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Florentinus Dika Octa Riswanto

Faculty of Pharmacy Universitas Sanata Dharma, Campus III Paingan, Maguwoharjo, Depok,
Yogyakarta 55282, Indonesia; Email: dikaocta@usd.ac.id

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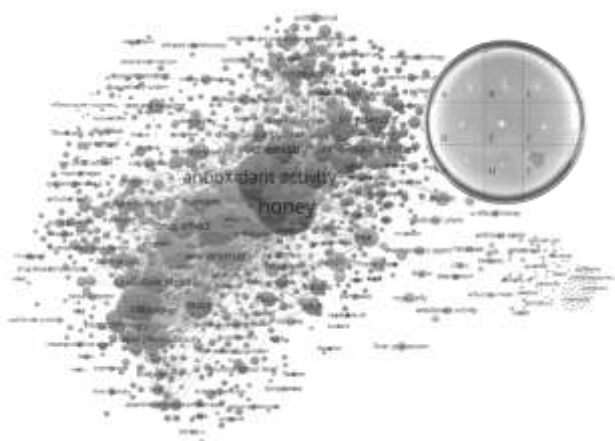
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See Khairunnisa *et al.*, p.64

Figure 2. Inhibition of W/O/W emulsion against *E. coli*; A (F1, formula with Cremophor RH 40 1% and Span 80 3.85%); B (FA, formula with Cremophor RH 40 1.5% and Span 80 3.85%), C (FB, formula with Cremophor RH 40 1% and Span 80 4.5%), and D (FAB, formula with Cremophor RH 40 1.5% and span 80 4.5%); E (F1 non-bacteriophage (N1)); F (non-bacteriophage FA (NA)); G (non-bacteriophage FB (NB)); H (non-bacteriophage FAB (NAB)); I (K + / non-formulation PT1b).

See Setyawan *et al.*, p.83

Figure 3. Network visualization of the topic by VOSviewer

Quality Assessment of Extemporaneous Capsule Preparation Containing Methylprednisolone, CTM, and Theophylline Using Spectrophotometrics and Chemometrics Techniques

Muhammad Darmawangzah¹, Florentinus Dika Octa Riswanto¹, Irnawati^{2*}

¹Division of Pharmaceutical Analysis and Medicinal Chemistry, Faculty of Pharmacy, Universitas Sanata Dharma, Yogyakarta, 55282, Indonesia

²Study Program of Pharmacy, Faculty of Pharmacy, Halu Oleo University, Kendari, 93232, Indonesia

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Article Info	ABSTRACT
<p>Received: 2024-06-04 Revised: 2024-07-03 Accepted: 2024-07-09</p> <p>*Corresponding author: Irnawati email: irnawati.vhina@gmail.com</p> <p>Keywords: Chemometrics; Chlorpheniramine maleate (CTM); Methylprednisolone; Theophylline; UV-Vis spectrophotometry</p>	<p>Currently, doctors in developing countries still prefer to prescribe compounding drugs because certain drugs are not available in ready-made dosage forms. It is considered that the capsule formulation can increase patient compliance because it requires a smaller amount of medication. In particular, for asthma patients, extemporaneous capsule preparation containing methylprednisolone, CTM, and theophylline is usually prescribed. However, theophylline, which has a narrow therapeutic index, combined with small doses of methylprednisolone and CTM, may result in inconsistent drug content in the compounded drug. This study aimed to assess the quality of the capsule mixture containing methylprednisolone, CTM, and theophylline formulated at the "X" Kolaka Community Health Center, Southeast Sulawesi, Indonesia. Extemporaneous capsules are tested using various methods such as organoleptic tests, moisture content tests, disintegration time tests, and content uniformity tests. The quality test results of the compounding capsule with the active substance a combination of methylprednisolone, CTM, and theophylline formulated at the "X" Kolaka Health Center met the quality requirements with organoleptic tests, moisture content tests, and disintegration time tests. The content uniformity test does not meet the requirements according to the Indonesian Pharmacopoeia VI edition based on the acceptance values of L1% and L2%. Extemporaneous capsule preparation containing methylprednisolone, CTM, and theophylline met the quality requirements with organoleptic tests, moisture content tests, and disintegration time tests. However, the content uniformity test does not meet the requirements according to the Indonesian Pharmacopoeia VI edition based.</p>

INTRODUCTION

Extemporaneous drug preparations are preparations that are formed by mixing medicinal preparations or active ingredients. Doctors are still interested in prescribing medicines in the form of capsule formulations; this happens because some medicines with certain doses are not available in a ready-to-use form (Putra *et al.*, 2017; Yuliani *et al.*, 2023). Apart from that, giving capsules is expected to

increase patient compliance in using medication because they do not take large amounts of medication (Andriani *et al.*, 2014).

Prescription of medicines in compound form (powder, divided powder, compound capsule) is very widely accepted at the "X" Kolaka Health Center, Southeast Sulawesi, Indonesia. In the process of compounding capsule preparations, the distribution of powder is still done visually. The visual method is the most

widely used division method because it is fast and practical. However, this method has many weaknesses, namely unable to guarantee uniformity in content and uniformity in weight of each compound capsule (Putra *et al.*, 2017). The risk that arises due to non-uniformity in the preparation of compound capsules is the non-uniformity of the drug dose received by the patient. Non-uniformity of drug doses can result in toxicity for patients if patients receive drugs with a narrow therapeutic index (Kasanah *et al.*, 2019). Accordingly, it is important to know the uniformity of the content of the compound capsule being made to ensure uniformity of drug dosage.

This study used a capsule preparation containing theophylline, CTM, and methylprednisolone which was prescribed to adult patients with asthma. Based on clinical risk analysis, small doses of CTM and methylprednisolone can potentially lead to non-uniformity in the content of the compounded drug which results in dose non-uniformity, namely the dose could be an underdose or overdose (Andriani *et al.*, 2014). Apart from that, one of the active substances used has a narrow therapeutic index, namely theophylline (Handiana and Indriyati, 2016). Theophylline has a narrow therapeutic index of 10-20 mg/L and is given every 6 hours (Katzung, 2012). Therefore, it requires monitoring of drug levels in the blood (Therapeutic Drug Monitoring). This further strengthens the importance of monitoring the quality of compounded preparations, which is the responsibility of a pharmacist (Betha *et al.*, 2019).

The content uniformity test in this study used a combination method of chemometrics-ultraviolet-visible (UV-Vis) spectrophotometry. The use of spectrophotometry in combination with chemometrics allows for the application of complex mixture analysis without component separation (El-Gindy and Hadad, 2012; Dzulfianto *et al.*, 2017). In another study, the determination of theophylline and methylprednisolone levels was successfully carried out using the UV-Vis spectrophotometric method (Maheswari, 2022). Analysis of the compound preparation containing CTM was successfully carried out using spectrophotometry (Hariyati and Yuliani, 2022). Therefore, the combination of chemometrics-UV-Vis spectrophotometry is a new, accurate, and fast technique that will provide accurate results for determining the quality of preparations (Shafirany *et al.*, 2018).

METHODS

Material

The materials used are capsule preparation at the "X" Kolaka Health Center with the active substances methylprednisolone, CTM, and theophylline; Methylprednisolone standard with a purity of 98.57%, CTM standard with a purity of 100.09%, and theophylline standard with a purity of 98.43% obtained from the Indonesian Food and Drug Authority (Indonesian FDA) (Central Jakarta City, Jakarta, Indonesia), and PT Ifars Pharmaceutical Laboratories (Waru, Pulosari, Kebakkramat Subdistrict, Karanganyar Regency, Central Java, Indonesia); and methanol P with a purity of 99.8% obtained from PT. Smart Lab Indo (Sidoarjo, East Java, Indonesia).

Instrumentation and Software

The instrument used was a UV-visible 1800 spectrophotometer (Shimadzu®); 1 cm quartz cuvette (Hellma®); a set of computers (ASUS®); Disintegration tester (Shanghai Develop Machinery BJ-2®); gram balance analytical scale with sensitivity 0.0001 (Fujitsu FS-AR®); micropipette (Eppendorf®) 0.5-10 µL, 10-100 µL, 20-200 µL, and 100-1000 µL; label paper (Kenjoy®); dropper pipette (Hawarilab®); glass beaker (Pyrex®); mortar and stamper; oven (Labtech Daihan®); filter paper; glass funnel (Pyrex®); measuring flask (Pyrex®) 5 mL, 10 mL, and 50 mL. UV spectral data were exported to Excel 2010 (Microsoft, USA®) and converted into a .csv format file for further data processing. Statistical analysis and multivariate calibration were performed using R software version 4.2.1 with the 'pls' package.

Sample Preparation

The samples tested in this research are capsule preparations with active substances methylprednisolone, CTM, and theophylline which were prepared at the "X" Kolaka Health Center with the following recipe:

R/ Methylprednisolone 4 mg	1/2 tab
CTM 4 mg	1/2 tab
Theophylline	100 mg
mf pulv da in caps dtd no LX	
S 3 dd 1 pc	

Sampling was carried out at the "X" Kolaka Health Center by filling the prescription twice. For the first prescription, 60 capsules were taken for organoleptic testing of 10 capsules, moisture content test of 8 capsules, disintegration time test of 12 capsules, and content uniformity test of 30 capsules. For the second prescription, 60 capsules were taken for chemical stability testing.

Organoleptic Test

The organoleptic test was conducted by visually observing the uniformity of the powder in the capsule and the physical condition of the capsule prepared at the "X" Kolaka Community Health Center. There were 10 capsules taken and divided into 2 parts to be observed on day 1 and day 30 for the specificity of the smell, capsule shape, and color of the samples tested.

Moisture Content Test

The moisture content test was conducted using the gravimetric method. At first, 8 capsules are taken and divided into 2 parts for day 1 and day 30. First, weigh and record the weight of the empty container, then the powder in the capsule will be weighed carefully in a container that has been weighed (initial powder weight), then dried in an oven at a heating temperature 105°C for 4 hours until constant, after that it is weighed and the weight of the container containing the powder is recorded (final powder weight), then the percentage of moisture content in the powder is calculated using the gravimetric method formula (Azmi, 2018).

Disintegration Time Test

The disintegration time test was conducted by preparing 12 capsules divided into 2 parts for day 1 and day 30. Prepare 6 capsules, and put each capsule into 6 tubes from the basket. A 10-mesh gauze is placed on the top plate surface of the basket assembly. The tool is turned on with the water temperature set to 37.0 ± 2.0 as the medium (Kemenkes RI, 2020). The tube was then dipped into a 1000 mL beaker containing water and then the apparatus was run for 30 minutes. Disintegration time was recorded as the time at which the capsule disintegrated into powder particles.

Content Uniformity Test

Preparation of Standard Solutions

After weighing 10 mg methylprednisolone, 10 mg CTM, and 50 mg theophylline, then each are dissolved separately into a 25 mL measuring flask to methylprednisolone and CTM, while theophylline into a 50 mL measuring flask using methanol as a solvent, this solution is labeled as a stock solution methylprednisolone, CTM, and theophylline. Furthermore, the standard solution

was read for absorbance using a UV-Vis spectrophotometer at a wavelength of 200-400 nm to ensure that there were overlapping spectra in the three standard solutions.

Preparation of Calibration Series and Validation Series Solutions

Next, 25 calibration series solutions (training set) and 10 validation series solutions (test set) were made. The concentration range methylprednisolone, CTM, and theophylline is a non-fixed number value that can be modified to suit the orientation results during testing. Calibration series and validation series are created at certain concentrations based on random numbers (actual concentrations) can be seen in Table 1. Then, the absorbance of each mixture was measured using a UV-Vis spectrophotometer at a wavelength of 200-400 nm. The absorbance data obtained were used to produce calibration and validation series models.

Multivariate Calibration Model Analysis

The absorbance values for each wavelength obtained from the calibration series and validation series solutions were analyzed statistically using R studio software. The PLS statistics package was used to perform chemometric data processing. This package was downloaded and installed using the install packages ("pls") function. Once successfully installed, the package was loaded using the library (PLS) function before further statistical analysis. Several multivariate calibration models such as principal component regression (PCR) and partial least squares (PLS) made for methylprednisolone, CTM, and theophylline. Then R studio software is also used to transform the initial data into several variations of data sets by creating new files such as SNV (standard normal variation), MSC (multiplicative scatter correction), D1 (first derivative), and D2 (Second derivative). Models built on multivariate calibration are evaluated statistically by assessing the coefficient of determination (R^2), root mean error of calibration (RMSEC), root mean square error of cross-validation (RMSECV), and root mean error of prediction (RMSEP). Next, a multivariate calibration model for each mixture that produces an R^2 value close to 1, and lower RMSEC, RMSECV, and RMSEP are selected for determination of levels (Rohman *et al.*, 2022).

Table 1. Calibration Series and Validation Series Solution Concentrations for Each Mixture











No	Calibration Solution Concentration ($\mu\text{g/mL}$)			No	Validation Solution Concentration ($\mu\text{g/mL}$)		
	Theophylline	CTM	Methylprednisolone		Theophylline	CTM	Methylprednisolone
1	145	6	7	1	66	13	14
2	122	7	11	2	88	13	3
3	101	7	10	3	73	19	7
4	106	2	12	4	116	8	8
5	57	7	10	5	111	15	17
6	145	7	1	6	128	11	12
7	78	12	14	7	123	8	19
8	146	9	20	8	139	6	13
9	144	1	12	9	61	17	18
10	120	19	19	10	79	3	2
11	112	10	8				
12	123	16	19				
13	90	16	15				
14	95	9	19				
15	107	7	1				
16	81	5	17				
17	73	17	2				
18	52	15	19				
19	147	17	11				
20	54	16	4				
21	81	17	2				
22	85	2	15				
23	111	3	7				
24	89	10	16				
25	137	12	11				

Determination of the container containing capsules methylprednisolone, CTM, and theophylline

A total of 10 capsule preparation samples were used for concentration determination methylprednisolone, CTM, and theophylline in capsule preparations. Each capsule was weighed using an analytical scale, dissolved with methanol in a different 25 mL volumetric flask, filtered using filter paper, and methanol added to the limit mark. Next, 125 μL was taken using a micropipette, 20-200 μL was put into a 5 mL measuring flask and methanol was added up to the mark. Next, it is measured using a UV-Vis spectrophotometer with a wavelength of 200-400 nm, and the absorbance values obtained were then processed using the multivariate calibration chemometric method.

The levels of theophylline, CTM, and methylprednisolone in the samples were obtained by entering the predicted/calculated level values (y) into the calibration curve equation created for each active ingredient, therefore that the actual values (x) were obtained. The x value obtained is then converted into a percent content according to the label. Then the acceptance value for the uniformity of sample content is calculated using the acceptance value (NP) formula. If it does not meet the required value, the previous procedure is repeated for the remaining 20 capsules (Kemenkes RI, 2020).

Table 2. Organoleptic test results

Samples	Day 1		Day 30	
	Results	Visual	Results	Visual
Sample 1	sample color : green sample consistency : hard sample odor : characteristic		sample color : green sample consistency : hard sample odor : characteristic	
Sample 2	sample color : green sample consistency : hard sample odor : characteristic		sample color : green sample consistency : hard sample odor : characteristic	
Sample 3	sample color : green sample consistency : hard sample odor : characteristic		sample color : green sample consistency : hard sample odor : characteristic	
Sample 4	sample color : green sample consistency : hard sample odor : characteristic		sample color : green sample consistency : hard sample odor : characteristic	
Sample 5	sample color : green sample consistency : hard sample odor : characteristic		sample color : green sample consistency : hard sample odor : characteristic	

RESULTS AND DISCUSSION

The recipe for compound capsule preparations with a combination of active ingredients methylprednisolone, CTM, and theophylline is a compounding prescription received from the "X" Kolaka Health Center as an asthma medication prescribed twice. For the first prescription, 60 capsules were taken for organoleptic testing of 10 capsules, moisture content test of 8 capsules, disintegration time

test of 12 capsules, and content uniformity test of 30 capsules. For the second prescription, 60 capsules were taken for chemical stability testing. Compounding capsule preparations if it is not in accordance with good compounding procedures will affect the quality of the compounding capsule preparation. This research is exploratory to see the quality of capsule preparations with the active substance a combination of methylprednisolone, CTM, and

theophylline received from the "X" Kolaka Community Health Center, whether they meet the criteria for quality test parameters for compound capsule preparations such as organoleptic test, moisture content test, disintegration time test, and content uniformity test.

Organoleptic tests are conducted to determine the physical condition of the compound preparation during the storage period in a tightly closed container away from sunlight at conditions. The organoleptic test results obtained in Table 2 show that during the storage period, on day 1 and day 30, all samples did not experience changes in organoleptic results during the storage period, which indicates that the compounded capsule preparation is physically stable because it is able to maintain its physical shape (Rahman *et al.*, 2018).

The moisture content test aims to determine the water content contained in the preparation. A good and stable powder in storage has a moisture content of less than 5% (Elisabeth, 2018). The results of the moisture content test are based on Table 3. The results on day 1 obtained an average of 2.601% and on day 30 an average of 4.312%, so it can be concluded that all the compound capsules met the requirements for the moisture content of the preparation, namely less than 5%. During the storage period, the percentage value of moisture content on the 30th day increases, which is influenced by the potential interaction between

the capsule preparation and water molecules in the storage environment, where drugs in the form of salt will more easily absorb moisture from the environment resulting in an increase in the percentage of moisture content during the storage period of the capsules (Armstrong *et al.*, 2014). This can also be influenced by the presence of excipients in the tablet packaging which does not specify the type of excipient, where some excipients are hygroscopic and therefore, they can affect the moisture of the sample (Varma, 2016).

The disintegration time test aims to determine the time required for the capsule to completely disintegrate. Capsules are able to provide a therapeutic effect if they are disintegrated into small particles and the contents of the capsule can be absorbed in the digestive tract (Nurani *et al.*, 2017). The results of the disintegration time test were obtained can be seen in Table 4, indicating that on day 1 and day 30 the same results. This shows that the capsule preparation combined with theophylline, CTM, and methylprednisolone meets the disintegration time requirements for solid oral preparation. This shows that there is no change in the disintegration time of the capsule during the 30-day storage period, then the capsule is able to disintegrate completely in less than 15 minutes. Capsule preparations are declared to meet the requirements if they are able to disintegrate completely in less than 15 minutes (Kemenkes RI, 2020).

Table 3. Moisture content test results

Capsule Samples	Day 1	Capsule Samples	Day 30
	Percentage of MC (%)		Percentage of MC (%)
Sample 1	2.372	Sampel 1	3.750
Sample 2	2.745	Sampel 2	4.132
Sample 3	2.500	Sampel 3	4.800
Sample 4	2.789	Sampel 4	4.564
Mean	2.601	Mean	4.312
SD	0.199	SD	0.465
CV	7.653	CV	10.796

Table 4. The disintegration time test data

Observation time	Observation results	
	Day 1	Day 30
1 minute	The capsule shell is soft throughout	The capsule shell is soft throughout
2 minutes	A little of the capsule shell remains	A little of the capsule shell remains
3 minutes	The powder in the capsules dissolves	The powder in the capsules dissolves
4 Minutes	The capsule preparation is completely disintegrated	The capsule preparation is completely disintegrated

Based on the data results presented in Figure 1, it is known that the spectra of compounds methylprednisolone, CTM, and theophylline showed overlapping spectra results. When the spectra of a mixture of compounds overlap, then the concentration of each compound cannot be determined without prior separation (Miller and Miller, 2010). This can be overcome by combining UV-Vis spectrophotometric methods with chemometrics, and using multivariate calibration with principal component regression (PCR) or partial least squares (PLS) models, because these models are able to predict well when there is a random linear baseline or principal component spectra which overlap (Dewi, 2021). Furthermore, the results obtained from scanning 25 concentrations of the calibration series solution and 10 concentrations of the validation series solution at a wavelength of 200-400 nm also showed the same pattern where overlapping occurred, therefore with the chemometric method this problem could be overcome. By combining UV-Vis spectrophotometry and chemometric methods, we can predict analysis results well if there are overlapping spectra (Dewi, 2021).

Multivariate calibration chemometric methods implemented in this study are principle component regression (PCR) and Partial Least Squares (PLS). All multivariate calibration models were built using R studio software (R Core Team, 2021), by utilizing a statistical package called 'PLS' (Mevik and Wehrens, 2019). This technique is applied to produce predictive models for methylprednisolone, CTM, and theophylline. Then, the absorption data that are processed include absorption data selected from several absorption data at wavelengths around 200-400 nm which can be seen in Table 5. This process is done to reduce absorption data that interfere with data processing to obtain the best calibration model (Sinulingga, 2021).

Absorption data processing begins by transferring the actual concentration value of each active substance along with the absorbance value of the absorption data to R studio software

by leaving one out of cross-validated PCR and PLS models. The resulting data obtained are the coefficient values used to calculate the calculated concentrations on each active substance (calculated). The leave-one-out cross-validation method can determine the number of PCR and PLS calibration model components that can characterize the data, while the selected components are considered to represent the number of components in each model (Sinulingga, 2021). The actual concentration value is the concentration created based on random numbers at the calibration and validation series solution-making stage, while the calculated concentration value is the concentration obtained from predictions from the PCR and PLS models (Riswanto, 2022).

The quality of the built multivariate calibration model was evaluated statistically by assessing several performances such as R^2 (R_{cal}^2 , R_{cv}^2 , and R_{val}^2) and RMSE (RMSEC, RMSECV, and RMSEP). The model will be better if the resulting R^2 value is quite good (a value between 0.7-0.9) or good (a value ≥ 0.9), and the resulting RMSE value is low (close to zero) (Rohman *et al.*, 2022). The higher the R^2 value means it represents a smaller difference between the actual value and the calculated value, while the lower the RMSE value indicates the minimum error (Rohman *et al.*, 2022).

Based on the data presented in Table 5, it was obtained that the selected model for methylprednisolone was a wavelength of 215-300 nm in the PLS model for the D1 (first derivative) spectrum with R_{cal}^2 , R_{cv}^2 , and R_{val}^2 are 0.9862, 0.9541, and 0.9937. The model error is expressed from RMSEC, RMSECV, and RMSEP with values of 0.7017, 1.2800, and 0.4564. The equality to correlate between actual values and calculated concentration value for methylprednisolone is $y = 0.9334x + 0.0861$ ($R^2 = 0.9937$). The component plot of leave-one-out cross-validation results, regression coefficient plot, and regression plot of methylprednisolone PLS multivariate calibration model are depicted in Figure 2.

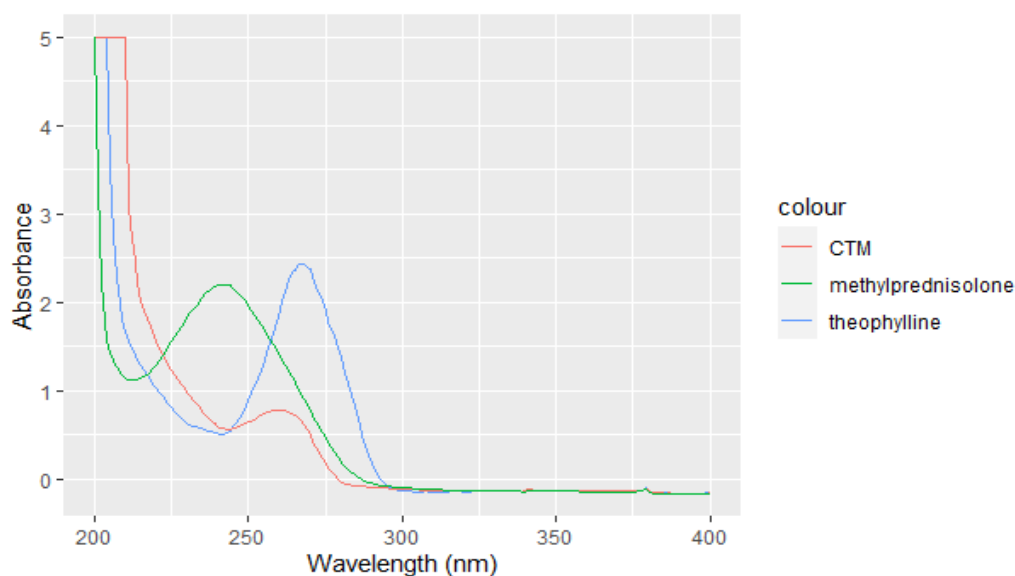


Figure 1. Spectra of standard solutions of methylprednisolone 400 µg/mL, CTM 400 µg/mL, and theophylline 100 µg/mL

Table 5. Analysis of calibration and validation model of *principal component regression* (PCR) and *partial least square* (PLS) for methylprednisolone, CTM, and theophylline

Analytes	Wavelength (nm)	Multivariate Calibration	Spectra	Comp. Number	R _{cal} ²	RMSEC	R _{cv} ²	RMSECV	R _{val} ²	RMSEP		
Methylprednisolone	215-300 nm	PLS	Original	10	0.9920	0.5332	0.9487	1.3540	0.9093	1.7358		
			D1	7	0.9862	0.7017	0.9541	1.2800	0.9937	0.4564		
			D2	12	0.9970	0.3248	0.4207	4.5490	0.9426	1.3804		
			MSC	9	0.9789	0.8683	0.7638	2.9050	0.8988	1.8334		
			SNV	10	0.9869	0.6829	0.8207	2.5310	0.9096	1.7322		
		PCR	Original	17	0.9931	0.4977	0.9545	1.2750	0.8962	1.8564		
			D1	11	0.9856	0.7179	0.9521	1.3080	0.9902	0.5715		
			D2	23	0.9916	0.5488	0.3674	4.7540	0.9215	1.6147		
			MSC	13	0.9754	0.9366	0.7992	2.6780	0.8895	1.9158		
			SNV	15	0.9830	0.7803	0.8462	2.3440	0.9013	1.8103		
		CTM	244-300 nm	PLS	Original	4	0.8383	2.1502	0.6292	3.2560	0.9651	0.8955
					D1	19	0.9680	1.0307	0.8633	1.7732	0.9473	1.1008
D2	5				0.9330	1.3845	0.8375	2.1560	0.9009	1.5100		
MSC	3				0.7338	2.7590	0.6059	3.3570	0.4470	3.5670		
SNV	3				0.7624	2.6068	0.6439	3.1910	0.7072	2.5958		
PCR	Original			4	0.8275	2.2209	0.6546	3.1430	0.9735	0.7805		
	D1			23	0.9618	1.1257	0.8228	2.2509	0.8699	1.7299		
	D2			10	0.9071	1.6304	0.8288	2.2127	0.8090	2.0967		
	MSC			3	0.7332	2.7624	0.6116	3.3330	0.4434	3.5787		
	SNV			3	0.7613	2.6130	0.6476	3.1740	0.7056	2.6027		
Theophylline	214-300 nm			PLS	Original	1	0.6895	16.4209	0.7828	12.4839	0.8034	11.8782
					D1	2	0.8565	10.1485	0.8162	11.4840	0.8529	10.2760
		D2	4		0.9084	8.2576	0.8738	9.5176	0.8911	8.8867		
		MSC	1		0.2133	26.1381	0.6302	17.9218	0.4140	20.5069		
		SNV	1		0.2035	26.3006	0.6481	17.4810	0.2840	22.6683		
		PCR	Original	1	0.8023	11.9126	0.7760	12.6780	0.8035	11.8738		
			D1	2	0.8567	10.1416	0.8193	11.3883	0.8369	10.6508		
			D2	7	0.8723	9.5713	0.8528	10.2788	0.8738	9.5176		
			MSC	2	0.2366	25.7489	0.6982	16.1884	0.5031	18.8835		
			SNV	2	0.2253	25.9279	0.7173	15.6681	0.4333	20.1671		

Notes: Selected model for each analyte were marked using bold fonts

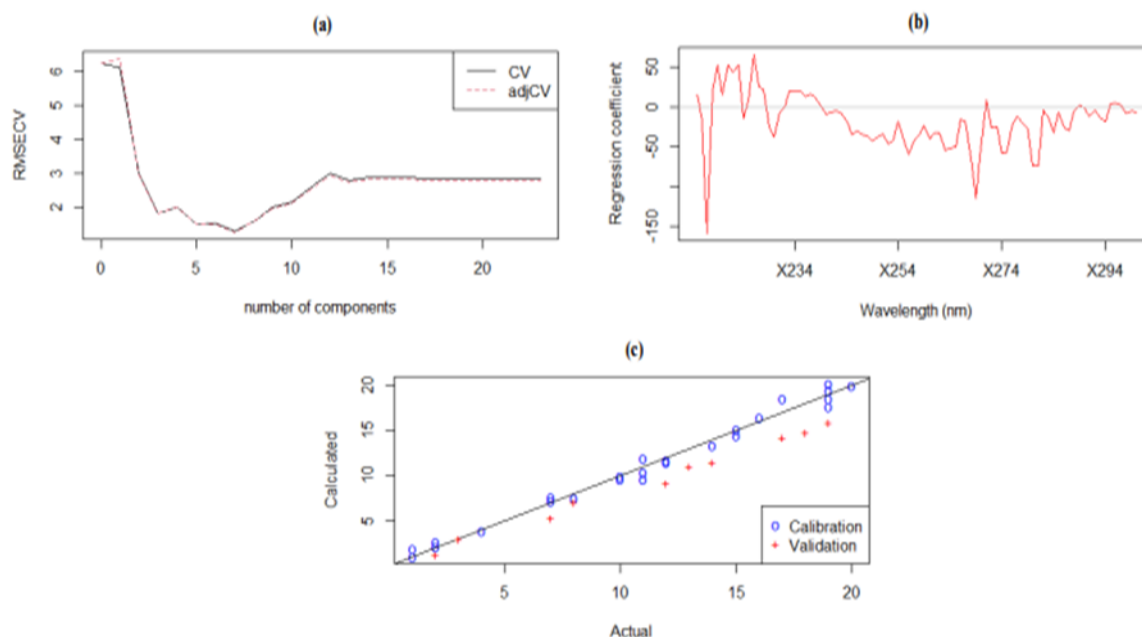


Figure 2. Results of cross-validation using *leave one out* (a), regression coefficient plot (b), and prediction plot (c) for methylprednisolone according to the best multivariate calibration model

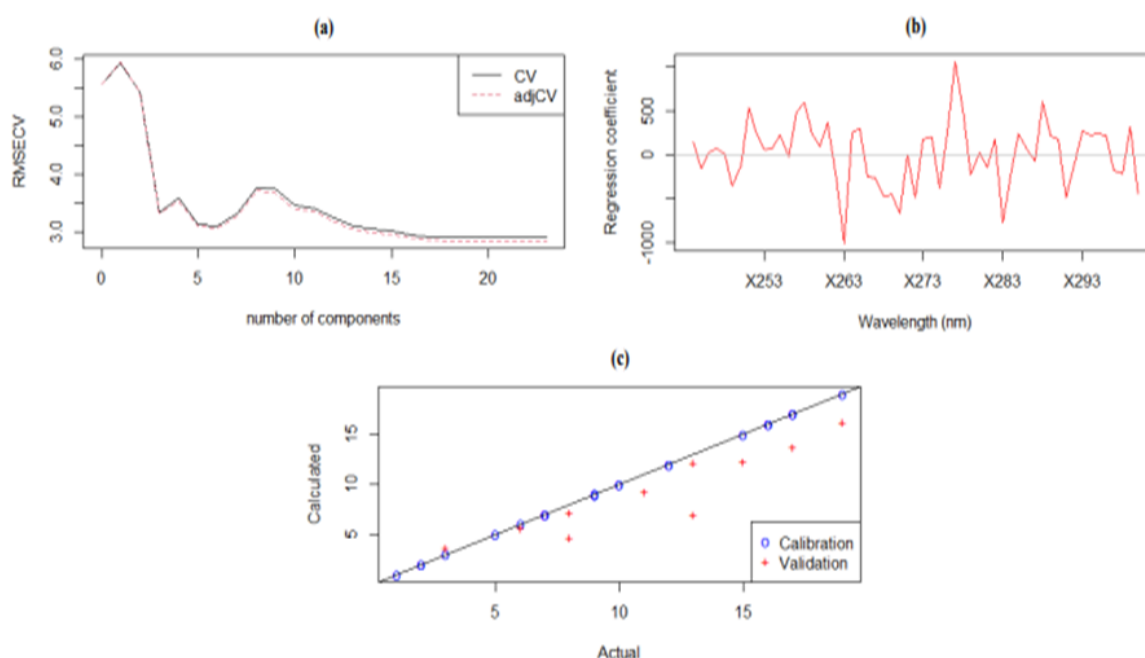


Figure 3. Results of cross-validation using *leave one out* (a), regression coefficient plot (b), and prediction plot (c) for CTM according to the best multivariate calibration model

The model chosen for CTM is wavelength 244-300 nm in the PLS model for D1 (first derivative) spectra with R_{cal}^2 , R_{cv}^2 , and R_{val}^2 are 0.9680, 0.8633, and 0.9473. The model error is expressed from RMSEC, RMSECV, and RMSEP

with values of 1.0307, 1.7732, and 1.1008 respectively. The equality to correlate between actual values and calculated concentration values for CTM is $y = 0.8764x + 0.4035$ ($R^2 = 0.9473$). The component plot of leave-one-out

cross-validation results, regression coefficient plot, and regression plot PLS CTM multivariate calibration model are depicted in Figure 3.

The selected model for theophylline is wavelength 214-300 nm in the PLS model for spectra D2 (second derivative) with R_{cal}^2 , R_{cv}^2 , and R_{val}^2 are 0.9084, 0.8738, and 0.8911. The model error is expressed from RMSEC, RMSECV, and RMSEP with values of 8.2576, 9.5176, and

8.8867. The equality to correlate between actual values and calculated concentration values for theophylline is $y = 1.0861x - 9.3643$ ($R^2 = 0.8911$). The component plot of leave-one-out cross-validation results, regression coefficient plot, and regression plot PLS theophylline multivariate calibration model are depicted in Figure 4.

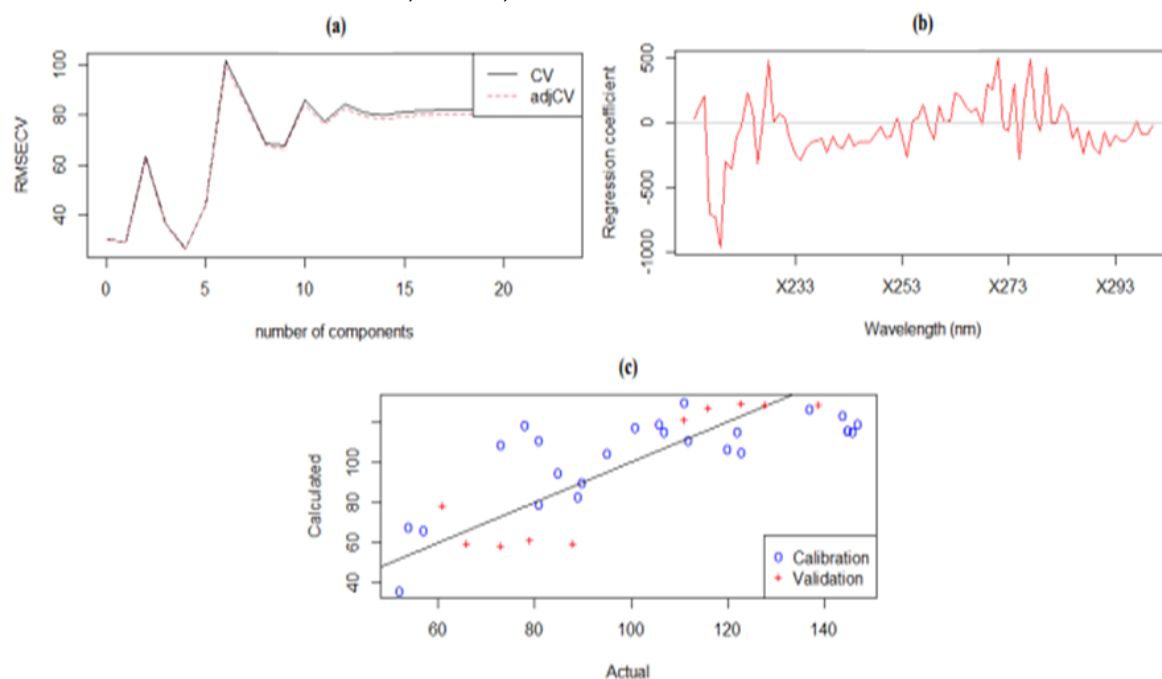


Figure 4. Results of cross-validation using *leave one out* (a), regression coefficient plot (b), and prediction plot (c) for theophylline according to the best multivariate calibration model

Table 6. Results of content uniformity test of extemporaneous capsules containing methylprednisolone, CTM, and theophylline

Content uniformity for 10 capsules			
Sample	Methylprednisolone content (%)	CTM content (%)	Theophylline content (%)
Mean	97.7426	95.0915	107.3021
SD	15.3952	15.8143	7.7957
CV	15.7507	16.6306	7.2652
NP L1%	38.5591	43.3219	23.2386
Content uniformity for 30 capsules			
Sampel	Methylprednisolone content (%)	CTM content (%)	Theophylline content (%)
Mean	102.4908	95.2949	111.8620
SD	17.1319	17.9856	10.5172
CV	16.7156	18.8736	9.4019
NP L2%	34.4219	40.9523	29.1658

Based on the data presented in Table 6, shows that the uniformity of the levels of the compound capsule does not meet the requirement of good acceptance value in the L1% value, namely 15.0, and the L2% value, namely 25.0. The discrepancy between the uniformity of the levels of acceptance values (NP) of L1% and L2% with those required can be caused by variations in capsule weight and the capsules tested are taken randomly so the levels of each capsule tested may be also not uniform.

The results of the content uniformity value of L2% in 30 units of capsule preparation showed that the uniformity value of methylprednisolone content with CTM was smaller than the content uniformity value of L1% in testing 10 units of capsule preparation, and the uniformity value of theophylline content was greater. This can be caused by random sampling, where at each random sampling the active substance levels are obtained that are not in accordance with those prescribed and have levels that are greater or smaller than in the random sampling of the 10 previously compound capsules (Pandhita, 2022).

Results that do not comply with the requirements for uniformity of content contained in the literature can be caused by the use of a blender when mixing capsule preparations and dividing the compound results visually. The blender has a part that allows the drug dose to be reduced due to the drug powder remaining in parts of the blender that are difficult to reach (Chalik *et al.*, 2019). Then, during compounding, the compound of powder is distributed by dividing the compound evenly on parchment paper visually in amounts according to the recipe. Even though this method is fast and practical, it cannot guarantee the uniformity of the resulting capsules, therefore it can affect the dosage and uniformity of the capsule content produced (Rahayu and Yulyuswarni, 2020).

Apart from that, the influence of limitations in accuracy, skill, and compounding time is also a factor causing variations in the weight of each compounded capsule (Putra *et al.*, 2017). This could be due to the fact that at the time of sampling, there were many patients visiting and redeeming medicines at the "X" Kolaka Health Center Pharmacy Installation, while the number of pharmacists was not that large. These several factors then cause variations in the content of each capsule preparation unit, thus causing the acceptance (NP) of determining the content uniformity level of L1% in 10 capsule preparation units and L2% in 30 capsule

preparation units to exceed the acceptance requirements.

The increase and decrease in levels of the active substances CTM and methylprednisolone may be caused by storage conditions. This can happen due to the compounded preparation's physical and chemical characteristics, which can change from the initial preparation time to the storage time (USP, 2019). On active substances, CTM contains amine groups and has the potential for N-oxidation to cause detrimental effects in the form of loss of activity or changes in the concentration of active substances that occur during storage (Baertschi *et al.*, 2016), whereas in the active substance methylprednisolone can undergo degradation caused by hydrolysis with acids or base catalysis at room temperature, the presence of hydroxyl groups causes methylprednisolone to be oxidized into aldehyde (Baertschi *et al.*, 2016). Due to the presence of OH groups that enter the primary alcohol group (Dangi and Oh, 2019). Some of these changes have the potential to cause detrimental effects such as loss of activity or changes in the concentration of active substances during the sample storage period (Baertschi *et al.*, 2016).

There is an increase in the levels of the active substance theophylline during storage, possibly due to the nature of the capsule which can absorb or release moisture (Srividya *et al.*, 2014). Moisture will increase molecular mobility and chemical reactivity (Golonka *et al.*, 2015). Then, the hygroscopic nature of theophylline causes clumping and affects the test results (Guo *et al.*, 2021). The potential for interaction between capsule preparations and water molecules in the storage environment has an impact on medicines in the form of salt which will more easily absorb moisture during the capsule storage period (Armstrong *et al.*, 2014). CTM is a drug in its salt form which is hygroscopic. CTM has the risk of experiencing instability because it is influenced by humidity, where CTM is hygroscopic in the form of maleic salt so it is likely to get wet (Kurniawan, 2014). Hygroscopic drugs have the ability to absorb water molecules, increasing the moisture content of the sample (Nurjanah *et al.*, 2021).

CONCLUSIONS

Capsule preparation with a combination of active substances methylprednisolone, CTM, and theophylline which was formulated at the "X" Kolaka Community Health Center has met the quality requirements with organoleptic tests, moisture content tests, and disintegration time

tests. However, the content uniformity test does not meet the requirements according to the Indonesian Pharmacopoeia VI edition based on the acceptance values of L1% and L2%.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

REFERENCES

- Andriani, D., Wijaya, I.N., and Utami, W., 2014. Profil Peresepan Sediaan Kapsul Racikan Di Apotek "X" Di Surabaya. *J Farm Komunitas*, 1(2), 41–4.
- Armstrong, B., Brockbank, K., and Clayton, J., 2014. Understand the Effects of Moisture on Powder Behavior. *Chem Eng Prog*, 110(10), 25–30.
- Azmi, M.H., 2018. Formulasi Tablet Ekstrak Etanol Daun Jamblang (*Syzygium Cumini* (L.) Dengan Variasi Konsentrasi Sodium Starch Glycolate Sebagai Superdisintegran. Skripsi, Fakultas Ilmu Kesehatan UIN Syarif Hidayatullah, Jakarta, Indonesia.
- Baertschi, S.W., and Alsante, K.M., and Reed, R.A., 2016. Pharmaceutical Stress Testing: Predicting Drug Degradation, CRC Press, ISBN 1439801800.
- Betha, O.S., Yardi, Y., Alvionita, Y., Zilhada, Z., and Siregar, B.J., 2019. Mutu Sediaan Racikan Puyer Di Kecamatan Ciputat Timur. *Pharm Biomed Sci J*, 1(1).
- Chalik, R., Rusli, R., and Hasanah, N., 2019. Identifikasi Medication Error Fase Compounding Pada Pasien Anak Rawat Jalan Di RSUD Labuang Baji Makassar. *Media Farm*, 13(2), 22–24.
- Dangi, B., and Oh, T.J., 2019. Bacterial CYP 154C8 catalyzes carbon-carbon bond cleavage in steroids. *FEBS letters*, 593(1), 67–79.
- Dewi, M.S., 2021. Uji Kualitas Sediaan Racikan Pulveres Campuran Ketotifen Fumarat Dan Siproheptadin HCl. Skripsi, Fakultas Farmasi Universitas Sanata Dharma, Yogyakarta, Indonesia.
- Dzulianto, A., Riswanto, F.D.O., and Rohman, A., 2017. The Employment of UV-Spectroscopy Combined with Multivariate Calibration for Analysis of Paracetamol, Propyphenazone and Caffeine. *Indones. J. Pharm*, 28, 191–197.
- El-Gindy, A., and Hadad, G.M., 2012. Chemometrics in Pharmaceutical Analysis: An Introduction, Review, and Future Perspectives. *J AOAC Int*, 95(3), 609–23.
- Elisabeth, V., 2018. Formulasi Sediaan Granul Dengan Bahan Pengikat Pati Kulit Pisang Goroho (*Musa acuminata* L.) Dan Pengaruhnya Pada Sifat Fisik Granul. *Pharmacon*, 7(4).
- Golonka, I., Kawacki, A., and Musial, W., 2015. Stability Studies of a Mixture of Paracetamol and Ascorbic Acid, Prepared Extempore, at Elevated Temperature and Humidity Conditions. *Trop. J. Pharm. Res*, 14(8), 1315–1321.
- Guo, M., Sun, X., Chen, J., and Cai, T., 2021. Pharmaceutical Cocrystals: A Review of Preparations, Physicochemical Properties and Applications. *Acta Pharm. Sin. B*, 11(8), 2537–2564.
- Handiana, I.R., and Indriyati, W., 2016. Formulasi Sediaan Tablet Lepas Lambat Teofilin Dengan Bahan Matriks Yang Berkarakteristik Hidrofilik. *Farmaka*, 14(1), 136–141.
- Hariyati, R.S., and Yuliani, S.H., 2022. Penetapan Kadar Racikan Kapsul Yang Mengandung Aminofilin, CTM, Dan Prednison. *J Heal Promot Serv Manag*, 1(1), 69–79.
- Kasanah, D.A., Putri, D.C.A., Yuliani, S.H., and Dwiastuti, R., 2019. Kajian Potensi Inkompabilitas Dan Instabilitas: Studi Kasus Sediaan Racikan Mengandung Amitriptilin, Trifluoperazine Dihidroklorida Dan Alprazolam. *JPSCR J. Pharm. Sci. Clin. Res*, 4, 120–131.
- Katzung, B.G., Masters, S.B., and Trevor, A.J., 2012. Basic & Clinical Pharmacology 12th Edition, McGraw-Hill Medical: New York, ISBN 9780071764025.
- Kemenkes RI, 2020. Farmakope Indonesia Edisi VI, Kementerian Kesehatan Republik Indonesia, Jakarta.
- Kurniawan, B.R., 2014. Stabilitas Resep Racikan yang Berpotensi Mengalami Inkompabilitas Farmasetika yang disimpan Pada Wadah Tertutup Baik. *Calyptra*, 2(2), 1–16.
- Maheswari, B.K.S., 2022. Kualitas Sediaan Racikan Kapsul Kombinasi Teofilin Salbutamol Sulfat Dan Metilprednisolon Di Rumah Sakit "X" Di Yogyakarta. Skripsi, Fakultas Farmasi, Universitas Sanata Dharma, Yogyakarta, Indonesia.

- Mevik, B., Wehrens, R., 2019. Introduction to the pls Package. Help Sect Pls Packag R Stud Softw.
- Miller, J.M., and Miller, J.C., 2010. Statistics and Chemometrics for Analytical Chemistry: Sixth, Pearson Education Limited: Harlow, ISBN 9780273730422.
- Nurani, L., Kumalasari, E., Rohman, A., and Widyarini, S., 2017. Formulasi Kapsul Ekstrak Etanol Akar Pasak Bumi (*Eurycoma longifolia* Jack) Dan Pengaruhnya Terhadap Vital Sign Manusia Sehat. *Tradit Med J*, 22(2), 91–6.
- Nurjanah, F., Sriwidodo, S., and Nurhadi, B., 2021. Stabilisasi Tablet yang Mengandung Zat Aktif Bersifat Higroskopis. *Majalah Farmasetika*, 6(1), 10–22.
- Pandhita, A.K., 2022. Keseragaman Kandungan Racikan Kapsul Kombinasi Aminofilin, Setirizin, Dan Salbutamol Di RS “X” Yogyakarta Dengan Metode Spektrofotometri UV Dan Kemometrika. Skripsi, Fakultas Farmasi Universitas Sanata Dharma, Yogyakarta, Indonesia.
- Putra, M.E., Ardana, M., and Fadraersada, J., 2017. Deteksi Dispensing Error Pada Peresepan Sediaan Kapsul Racikan di Apotek Wilayah Kecamatan Samarinda Ulu. *Proceeding of Mulawarman Pharmaceuticals Conferences*, 6(1), 141–145.
- R Core Team R Development Core Team, R A Lang., 2021. R A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, 55, 275–86.
- Rahayu, P., and Yulyuswarni, E.R.M., 2020. Pelatihan Peracikan Yang Bertanggungjawab Bagi Tenaga Teknis Kefarmasian Dan Juru Racik Di Apotek Kota Bandar Lampung. *J. Pengabd. Kpd. Masy. Sakai Sambayan*, 4(3), 181–184.
- Rahman, Z., Dharani, S., Ali, S.F.B., Afrooz, H., Reddy, I.K., and Khan, M.A., 2018. Effect of Processing Parameters and Controlled Environment Storage on the Disproportionation and Dissolution of Extended-Release Capsule of Phenytoin Sodium. *Int J Pharm*, 550(1-2), 290–299.
- Riswanto, F.D.O., 2022. Kemometrika Pengenalan Pola Dan Kalibrasi Multivariat Dengan Perangkat Lunak R; First, Sanata Dharma University Press, ISBN 6236103801.
- Rohman, A., Irnawati, and Riswanto, F.D.O., 2022. Analisis Farmasi Dengan Spektroskopi UV-Vis Dan Kemometrika, UGM Press: Yogyakarta.
- Shafirany, M.Z., Susilawati, Y., and Musfiroh, I., 2018. Aplikasi Kemometrik Dalam Penentuan Mutu Tumbuhan Obat. *Maj Farm Sains, Dan Kesehat*, 4(2), 6–14.
- Sinulingga, C.A., 2021. Kualitas Sediaan Racikan Pulveres Kombinasi Ambroxol HCl Dan Alerfed Di Rumah Sakit “X” Tipe C Di Semarang. Skripsi, Fakultas Farmasi Universitas Sanata Dharma, Yogyakarta, Indonesia, 2021.
- Srividya, B., Sowmya, C., and Reddy, C.S.P., 2014. Capsules and it’s technology: An Overview. *Int J Pharm. drug Anal*, 727–733.
- United States Pharmacopeia Conversion (USP), 2019. USP General Chapter <795> Pharmaceutical Compounding-Nonsterile Preparations, USP 42-NF 37, Rockville
- Varma, K., 2016. Excipients Used in the Formulation of Tablets. *Res Rev J Chem*, 5(2), 143–154.
- Yuliani, S.H., Putri, D.C.A., Virginia, D.M., Gani, M.R., Riswanto, F.D.O., 2023. Prevalence, Risk, and Challenges of Extemporaneous Preparation for Pediatric Patients in Developing Nations: A Review. *Pharmaceutics*, 15, 840.