preparation within 5 w.

Conclusion: This study successfully determined the BUD of cetirizine hydrochloride syrup by analyzing cetirizine concentrations using HPLC with a UV detector. The results revealed a progressive decrease in cetirizine concentration over five weeks of storage, and the BUD was established at 25 d. This finding is significant, providing valuable guidance for pharmacists and healthcare providers in managing the use of the medicine after the primary packaging is opened.

Keywords: BUD, Cetirizine, HPLC

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INTRODUCTION

The drug quality, safety, and efficacy must be ensured during production until they are delivered to patients [1]. The concept of drug stability is central to maintaining these standards, which encompasses preserving chemical, physical, microbiological, therapeutic, and toxicological characteristics from production through storage and use [2]. Pharmaceutical preparations achieve stability when they retain these attributes unchanged, underscoring the importance of rigorous quality control measures [3]. These measures safeguard the integrity of medications and ensure that patients receive effective and safe treatments. As outlined by regulatory bodies and pharmacopeial standards, adherence to stability guidelines forms the foundation for pharmaceutical manufacturers and healthcare providers to uphold high standards of patient care and therapeutic outcomes.

Active ingredients can degrade under specific conditions and over time, prompting the pharmaceutical industry to imprint Expiration Dates (ED) on packaging as a guideline for safe use before the primary packaging is opened [4]. The ED signifies the duration until the medication is deemed safe and effective if stored under recommended conditions. BUD, on the other hand, pertains to medications after their primary packaging has been opened or when compounded [5]. It denotes the period during which the medication retains its potency and remains safe under specified conditions [6]. Despite its importance, awareness of BUD among the public varies, and regulations regarding its determination can differ across countries. For compounded drugs, the United States Pharmacopeia (USP) provides guidelines for establishing BUD [6], emphasizing factors like temperature and humidity that can influence stability. However, standardized guidelines for BUD may not exist for industrially produced drugs, underscoring the need for careful consideration of external factors in determining safe usage periods for medications worldwide.

Cetirizine is a widely used second-generation antihistamine known for its effectiveness in treating allergic rhinitis, chronic urticaria, and other allergic conditions [7]. Its popularity stems from its non-sedating properties compared to older antihistamines, making it suitable for adults and children [8, 9]. Cetirizine HCl preparations were most frequently used at 72.48% of the total use of antihistamine drugs in the hospitals in Bandung, West Java, Indonesia. The increased use of cetirizine also occurred in Central Java, Indonesia, with a percentage between 10-19% [10].

The Cetirizine HCl preparation, which is widely distributed in the market, is an oral syrup preparation. Syrup is preferred because of its easy use, especially for pediatric and geriatric patients who have difficulty swallowing solid preparations. However, the stability of syrup (liquid) preparations is relatively lower than that of solid preparations, such as tablets [11, 12]. Therefore, paying attention to the stability of syrup preparations related to the beyond-use date product is important. Understanding the BUD of cetirizine syrup is crucial for ensuring its safety and efficacy. Compliance with BUD guidelines help maintain the medication's effectiveness and reduces the risk of potential side effects, ensuring optimal therapeutic outcomes.

This study was conducted to determine the BUD of cetirizine HCl syrup preparation. The determination of BUD is based on the decrease in active substance levels (Cetirizine HCl) measured by using HPLC with UV-detector. This study is expected to provide information on the BUD of cetirizine preparations circulated in Indonesia.

MATERIALS AND METHODS

Materials

The materials used in this study were cetirizine HCl standard (Sigma-Aldrich, Germany), potassium dihydrogen phosphate (Merck, Germany), phosphoric acid (Merck, Germany), acetonitrile (Merck, Germany), aqua pro injection (Ikapharmindo, Indonesia), nylon syringe filter 0.45µm (Whatman, USA), 5 brands of cetirizine HCl 5 mg/5 ml syrup purchased at several pharmacies in the East Jakarta, Indonesia area.

Methods

Optimization of wavelength analysis

The UV spectrum of cetirizine HCl was obtained by measuring the standard solution of cetirizine HCl in acetonitrile 10 µg/ml with UV-VIS spectrophotometry (Shimadzu, UV-1900i, Japan) in the 200-400 nm range. Maximum absorption wavelength was used for HPLC analysis.

Optimization of chromatography condition

A 20 µl solution of cetirizine HCl was injected into the HPLC (Shimadzu® LC-20 AT, Japan) system at the maximum wavelength. The mobile phase used in the test was acetonitrile-phosphate buffer 0.05M pH 3 with a composition of 40:60, 50:50, and 60:40 (v/v) at a flow rate of 1 ml/min. The mobile phase composition was selected based on the parameters evaluation of retention time (tR), tailing factor value (Tf), Height Equivalent to a Theoretical Plate (HETP), and theoretical plate number (N) [13, 14].

System suitability test

Under optimum analytical conditions, a 20 µl cetirizine HCl solution (10 µg/ml) was injected into the HPLC system. The test was carried out six times. The system suitability test result was evaluated based on the parameters of analysis time, number of theoretical plates (N), HETP, tailing factor (Tf), and CV value. The result should comply with the following criteria: relatively faster analysis time, number of theoretical plates (N)>2000, Tf value close to 1, small HETP value, and CV ≤ 2% [13-14].

Validation of method analysis

Selectivity test

The selectivity test was performed by comparing the chromatogram profile of the cetirizine HCl standard solution (10µg/ml) and blanks. The sample (20 µl) was injected into the HPLC system using the selected method. The analysis was carried out on blanks, standard cetirizine HCl (10 µg/ml), simulation matrix (consisting of syrup us simplex 65%, methylparaben 0.2%, and aquadest), and samples of cetirizine HCl syrup (final concentration of 10 µg/ml). The selectivity test results fulfill the criteria if there is no other peak or interference at the time of analyte release [13].

Linearity test

A linearity test was performed on six concentrations of cetirizine HCl standard solution, namely 4, 8, 10, 16, 20, and 32 µg/ml. The solutions (20 µl) were injected into the HPLC system and analyzed using the selected method. The linear regression line equation (from the calibration curve) was calculated. The linearity test fulfills the requirements if the correlation coefficient value (r) is ≥ 0.9990 and V_{x0} ≤ 2% [13, 14].

Limit of detection (LOD) and limit of quantification (LOQ)

Limits of detection and quantitation were obtained based on statistical calculations through linear regression equations of the cetirizine HCl calibration curve. The LOD and LOQ were calculated by the following formula [13].

$$LOD = \frac{3.3\left(S_{\frac{y}{x}}\right)}{S} \quad LOQ = \frac{10\left(S_{\frac{y}{x}}\right)}{S}$$

$S_{y/x}$ is the standard deviation of the residual, and S is the slope of the calibration curve between the response area and the analyte concentration in the linear regression equation.

Accuracy and precision test

This study applied simulation (spiked-placebo recovery) as an accuracy test method. The test was conducted by making a simulation formula of cetirizine HCl syrup with three concentration levels, namely 80% (16 µg/ml), 100% (20 µg/ml), and 120% (24 µg/ml). The test was performed thrice (100% level was carried out six times). A sample solution of 20 µl was injected into the HPLC system. The accuracy test results are satisfying if the recovery value is 98-102%. Precision test results meet the requirements if Coefficient of Variation (CV)<2% [13, 14].

Robustness test

Robustness testing is performed by changing variations in the selected analytical method to ensure no significant measurement changes occur. In this study, the factors that changed were flow rate and mobile phase composition. A standard solution of cetirizine HCl with a volume of 20 µL was injected into the HPLC. The cetirizine HCl solution was injected 3 times in each variation of conditions. The results satisfy the requirements if the CV value is ≤ 2% [13, 14].

Ruggedness test

In the ruggedness test, the selected method was tested on different HPLC instruments to evaluate the reproducibility. A 20 µl standard cetirizine HCl (10 µg/ml) was injected into the HPLC system. The cetirizine standard solution was injected 3 times (in triplicates), and the result was evaluated. The analysis results fulfill the requirements if the CV value is ≤ 2% [13].

The ruggedness test was conducted using different instruments. The test objective is to evaluate the reproducibility of the method. Cetirizine HCl standard solution (10 µg/ml) was injected into the HPLC system three times (triplicates). The result was evaluated. The test results meet the requirements if the CV is ≤ 2% [13].

Assay

The assay was performed on five cetirizine HCl syrup brands (the dosage strength is 5 mg/ml) that are commercially available on the market. In each brand, the assays were carried out using three samples (triplicate). The assay procedure is a modification from the previous report [11]. Before the assay, the specific gravity of each dosage brand was determined. The cetirizine HCl syrup sample was weighed equivalent to 2 mg of cetirizine HCl and put into a 10 ml volumetric flask. Then, the mobile phase was added to half the volumetric flask and sonicated for 5 min. Next, the solution was added to the mobile phase to obtain a 200 µg/ml sample concentration. The sample solution was diluted tenfold by mobile phase to obtain a concentration sample of 20 µg/ml. After that, the sample solution was filtered using a 0.45 m nylon syringe filter. The sample solution was injected into the HPLC system, and sample content was calculated.

Determination of beyond-use date (BUD)

The BUD determination of cetirizine HCl syrup was carried out by quantitative analysis of the cetirizine HCl syrup content since the primary packaging was opened (day 0) for 5 w of storage. According to the ICH Q1F guidelines, the sample was stored in zone IVB at 30 °C±2 °C and in a dry place. The sample was opened occasionally according to the dose regimen three times a day and stored in a medicine box so that storage conditions comply with storage guidelines. The test interval is shown in table 1.

Beyond use, date was determined based on changes in cetirizine HCl content in the syrup sample. According to the 6th Indonesian Pharmacopoeia (FI VI), the general content requirement of a cetirizine syrup is not less than 90.0% and not more than 110.0% of the amount stated on the label [15]. The BUD of the sample was determined when the sample concentration no longer met the general level requirement, which is less than 90.0% of the amount stated on the label.

Data analysis

The chromatograms were processed using the Shimadzu LC solution program. The data analysis was processed using the Microsoft® Excel for Mac application version 16.61.1, and statistical testing was processed using the IBM SPSS application version 28.0.1.1 spectrophotometer (Tokyo, Japan).

Table 1: Sampling schedule and analysis of ambroxol HCl syrup preparation

Week	Day						
0	**0**	**1**	**2**	**3**	**4**	**5**	**6**
1	7	8	9	10	11	12	13
2	14	15	16	17	18	19	20
3	21	22	23	24	25	26	27
4	28	29	30	31	32	33	34
5	35	36	37	38	39	40	41

Note: the black highlighted part shows the sampling time.

RESULTS AND DISCUSSION

The study starts with determining cetirizine HCl maximum absorbance wavelength by Ultraviolet-Visible (UV-VIS) spectrophotometry. It is essential to conduct the measurement at the maximum absorption wavelength since it provides the most sensitive and accurate measurement of the concentration of a substance. In this study, the maximum absorption wavelength of cetirizine HCl obtained using UV-VIS spectrophotometry was 232 nm. This result is in accordance with the certificate of analysis of cetirizine HCl standard. The UV spectrum of cetirizine HCl can be seen in fig. 1.

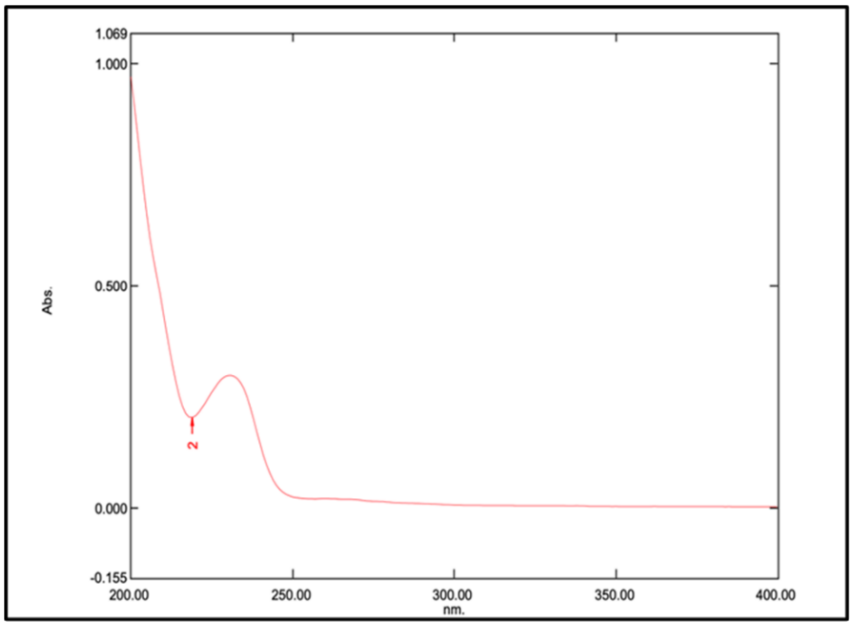

Fig. 1: UV Spectrum of cetirizine HCl (10µg/ml) in acetonitrile

The mobile phase composition optimization was performed to obtain the optimum conditions for the analysis. The mobile phase compositions tested were acetonitrile-phosphate buffer pH 3 with a ratio of 60:40 (v/v), 50:50 (v/v), and 40:60 (v/v). The mobile phase commonly used in reversed-phase HPLC systems is a water mixture with organic solvents, such as acetonitrile, methanol, or Tetrahydrofuran (THF) [16]. This study chose acetonitrile as the organic solvent because it has a low viscosity (0.36 cP), whether in single-use or when mixed with water. A mobile phase with low viscosity is a good candidate because it facilitates solute transportation when passing through the column (stationary phase) and prevents high back pressure [17, 18]. In addition, acetonitrile has a greater elution strength than methanol [19].

The addition of phosphate buffer aims to suppress ionization and control the unreacted degree of ionization of free silanol groups to minimize the tailing factor and improve chromatogram performance [16]. The buffer addition also stabilizes the pH of the mobile phase. The mobile phase pH>1.5 units from the pKa of the analyte will produce a stable analyte retention time [17]. The pKa of cetirizine HCl is 8.0, and the pH of the mobile phase used is 3.0.

The mobile phase composition optimization data can be seen in table 2. The selected mobile phase composition is acetonitrile-phosphate buffer pH 3 50:50 (v/v). It has the greatest area compared to the others. Usually, the retention time is a significant evaluation parameter. The retention time of the 50:50 (v/v) mobile phase was slightly longer than 60:40 (v/v), but other parameters, such as the number of theoretical plates (N) values, HETP, area, and tailing factor, were superior. The N, HETP, and tailing factor parameters in the 40:60 (v/v) mobile phase are better than the 50:50 (v/v) mobile phase, with an extended retention time. A long retention time will result in good separation, but the peak may be broader. In addition, the analysis cost must be considered due to the extended analysis time. Therefore, we selected the 50:50 composition for the analytical method validation.

Compared with the other report, the chosen mobile phase system is more straightforward to prepare. Jaber *et al.* use a combination of phosphate buffer, methanol, acetonitrile, and THF at a pH of 5.5 to determine cetirizine and related impurities [20]. The chosen mobile phase system also provides similar sensitivity and selectivity parameters compared to the report by Souri *et al.*, which uses the compositions of 60:40 and pH 3.5 for the kinetic measurement of cetirizine [21]. Several studies have reported that cetirizine HCl and similar antihistamine preparations are stable under acidic conditions, which supports this study's choice of a mobile phase with a pH of 3.0 [22-24].

Table 2: The optimization mobile phase composition data, (data are described as mean with experiment number n = 3)

Parameter	Mobile phase composition		
	Acetonitrile-phosphate buffer pH 3 (60:40 v/v)	Acetonitrile-phosphate buffer pH 3 (50:50 v/v)	Acetonitrile-phosphate buffer pH 3 (40:60 v/v)
Retention time (minutes)	3.23	4.35	8.93
Area (mV/s)*	312080±13908	432917±12533	422316±16346
Number of theoretical plate (N)	43597.33	56444.67	83885.67
HETP	22.938	17.750	11.923
Tailing Factor (Tf)	1.28	1.21	1.11

*Data expressed as mean±SD (n = 3), SD = standard deviation

The system suitability test results can be found in table 3. The system suitability test was conducted to verify that the system measurements and operations related to the analysis procedure met the requirements and improved the detection of potential failures [14]. The system suitability test results showed that the theoretical plate number (N) was more than 2000, the Tf value was less than 2, and relatively stable. The CV value from retention time and peak area data was 0.18 % and 1.87 %, respectively. The result shows that the system suitability test meets the requirements.

Table 3: System suitability test result

Injections (n = 6)	Parameter				
	Retention time (min)	Area (mV/s)	Number of theoretical plate (N)	HETP	Tf
1	4.31	476024	58016	17.236	1.27
2	4.31	481160	57486	17.396	1.27
3	4.31	460081	56658	17.650	1.26
4	4.31	466388	57112	17.510	1.27
5	4.33	474662	57227	17.474	1.27
6	4.32	483434	58746	17.022	1.27
Mean	4.32	473624.83	57540.83	17.381	1.27
RSD	7.78	8895.36			
CV (%)	0.18	1.87			

The selectivity test aims to determine that there are no peaks from other compounds at the retention time of the analyte [14]. The selectivity results showed that there were no components that interfered with the analyte analysis time. The selectivity test result is fig. 2.

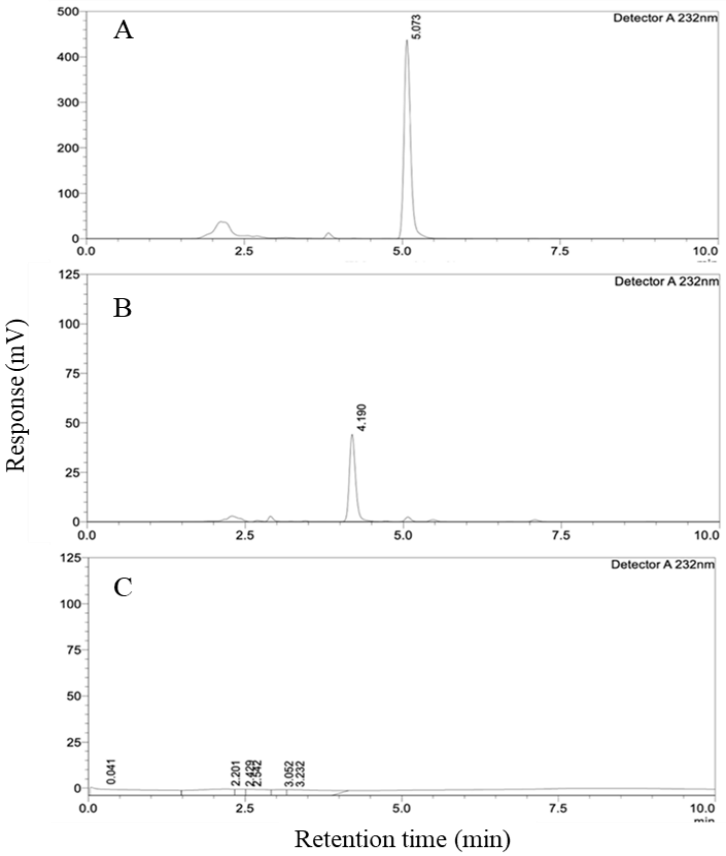

Fig. 2: Chromatogram of the selectivity test (A) cetirizine HCl standard (10 µg/ml); (B) matrix simulation; (C) blank. Analytical conditions: YMC C18 column (250 mm x 4,6 mm, 5µm); Mobile phase acetonitrile-phosphate buffer pH 3 (50:50 v/v); flow rate 1.0 ml/min; UV detector 232 nm, injection volume 20 µl, analysis time 10 min

The linearity test was conducted by injecting six concentrations of standard cetirizine solution (4, 8, 10, 16, 20, and 32 µg/ml). The standard calibration curve of cetirizine HCl produced a linear regression equation y = 24179x-1183.7 with the values of r (correlation coefficient) and V_{x0} (coefficient of variation of the regression function were 0.9998 and 1.16%, respectively. Both values meet the parameters of the linearity test ($r \geq 0.999$ and $V_{x0} \leq$ 2%). LOD and LOQ were determined from calculations based on linear regression equations. From these calculations, the LOD value of cetirizine HCl obtained was 0.57 µg/ml, and LOQ was 1.74 µg/ml.

The average recovery values of the accuracy test (at the concentration of 80%, 100%, and 120%) were 99.87%, 100.41%, and 99.05%, respectively. At the same time, the %CV value (at 100% concentration) is 0.58%. The results showed that the method met the test requirements for accuracy and precision (98-100% recoveries; %CV<2%). Accuracy and precision data are shown in table 4.

Table 4: Accuracy and precision test result

Concentration (µg/ml)	Area (mV/s)	Concentration measured (µg/ml)	*Recovery* (%)	Average recovery±SD (%)	CV (%)
16	395325	16.04064	100.25	99.87±1.51 (n = 3)	1.51
	387240	15.71357	98.21		
	398903	16.18539	101.16		
20	493596	20.01617	100.08	100.41±1.03 (n = 6)	0.58
	493537	20.01378	100.07		
	498501	20.2146	101.07		
	498526	20.21561	101.08		
	484599	19.6522	98.26		
	492796	19.98381	99.92		
24	590474	23.93534	99.73	99.05±0.82 (n = 3)	
	587824	23.82814	99.28		0.83
	580995	23.55187	98.13		

The robustness test was performed to evaluate the method, which undergoes minor changes in analysis conditions [25-27]. The factors that changed were flow rate and mobile phase composition. The flow rate was changed to 1.2 ml/min and 0.8 ml/min. In contrast, the mobile phase composition was changed to acetonitrile-phosphate buffer pH 3 40:60 (v/v) and 60:40 (v/v). Each condition was repeated three times. The test results showed that the CV values from the flow rate changes (0.8 ml/min and 1.2 ml/min) were 1.46% and 0.96%, respectively. The CV values from the mobile phase composition change (40:60 v/v) and (60:40 v/v) were 0.83% and 1.15%, respectively. The selected analysis conditions were tested on different HPLC instruments in the ruggedness test. The test was performed three times. The average peak area was 827534.5, with a CV value of 1.84%. The ruggedness test meets the requirements (CV value ≤ 2%).

BUD determination of cetirizine HCl syrup was carried out by analyzing the levels of cetirizine HCl syrup for six weeks from day 0 to 41. Tests were conducted on five different brands, each with three bottles of medicine. The bottles were opened once a day for seven days and stored in the medicine box. This is to match the conditions in which the syrup is used. Based on the curve of changes in cetirizine levels, it can be observed that the active substance levels in sample a decreased until the end of the measurement day. On the 41st day, the cetirizine content reached 87.57%. The active substance level decreased past the active substance acceptance requirement, which is less than 90%. The decrease of active substances in all samples is shown in fig. 3.

As for sample B, the decrease was observed from 0 to 41st d. On the last measurement day, the active substance level reached 88.39%. There was also a decreasing active ingredient level of samples C, D, and E. On the last day of the test, the cetirizine levels of samples C, D, and E were 84.28%, 79.77%, and 67.14%, consecutively (fig. 3). The active substance levels in syrup preparations have reached below 90%.

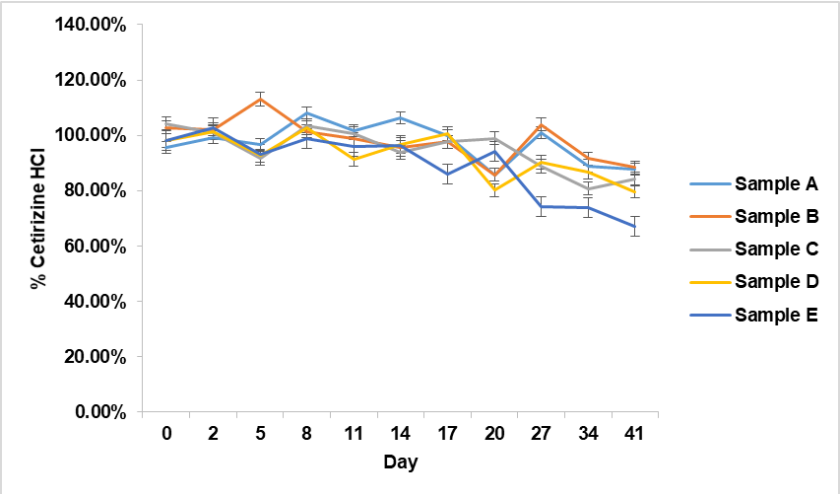

Fig. 3: The curve of % cetirizine HCl content (average data from each sample, n = 3) on each analysis time

A normality test determined the data distribution (active substance levels). The results showed p>0.05, which indicates that the data was not normally distributed. The result might be due to non-linear degradation patterns of cetirizine HCl in the syrup, potentially influenced by environmental factors like temperature or light exposure, which can cause irregular declines in the concentration of

the active ingredient over time. Furthermore, the homogeneity test was carried out on the variance. The results show a value of p>0.05, so the data has a homogeneous variance. Namely, the degree of variability in cetirizine HCl levels is similar across the different syrup formulations. The result suggests that while the degradation rate varies between samples, the level of variance between them is consistent, implying that the differences observed in active ingredient degradation across samples are not due to fluctuations in variance but rather differences in the formulations themselves or storage conditions.

Subsequently, the data were tested with One Way ANOVA. According to this test, the sample data between groups did not show significance (p>0.05). This means that although there is a decline in cetirizine levels in all samples, these declines are not statistically different enough to suggest that one sample degrades significantly faster or slower than the others. This could imply that the various formulations or conditions tested exhibit similar degradation behavior over time. These results were confirmed in the Post Hoc test, where the significance value between samples was p>0.05. The test results indicate that there is no significance between sample groups. It reinforces that there is no significant difference in cetirizine degradation between the sample groups. Even though there are numerical differences in cetirizine levels ranging from 88.39% in sample B to 67.14% in sample E—these differences are not statistically significant. This indicates that all the samples follow a similar degradation trend, and the observed variations could be due to random fluctuations rather than meaningful differences in stability.

The fact that there is no significant difference between the sample groups implies that factors such as formulation or storage conditions may not drastically influence the degradation rate, at least within the parameters tested. However, the decreasing trend in active ingredient levels (especially in sample E, which reached 67.14%) demonstrates that degradation is occurring at a meaningful rate, potentially affecting the efficacy of the syrup over time.

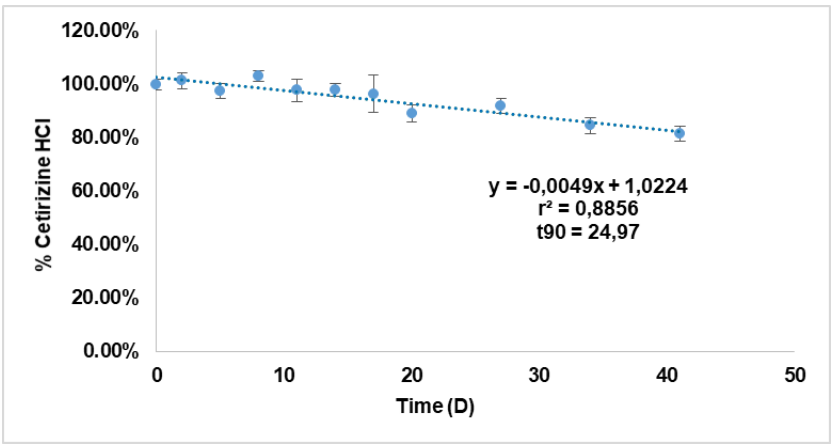

Fig. 4: The curve of % cetirizine HCl level (average data of n = 5 obtained from all samples) versus analysis time. The linear regression line obtained from the curve was used for BUD determination

Therefore, the data of all samples can be combined (averaged) to calculate cetirizine BUD. The average levels of the samples against time were graphed to obtain a linear regression equation. The BUD value was obtained by substituting y = 0.9 (t90) into the linear regression equation. From the linear regression equation y =-0.0049x+1.0224, the t90 value obtained was 24.59 or 25 d. This value is below the USP guideline standard of 35 d [6]. One of the samples listed the BUD of the sample as 14 d, so this result still complies with the claim on the label. Organoleptic tests were also conducted on each sample. The results showed no significant organoleptic changes (color and odor) in all samples until the last day of BUD testing.

The obtained cetirizine BUD was relatively fast compared to another study with different active ingredients. The author also conducted the same experiment for ambroxol hydrochloride syrup preparation, and the BUD was 49 d [28]. Regarding the cetirizine HCl, Wang *et al.* reported the degradation of cetirizine in an aqueous solution is about 30 d, which is almost a similar result compared to this study. They tested cetirizine hydrochloride degradation in various aqueous environments (pH, temperature, and time) [29]. Another study report by Patel *et al.* showed that cetirizine HCl oral solutions stored in cool, dry conditions demonstrated cetirizine stability for 6 mo. The study showed that cetirizine retained its stability for quite a long time when the primary packaging was not opened [11]. The comparison result suggests that temperature, light exposure, and humidity significantly affect the cetirizine stability in syrup preparation. Apart from that factor, the formulation differences also considerably affect the stability and BUD of the final product. For example, formulations that include preservatives or moisture barriers could prevent degradation and hydrolysis, resulting in longer BUDs than formulations lacking these protective components.

Finally, the findings from this study highlight the importance of a well-defined BUD for cetirizine HCl syrup, ensuring that patients receive the full therapeutic benefit of the medication within 25 d. Pharmacists and healthcare providers should emphasize the importance of adhering to this BUD and proper storage and disposal practices. For patients, clear communication regarding the expiration date, storage instructions, and the need to discard unused syrup after the BUD period will help maintain the efficacy and safety of cetirizine HCl syrup.

CONCLUSION

The method used for the determination of BUD cetirizine syrup was YMC® C18 column (250 mm x 4.6 mm, 5 µm), mobile phase acetonitrile-phosphate buffer pH 3 (50:50), flowrate 1 ml/min with a UV detection at 232 nm. The method fulfills validation criteria such as selectivity, sensitivity, linearity, accuracy, precision, robustness, and ruggedness. According to the analysis of cetirizine concentrations in the sample for 5 w, the BUD of cetirizine hydrochloride syrup was 25 d. The information can be used as a reference to enlighten the public about beyond use date.

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Nil

CONFLICTS OF INTERESTS

The authors have declared no conflict of interest

AUTHORS CONTRIBUTIONS

Catur Jatmika designed and supervised the experiment and prepared the manuscript, Ghina Salma Fadhila conducted the experiment, and Raditya Iswandana proposed the data analysis and revised the manuscript.

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