Penentuan Simultan Parasetamol dan Ibuprofen dalam Campuran Biner Menggunakan Metode Spektrofotomeri Luas Daerah di Bawah Kurva

Simultaneous Determination of Paracetamol and Ibuprofen in Binary Mixture using Area Under Curve Spechtrophotomery Method

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INTISARI

Kombinasi parasetamol (PAR) dan ibuprofen (IBU) adalah obat bebas yang paling umum digunakan untuk demam dan nyeri. Penelitian ini bertujuan untuk menentukan kadar PAR dan IBU dalam campuran biner secara simultan dengan metode spektrofotometri luas daerah di bawah kurva.

Metode ini menggunakan area di bawah kurva setiap spektrum dalam berbagai konsentrasi untuk menganalisis rentang panjang gelombang yang dipilih dengan pelarut metanol. Kemudian, metode ini diterapkan untuk menentukan kadar PAR dan IBU dalam campuran biner.

Hasil dari metode ini adalah analisis rentang panjang gelombang terpilih PAR dan IBU pada rentang panjang gelombang masing-masing 244-254 nm dan 220-230 nm. Rata-rata % Recovery adalah 99,35% dan 99,49% untuk PAR dan IBU, masing-masing. Metode tersebut berhasil diterapkan untuk menentukan PAR dan IBU dalam campuran biner secara bersamaan dan memenuhi syarat validasi.

Kata kunci : Parasetamol; Ibuprofen; Spektrofotometri, Area under curve

ABSTRACT

The combination of paracetamol (PAR) and ibuprofen (IBU) is the most commonly used over-the-counter medication for fever and pain. This study aimed to determine simultaneously levels of PAR and IBU in binary mixture using area under curve spechtrophotometry method.

This method uses the spectral area under curves of each spectrum in various concentrations to analyze the selected wavelength range with methanol as the solvent. This method was then applied to determine the PAR and IBU levels in the binary mixtures.

The result of this method is an analysis of the selected wavelength range of PAR and IBU in the wavelength ranges of 244-254 nm and 220-230 nm, respectively. The average recovery rates were 99.35% and 99.49% for PAR and IBU, respectively. This method determines the PAR and IBU simultaneously in binary mixtures and is successfully applied to meet the validation requirements.

Keyword : Paracetamol; Ibuprofen; Spechtrophotometry; Area under curve

1. INTRODUCTION

The combination of paracetamol (PAR) and ibuprofen (IBU) is the most commonly used over-the-counter medication for fever and pain [1][2]. PAR or

paracetamol is chemically N-acetyl-p-aminophenol with analgesic and antipyretic properties [3][4]. IBU is chemically 2- (4-isobutylphenyl) propionic acid, a non-steroidal anti-inflammatory drug with analgesic, antipyretic and anti-inflammatory properties [5][6][7][8]. PAR and IBU suppress the production of prostaglandins [1].

Reported methods for estimating PAR and IBU alone or in combination with other bulks and formulations include HPLC[9][10], RP-HPLC [9], spectrophotometry [12], FT-IR [13], voltametric [14][15], RP-UPLC [16].

The main challenge in spectrophotometric analysis of binary mixtures is to determine two compounds in the same mixture without first separating them. Area under curve (AUC) is a spectrophotometric method used in routine analysis to analyze several drug mixtures without prior separation. This method is simple, accurate, and precise, with no interference from excipients [17]. However, no references were found for the AUC spectrophotometric method's simultaneous estimation of PAR and IBU in binary mixtures. Therefore, this study aims to develop the AUC spectrophotometric method to determine the levels of PAR and IBU in tablet dosage forms.

2. MATERIAL AND METHODS

2. 1. INSTRUMENT AND MATERIALS

A shimadzu 1800 Ultraviolet-visible spectrophotometer, pharmaceutical grades of PAR and IBU were from the Food and Drug Administration of Indonesia, methanol (Merck), tablet sample with label claim PAR 350 mg and IBU 200 mg per tablet were purchased from local pharmacies.

2. 2. METHODS

Standard Solution Preparation

Separately, 50 mg of PAR and IBU standards were accurately weighed and transferred into a 50 mL volumetric flask before being dissolved in methanol to yield solutions containing 1000 µg/mL PAR and IBU.

Analytical Wavelength Selection

PAR and IBU solutions were prepared in diluent with appropriate dilution, and the spectrum was recorded. The absorption spectra of solutions prepared at various PAR (3-9 µg/mL) and IBU (5-13 µg/mL) concentrations were scanned in the 200-400 nm range. To selected wavelength range analysis, AUC in various concentrations is calculated.

Application for Pharmaceutical Tablet Dosage Form

Twenty tablets were precisely weighed, and their average weight was determined. Tablets were crushed into fine powder, which was then precisely weighed to yield 350 mg PAR and 200 mg IBU and transferred into a 250 ml volumetric flask. 15 mL of methanol was added to this and sonicated for 10 minutes to dissolve completely. After that, it was shaken and the volume was adjusted with diluent. The solution was then filtered using Whatman filter paper. Pipette 0.2 ml of the filtrate and exchange it to a 50-mL volumetric flask, filled with methanol to the line check to get a arrangement containing 6 µg/mL Standard and 9 µg/mL IBU. The

proposed method was used to analyze the resulting solution. Quantification was performed by keeping these values in the linear equation of the calibration curve.

Validation of Method

This method was validated in terms of accuracy, precision, linearity, LOD, and LOQ in accordance with International Conference of Harmonization (ICH) guidelines [18].

Linearity

The proposed method's linearity is assessed by calculating the correlation coefficient. [19].

Accuracy

Recovery studies estimate the accuracy of the proposed method by measuring the recovery rate at three specific points (i.e. 80 % , 100 % and 120 %) [12][20] [21].

Precision

The proposed method's precision is expressed as a percentage of RSD using the formula [%RSD = (standard deviation/mean) × 100%] [20].

LOD and LOQ

The developed method's LOD and LOQ are computed using the following formula: LOQ=10*SD/SLOPE; LOD=3.3*SD/SLOPE; SD stands for Standard Deviation [22][23] [24][25].

3. RESULT AND DISCUSSION

Analytical Wavelength Selection

Figure 1 depicts the wavelength range of the PAR and IBU analysis for PAR (λ = 244-254) nm and IBU (λ = 220- 230) nm, as well as the binary mixture of PAR and IBU. The wavelength range chosen is to provide linearity with a correlation coefficient value of ≤1 [17][18]. It means that this method is excellent because it has linearity ≤1 (Table 1).

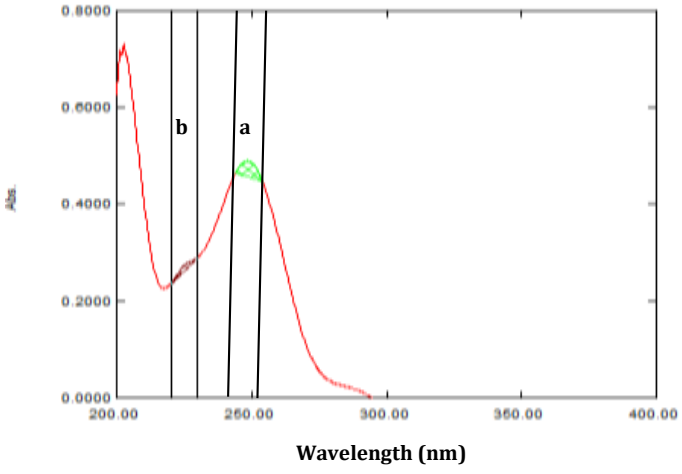

Figure 1. Curve Absorption of AUC For Binary Mixture PAR and IBU

(a) PAR (244-254 nm), (b) IBU (220-230 nm)

Based on Figure 1, we are able to conclude that there`s no covering AUC of each wavelength for PAR (244-254 nm) and IBU (220-230 nm) and influencing one to another. Based on these findings, UV spectrophotometry using the AUC method can be used to determine the drug content of multiple components simultaneously. [17][18].

Validation of Method

The method is validated using accuracy, linearity, precision, LOD, and LOQ. Table 1 shows the validation results.

Table 1. Validation Parameters of PAR and IBU

Parameters	PAR	IBU
Linearity	0.9979	0.9917
Accuracy (%)	99.35	99.49
Precision (%)	0.96	0.80
LOD (µg/mL)	0.69	0.68
LOQ (µg/mL)	2.300	2.2900

According to table 1, the linearity of PAR 0.9979 and IBU 0.9917 gives a good linearity with a correlation coefficient value of ≤1. The accuracy for PAR is 99.35% and 99.49% for IBU, this meets the requirements of the accuracy range between 98% to 102%. The precision for PAR was 0.96% and 0.80% for IBU, this met the precision requirement of less than 2%. LOD PAR 0.69 µg/mL and IBU 0.68 µg/mL, LOQ PAR 2,300 µg/mL and IBU 2.2900 µg/mL. Since all parameters of the validation test comply with the validation requirements of the ICH guidelines, this study yields good results for validation methods for simultaneously measuring PAR and IBU in binary mixtures. This indicates that these methods met the validation requirements. Several studies on spectrophotometry using the AUC method have been reported, with good results in verifying the method. [17][18][19][23].

Applying The Procedure In Tablet Dosage Form

Table 2 shows the results of using the proposed method to determine PAR and IBU in their combined tablet dosage forms.

Table 2. Result of Quantification PAR and IBU in Binary Mixtures

Drugs Content	Amount Found		Content in etiquette	Level Requirements Pharmacopeia Edition V	
	%	Mg		%	mg
PAR	100.36 ± 0.18%	350.4	350 mg	98.0-110.0%	343-385
IBU	100.40 ± 0.31%	200.1	200 mg	97.0-103.0%	194-206

According to Table 2, the levels obtained for PAR 100.36± 0.18% and IBU 100.40±0.31%, indicating that the levels obtained meet the requirements of the Indonesian Pharmacopeia Edition V, 98.0-110.0% for PAR and 97.0-103.0% for IBU. Therefore, a binary mixture of PAR and IBU can be measured simultaneously. Several studies, however, have been reported [18][19], and the proposed method has the potential to be used in routine drug analysis based on these findings.

4. CONCLUSION

The spectrophotometric AUC method can be used to simultaneously measure PAR and IBU in a binary mixture without prior separation.

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