International Journal Of Health, Engineering And Technology (IJHET) *E-ISSN 2829 - 8683*
Volume 4, Number 6, March 2026, *Page. 2450 - 2456*
Email : editorijhess@gmail.com

Verification Of the Analysis Method For Determining Cetirizine HCl Levels in Cetirizine Syrup Preparations By High-Performance Liquid Chromatography According To The Compendial Method Of The Indonesian Pharmacopoeia, VIth Edition, 2020

Nanda Putri Kamilah[1)], Hasriyani[2)], M. Khudzaifi[3)]
[1,2,3)] Faculty of Pharmacy, Muhammadiyah University of Kudus

*Corresponding Author
Email : hasriyani@umkudus.ac.id

Abstract

Cetirizine Hydrochloride is a second-generation antihistamine that is effective for allergy therapy and is widely used in syrup dosage forms. The quality of drug preparations requires a valid assay analysis method to ensure the active substance content meets the requirements. This study aims to verify the analysis method for determining the content of Cetirizine Hydrochloride in syrup preparations using High Performance Liquid Chromatography (HPLC) in accordance with the Indonesian Pharmacopoeia Edition VI 2020 standards. The study was conducted at the Quality Control Laboratory of PT. X using an HPLC system equipped with an L10 column and UV detector set at 233 nm. Method verification parameters include system suitability testing, specificity, accuracy, precision, as well as linearity and range in determining the content of Cetirizine Hydrochloride. The results demonstrated that all verification parameters met the acceptance criteria. The system suitability test gave good results with an area RSD value of 0.232% and a tailing factor of 1.389. The method was proven to be specific with a retention time of 24.842 minutes without interference from the matrix. The accuracy of the assay method was confirmed with an average recovery value of 101.06% in the concentration range of 80–120% of the nominal concentration, and excellent precision with an RSD value of 0.31%. Linearity and range tests showed an excellent linear relationship in the concentration range of 80–120% with a correlation coefficient (r) of 0.9996. Based on these results, the analysis method for determining the content of Cetirizine Hydrochloride in syrup preparations was declared valid and suitable for use in routine quality control analysis.

Keywords: Cetirizine Hydrochloride, Syrup, High Performance Liquid Chromatography (HPLC), Verification Of Analytical Method.

INTRODUCTION

Cetirizine hydrochloride is a second-generation antihistamine that is effective in treating allergy symptoms such as sneezing, runny nose, and itching. It has the advantage of minimal sedation compared to first-generation antihistamines, making it safe for long-term therapy. The use of this medication in syrup form is increasingly popular due to its ease of consumption, especially in children and patients who have difficulty swallowing solid preparations such as tablets [Ramadhana & Hendriani, 2019]. This phenomenon is driven by the high prevalence of allergies among pediatric patients, where cetirizine syrup offers a rapid onset of action and improved quality of life [Ritonga & Daulay, 2023].

The cetirizine HCl syrup dosage form facilitates pediatric patient compliance through improved taste and flexible dosing, reducing the risk of overdose or underdose in this vulnerable population [Shadrina et al., 2024]. Furthermore, a meta-analysis confirmed the effectiveness of cetirizine in managing seasonal allergic rhinitis in children, with additional benefits for allergic conjunctivitis.

The quality of cetirizine syrup requires a valid analytical method to ensure the active ingredient meets specifications, as formulation variations can affect stability and efficacy [Ramadhana & Hendriani, 2019]. High-performance liquid chromatography (HPLC) is the primary choice due to its high resolving power, good sensitivity, and rapid analysis of complex samples such as syrup [Chrissanti et al., 2020]. However, the application of the compendial method requires verification to ensure reliability in local laboratories [Riyanto, 2014][Ramadhan & Musfiroh, 2021].

Problems arise from the potential for syrup matrix interference, which can compromise the accuracy of cetirizine HCl assays, necessitating confirmation of specificity and precision.

Furthermore, fluctuations in laboratory environmental conditions can impact HPLC performance, emphasizing the importance of verifying parameters such as linearity and accuracy according to the Indonesian Pharmacopoeia, Edition VI (2020) [Ministry of Health, 2020]. Without verification, the risk of invalid data can compromise routine quality control [Riyanto, 2014][Ramadhan & Musfiroh, 2021].

This study aims to verify the compendial HPLC method of the Indonesian Pharmacopoeia VI Edition (2020) for the determination of cetirizine HCl levels in syrup, evaluating the system parameters of suitability, specificity, accuracy, precision, linearity, and range [Ministry of Health of the Republic of Indonesia, 2020]. The urgency lies in the need of Indonesian pharmaceutical laboratories for a verified method that supports the quality control of the widely circulated generic cetirizine syrup preparations [Ramadhan & Musfiroh, 2021]. The novelty of this study is the application of complete verification under local laboratory conditions of PT. X with an L10 column and a 233 nm UV detector, complementing the limited data for cetirizine syrup in Indonesia [Chrissanti et al., 2020].

RESEARCH METHODS

Types of research

This type of research is experimental by analyzing standard solutions and Cetirizine Syrup samples using High Performance Liquid Chromatography.

Population and Sample

The population in this study is a series of analyses of Cetirizine Hydrochloride in syrup preparations using High Performance Liquid Chromatography and the sample used is Cetirizine Syrup.

Tools and materials

The tools and materials used in this study are High Performance Liquid Chromatography (HPLC), L10 Column, Analytical Balance, Sonicator, Volumetric Flask, Beaker Glass, Volumetric Pipette, Dropper Pipette, 0.2 µm membrane filter. Reference Standard Cetirizine Hydrochloride BPFI, Cetirizine Syrup, Placebo, KH_2PO_4, H_3PO_4, Aquadest, Acetonitrile P.

Chromatography System

Tool : KCKT
Column : L10, 4.6 mm x 250 mm, 5 µm
Detector : UV 233 nm
Flow rate : 2.0 mL/minute
Injection volume : 20 µL
Column temperature : 50ºC
Mobile phase :*Gradient*

Time (minutes)	Solution A (%)	Solution B (%)
0	5	95
15	5	95
22	25	75
35	25	75
40	5	95
50	5	95

Verification of Analysis Method

Specificity

Standard solutions, samples (equivalent to 10 mg of active ingredient in 100 mL), placebo, and mobile phase were each prepared and injected separately into the HPLC system. Chromatograms were compared to ensure there were no interfering peaks at the retention time of the analytes.

Accuracy

The working standards were weighed at 80 mg, 100 mg, and 120 mg, respectively, and 1 mLxBJ placebo was added, then dissolved in a 100 mL volumetric flask and diluted according to the procedure to obtain concentrations of 80%, 100%, and 120%. Each level was made in three replications, injected into HPLC, and then the percent recovery (% recovery) was calculated.

Precision

The sample solutions were prepared ten times separately with concentrations (equivalent to 10 mg in 100 mL), then each was analyzed using HPLC and the RSD value was calculated to assess the repeatability of the method.

Linearity and Range

Standard solutions were prepared at five concentration levels of 80-120%, namely weighing 80 mg, 90 mg, 100 mg, 110 mg, and 120 mg in a 100 mL volumetric flask, then analyzed using HPLC. A calibration curve was made from the relationship between concentration and area to obtain the regression equation and correlation coefficient (r).

Data analysis

Data analysis used in this study was carried out by looking at the results of each test parameter, including Specificity, Accuracy, Precision, Linearity and Range Tests.

RESULTS AND DISCUSSION

Verification of Analysis Method

Method verification is a confirmation process aimed at ensuring that a method or analytical procedure meets established standards and criteria. Furthermore, verification serves to demonstrate that the laboratory in question has the capability to correctly implement the method and produce accurate, valid, and accountable data and test results.(Ramadhan & Musfiroh, 2021).

System Suitability Test

Before sample content determination was carried out, a system suitability test was conducted to verify that the analytical instrument and method provided valid, reliable, and consistent results. The results of the system suitability test are shown in Table 1.

Table 1. System Suitability Test Results

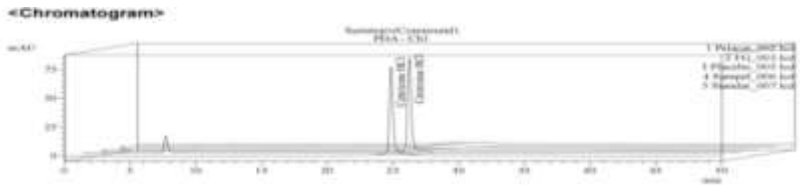
Injection number	Area
1	1644373
2	1641968
3	1650921
4	1649262
5	1651457
6	1649255
	Average : 1647873
	RSD (%) : 0.232
	Tailing Factor : 1.389
Acceptance Criteria	**RSD : No more than 1.0%**
	Tailing Factor : No more than 1.5

Based on the results presented in Table 1, the analysis showed that the mean peak area of Cetirizine Hydrochloride was 1647873, with a relative standard deviation (RSD) of 0.232% and a tailing factor of 1.389.

Specificity

Specificity testing was conducted to prove that the analytical method was able to identify the analyte accurately without interference from other components such as placebo and mobile phase. In Figure 1, the Chromatogram of Specificity Test Results of the placebo solution, solvent, and mobile phase did not find any response or interference peak at the same retention time as Cetirizine Hydrochloride. This indicates that the analytical method used has good specificity because it is able to separate the main analyte without interference from the carrier matrix, in accordance with the requirement that the mobile phase and placebo should not provide a response at the retention time of the analyte.

Figure 1.Specificity Test Results Chromatogram



Accuracy

Accuracy describes the closeness of the analysis results to the actual value.(Susanti & Dachriyanus, 2017)The accuracy of the analytical method is assessed based on the percent recovery (% recovery) of the test solution injections at various concentrations. The accuracy test results are shown in Table 2 below:

Table 2. Accuracy Test Results

Cetirizine Hydrochloride Concentration		Peak Area	Content (%)	Average Content (%)	Recovery (%)	Average Recovery (%)	RSD (%)
%	mg/mL						
80	0.08	1338764	80.41	80.32	101.54	101.43	0.09
		1336729	80.28		101.40		
		1336426	80.26		101.36		
100	0.10	1654683	99.38	99.47	100.42	100.38	0.23
		1654765	99.38		100.13		
		1659088	99.64		100.59		
120	0.12	2006244	120.49	120.40	101.47	101.36	0.09
		2004868	120.41		101.31		
		2003106	120.30		101.31		
Average recovery (%) :					101.06		
Acceptance Criteria		**RSD : ≤ 2%** **Average recovery: 98.0 – 102.0%**					

Based on Table 2, the average recovery of Cetirizine Hydrochloride was 101.06%, with the smallest RSD being 0.09% and the largest being 0.23%. These results demonstrate the accuracy of the method used.

Precision

Precision (repeatability) is carried out to determine the closeness of the results between one test and another test under the same conditions in a short time interval.(Susanti & Dachriyanus, 2017). Precision test results data can be seen in Table 3 below:

Table 3. Precision Test Results

Sample Number	Detected Area	Concentration (%)
1	1687065	101.31
2	1676904	100.71
3	1676170	100.66
4	1672460	100.42
5	1678768	100.83
6	1673231	100.49
7	1672815	100.43
8	1685003	101.16
9	1672559	100.44
10	1674762	100.56
		Average: 100.70
		SD : 0.31
		RSD : 0.31
Acceptance Criteria: RSD not more than 2%		

Based on Table 3, the average concentration of Cetirizine Hydrochloride was 100.70% with an RSD of 0.31%. These results demonstrate that the method used has good precision and repeatability.

Linearity and Range

Linearity was carried out to determine the ability of the analysis method to provide a response that is comparable to the concentration of Cetirizine Hydrochloride in the syrup preparation.(Susanti & Dachriyanus, 2017). The measurement results and graphs can be seen in Table 4 and Figure 2 below:

Table 4. Linearity Test Results

Cetirizine Hydrochloride Concentration		Detected Area
%	mg/mL	
80	0.08	1430332
90	0.09	1576231
100	0.10	1701682
110	0.11	1838011
120	0.12	1961451
Regression: y = bx + a **a = 381548.055** **b = 13191490.6** **r = 0.9996**		
Acceptance Criteria: r is greater than 0.999		

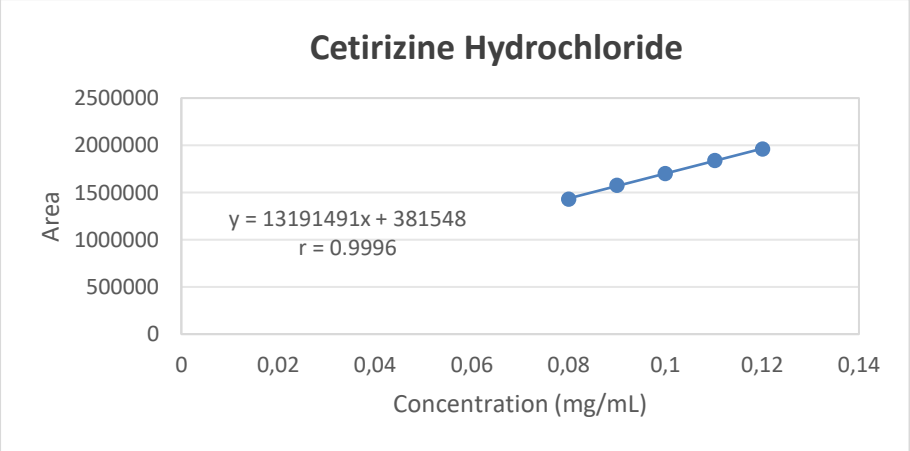


Figure 2. Linearity Test Results Graph

These results prove that the analysis method has good linearity over the test concentration range.

CONCLUSION

This study successfully verified the compendial HPLC method of the Indonesian Pharmacopoeia VI Edition (2020) for the determination of cetirizine HCl levels in syrup, with the main findings being the fulfillment of all parameters: system suitability (RSD area 0.232%, tailing factor 1.389), specificity (retention 24.842 minutes without matrix interference), accuracy (average recovery 101.06%, RSD ≤0.23%), precision (RSD 0.31%), and linearity (r=0.9996 in the 80-120% range). These results confirm the validity of the method for routine quality control analysis, supporting the consistency of active ingredients according to specifications [Ramadhan & Musfiroh, 2021]. The practical implication is to increase the reliability of testing in Indonesian pharmaceutical laboratories, minimizing the risk of variations in generic cetirizine syrup products widely used in pediatric patients.

However, limitations of this study lie in the use of a single sample batch and single laboratory conditions at PT. X, which may not capture the wide variety of commercial syrup matrices or long-term stability. Suggestions for future research include multi-batch studies, robustness testing against temperature/humidity fluctuations, and integration of MS detection for the identification of degradation products to strengthen industrial applications. This approach will enrich the HPLC verification data for antihistamine syrup preparations at the national level.

REFERENCES

Chaudhari, V., & Ubale, M. (2012). A validated stability-indicating HPLC assay method for cetirizine HCl in bulk drugs. International Journal of Advances in Pharmacy, Biology and Chemistry, 1(3), 136–142.

Chrissanti, RD, Darmawati, A., & Yuwono, M. (2020). Optimization of the HPLC method for determining the levels of 4-isobutylacetophenone and 2-(4-isobutyrylphenyl)propanoic acid in ibuprofen tablets. Indonesian Journal of Pharmacy and Pharmaceutical Sciences, 7(1), 26.

Ministry of Health of the Republic of Indonesia. (2020). Indonesian Pharmacopoeia, VIth Edition. Ministry of Health of the Republic of Indonesia.

Hasan, N., Chaiharn, M., Toor, U.A., Mirani, Z.A., Sajjad, G., Sher, N., & Siddiqui, F.A. (2016). Development, validation and application of RP-HPLC method: Simultaneous determination of antihistamines and preservatives with paracetamol in liquid formulations and human serum. The Open Medicinal Chemistry Journal, 10, 33–43.https://doi.org/10.2174/1874104501601000033

Ramadhan, SA, & Musfiroh, I. (2021). Review article: Verification of drug analysis methods. Farmaka, 19(2), 87–92.https://doi.org/10.24198/farmaka.v19i3.32328

Ramadhana, AF, & Hendriani, R. (2019). Problems and development of drug formulations for children's dosage forms. Pharmaceutical Magazine, 4(4), 230–239.https://doi.org/10.37376/mfarmasetika.v4i4.23064

Ritonga, M., & Daulay, A. (2023). Application of UV-spectrophotometry method in determining the levels of generic and trade-name cetirizine tablets. Traditional Health Journal, 1(2), 94–101.https://doi.org/10.47134/jkt.v1i2.290

Riyanto. (2014). Validation & verification of test methods: In accordance with ISO/IEC 17025 testing and calibration laboratories. Deepublish.

Shadrina, JA, Hilmi, IL, Sudarjat, H., Affandhy, AK, & Dzannuba, FL (2024). Clinical preference for cetirizine or chlorpheniramine maleate in the treatment of allergies. Journal of Public Health, 8(3), 7564–7575.https://doi.org/10.12345/jkm.v8i3.37749

Shamshad, H., Naz, A., & Mirza, A.Z. (2021). Reverse phase HPLC method for the simultaneous determination of cetirizine, verapamil/diltiazem and amlodipine. Analytical and Bioanalytical Chemistry Research, 8(2), 120–130.

Susanti, M., & Dachriyanus. (2017). High-performance liquid chromatography. LPTIK Andalas University.

Wang, DY, et al. (2022). Cetirizine for the treatment of allergic diseases in children: A systematic review and meta-analysis. Frontiers in Pediatrics, 10, Article 940213.https://doi.org/10.3389/fped.2022.940213

Zuberbier, T., Aberer, W., Asero, R., Bindslev-Jensen, C., Brzoza, Z., Canonica, GW, Church, MK, Ensina, L.F., Giménez-Arnau, A., Godzik, P., Hoffmann-Sommergruber, K., Hossenbaccus, D., Klimek, L., Mosges, R., Nakahara, T., Nasser, S., Nogueiras, J., et al. (2024). Cetirizine. In StatPearls. StatPearls Publishing.