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Original Article

GREEN METHOD FOR ACETAMINOPHEN AND IBUPROFEN SIMULTANEOUS ASSAY IN THE COMBINATION TABLET USING FTIR

ILMA NUGRAHANI, FARAH NUR KHALIDA

Institute Technology of Bandung, Jl. Ganesha No.10, Lb. Siliwangi, Coblong, Kota Bandung, Jawa Barat 40132, Indonesia
Email: ilma_nugrahani@fa.itb.ac.id

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ABSTRACT

Objective: The purpose of this study was to develop a green method for assay the tablet consists of a combination of acetaminophen (ACT)-ibuprofen (IBU). FTIR (Fourier Transform Infrared Spectroscopy), which is commonly used for qualitative analysis, was developed to measure the tablet contents, directly and quantitatively.

Methods: Standard for ACT and IBU was respectively mixed with KBr crystal in varied and measured using FTIR. The transmission spectrum yielded later was converted into its absorbance-derivatized forms which then a calibration curve was composed using the data. Once validated, the analytical method was conducted on samples of the branded ACT-IBU combination tablet.

Results: ACT had a specific wavenumber of a group N-H stretch, meanwhile IBU was represented by the C = O spectrum. These peaks then used for quantitative calculation basis levels respectively. The limits of detection and quantitation of ACT consecutively were 3.249×10^{-5}% w/w and 1.083×10^{-4}% w/w and IBU were 6.6652×10^{-4}% w/w and 2.2174×10^{-3}% w/w. Next; the method was carried out successfully to evaluate the content of sample tablet from the market.

Conclusion: The analytical method of ACT-IBU was proven applicable and suitable for the quantitative purpose. The method shows meet with the expectation such as simple and easy to perform and reduce the use of solvents.

Keywords: FTIR, Green method, Acetaminophen, Ibuprofen, Assay

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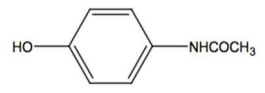
INTRODUCTION

Analgesic, antipyretic and anti-inflammatory are widely used around the world because almost of all disease are characterized by pain and fever symptoms. The many different types of drugs and forms under various trade names and circulated in the free market, pharmacies, hospitals, and community health centres. Among the types of pain-reducing and antipyretic drugs, generally contains a single drug or combined drug with an anti-inflammatory. Recently, acetaminophen (ACT) has been combined with ibuprofen (IBU) to produce a potentiation effect in relieving pain, reducing fever, and inflammation. Nonsteroidal anti-inflammatory drugs (NSAID), like IBU, work by inhibiting prostaglandin synthesis, suppress inflammation and pain. Meanwhile, ACT or commonly known as paracetamol works as a pain reducer and temperature control [1-3]. In the market, this combination can be found as a tablet dosage form [4]. Therefore, we need a suitable method for determining the levels of each active ingredient in tablet dosage combination of the two substances.



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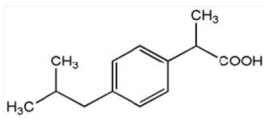

b

Fig. 1: Structure of A. ACT; B. IBU

The structure of ACT and IBU is shown in fig. 1 [5, 6]. The method commonly used in compendia to determine the levels of the substance in a pharmaceutical preparation is by using high-performance liquid chromatography instrument. Several researches also have reported the development of this compendia's method [7-12]. However, these methods still required amounts of solvents as the mobile phases. Meanwhile, the green pharmacy/green chemistry much be recommended for maintain the environment, one of which is to reduce the use of organic solvents [13].

Along the periods, Fourier Transform Infra Red (FTIR) has been more widely available due to this important function for identification to meet the compendia requirements. Infrared spectrum analysis has differences with others in the form division of two regions of the spectrum, which are the area of functional groups and the fingerprint region. The fingerprint area is a special characteristic of each compound. There are some regions of the spectrum of infrared but it used the range of the wave number of 4000-400 cm^{-1} [12].

The method used in this research was based on the vibration of atoms of a molecule that will generate the spectrum in the form of transmission and absorbance. The infrared spectrum was used by passing the infrared radiation to a sample, further determines the fraction that used the partial absorption of energy. The absorbance of infra-red follows Lambert Beer's Law; as same as the other spectroscopy method. Therefore, FTIR also will be tried to be conducted as a tool for quantitative analysis [14-17].

The vibration energy uses the energy which records almost all of the interaction in the structures. Hence, infrared is known to have the low specificity. In the previous researches, we have tried to develop the quantitative method using derivative mathematically. This technique has been frequently used to separate the overlaid spectra in other spectroscopy methods, such as uv-visible as well as spectrofluorometry [18-20]. Using the derivatisation, the lack of specificity can overcome successfully. The previous experiments also have proven that infrared derivation method is appropriate for drugs assay after increasing the sensitivity [21, 22]. The other advantages shown by the experiments are: the simpler preparation and did not need a solvent. Besides that, compared to the other methods which use extraction and dilution, it should be less time

consumption, then totally became less costly. Moreover, FTIR spectroscopy can be considered as a green analytical method which much be recommended nowadays [13, 21, 22].

So far, derivative spectra FTIR for ACT and IBU determination has never been reported. Meanwhile, the measurement of the area under the curve (AUC) of derivative of absorbance spectra of some drugs has been reported in the previous journal [21, 22]. Considering their structure, some infrared spectrums of these drugs was predicted can be used for the quantification method. Hence, the purpose of this study was to develop and validate FTIR method for the assay of ACT and IBU in the tablet directly and simultaneously.

MATERIALS AND METHODS

Materials

Reference standards of ACT, IBU, potassium bromide, lactose, aerosil, magnesium stearat, and two samples of the brand name of ACT-IBU tablets.

Instrument

This experiment was using FTIR Jasco-4200 Type A, Japan for the record the infrared spectra.

Methods

The method arranged to follow the previous research development of the direct assay using FTIR using derivated absorbance spectra has been reported previously [21, 22]. The derivative spectral has been commonly used in other spectrometry, such as uv-visible and fluorometry [18-20]. Standards of ACT and IBU are respectively mixed with KBr in a varied ratio, beaten into pellets at pressure 10-20 Mpa, and measured the spectrum. Then the spectrums recorded are converted into absorbance. The results next were changed to its derivatized form. Derivatization included baseline spectrum correction. Wavenumber that showed a clear and distinctive peak of each active ingredient is selected and calculated AUC.

Validation method conducted specificity, linearity, accuracy, precision, limit of detection (LOD), limit of quantitation (LOQ), and range [23-26]. Once validated, the analytical method is conducted on samples of ACT and IBU combination tablet in the market.

Validation method

The method was validated for its specificity, linearity, accuracy, precision, LOD, LOQ, and range [23-26]. Specificity was evaluated by comparing the derivated spectrum of the matrix with simulation tablet. The selected range over the spectrum is only found in simulation tablet. Linearity was tested for each analyte in concentration range in KBr. Linearity was determined by plotting the AUC with concentration (%). The acceptance criteria for linearity are as follows (r) ≥ 0.999 and variance of regression function (Vxo) ≤ 2% [8].

Accuracy was evaluated by formulating tablets with the amounts of ACT and IBU were 80, 100, and 120%, respectively. Then a number of analytes are mixed with KBr into 100 mg. The acceptance criterion for accuracy is the recovery value of 98–102% [8]. Precision was tested for each number of ACT and IBU with KBr in 100 mg simulation tablet and was done by repeating measurements six times a day. Measurements were also made within three days of different analysis times. The precision acceptance criterion is relative standard deviation of<2%. Determination of range was evaluated by the value of linearity, accuracy, and precision.

LOD and LOQ were proceeded from the calibration curve [9]. The equations are: LOD = $\frac{3\,Sy/x}{b}$; LOQ = $\frac{10\,Sy/x}{b}$; with Sy/x = $\left[\frac{\sum(yi-\hat{y}i)^2}{n-2}\right]^{\frac{1}{2}}$. Content of tablet combination of ACT and IBU assay was performed by sampling 20 tablets from each product. Then tablets were weighed, crushed, and mixed homogeneously. Several of them were sampled and mixed by means trituration with KBr into 100 mg. Measurement by FTIR and determined the AUC over the range of corresponding wavenumbers. The concentration of each active substance in each sample product can be determined.

RESULTS AND DISCUSSION

Content determination ACT and IBU in tablet sample

The experiment was begun with measured the FTIR spectrum of each active substance. Then the spectrum produced each transformed into an absorbance. Changing the relationship is because of absorbance values proportional to the concentration. Here is a combination of transmission spectral of a series concentration of ACT-IBU, which then was converted from the transmission into absorbance.

The ACT's absorbance-curve is shown in fig. 2.

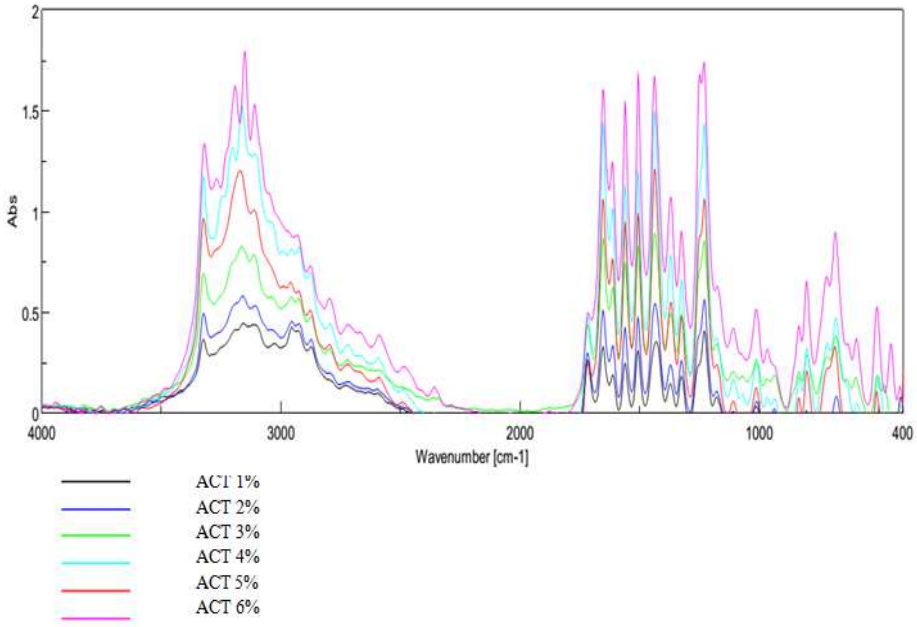

Fig. 2: Absorbance of the ACT

Next, the IBU's spectral is shown in fig. 3.

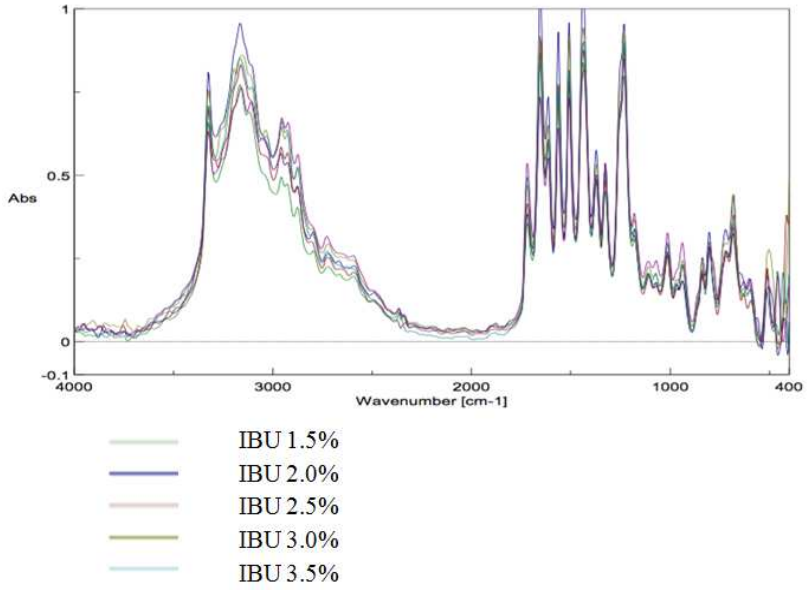

Fig. 3: Absorbance of IBU

To enhance the specificity, all the absorbance spectrums were derivated [18-22]. The result is shown in fig. 4 for ACT and 5 for IBU.

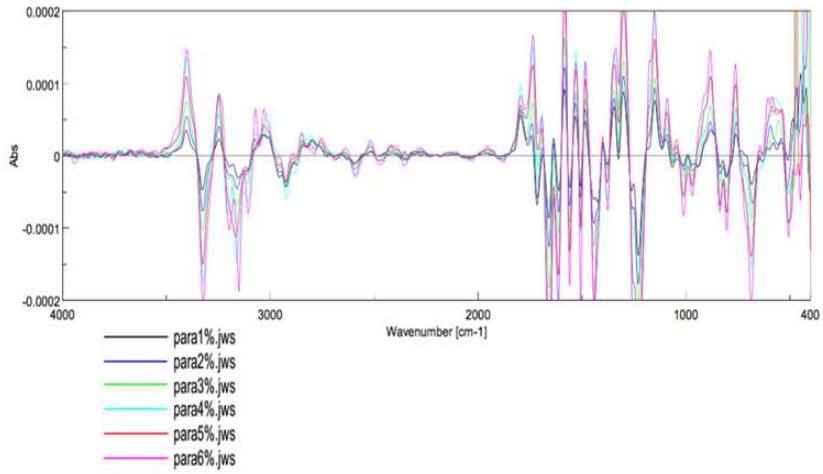

Fig. 4: Derivative absorbance spectra of ACT

Fig. 4 shows the absorbance from six concentrations: 1–6 % w/w; which were measured 3 times for each. Moreover, the derivative of absorbances based on the data spectra in fig. 4 is shown in fig. 5. From the derivative absorbance, the AUC (AUC) was measured. Afterwards, resulted from the data of ACT which are listed in table 1.

Table 1: ACT's concentrations versus AUCs of absorbance derivate curve

Concentration in mixture with KBr (%w/w)	AUC at the specific area of (cm^{-1})			
	3502-3355 (10^{-3})	3289-3220 (10^{-3})	1619-1554 (10^{-3})	798-732 (10^{-3})
1	1.6385	0.8205	1.6528	0.7453
2	3.0070	1.2398	2.4142	0.9360
3	4.1971	1.6242	3.1732	1.5481
4	5.7798	2.0456	3.8596	1.9992
5	6.9875	2.5350	8.2043	3.0566
6	8.5576	2.9084	10.1830	3.0566
r^2	0.9986	0.9989	0.8831	0.9551
Coefficient correlation (r)	0.9992	0.9994	0.9397	0.9772

*AUC: area under the curve, **Each value is represented as a mean, n=3; SD in this table is not displayed due to the restricted space.

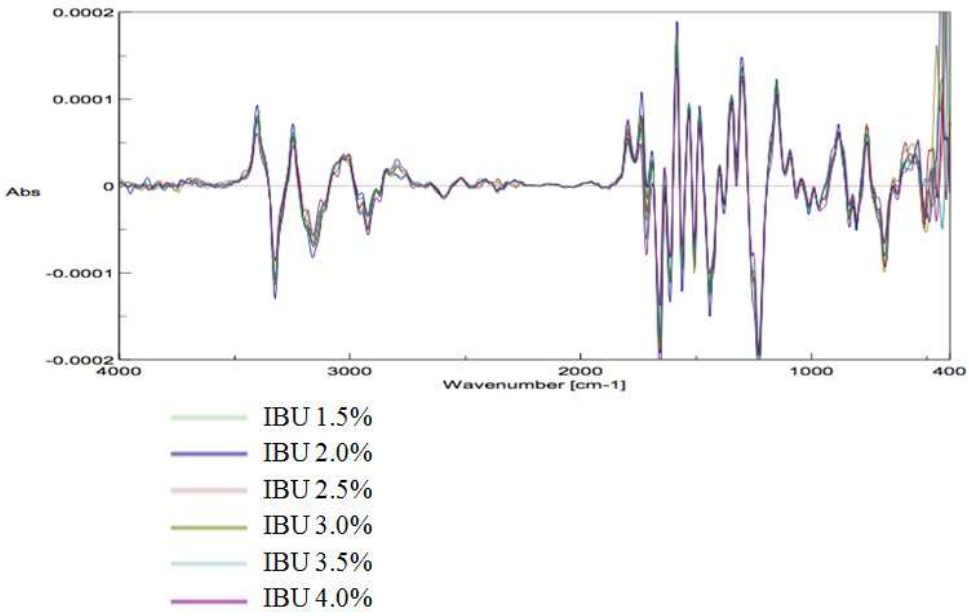

Fig. 5: Derivative absorbance spectra of IBU

Based on the selected range of wavenumbers in table 1, the highest linearity shown by the spectrum at 3289-3220 cm^{-1}, which has r = 0.9994. This is indicated as a group N-H stretch [14]. In addition, after the corrections to the matrix, this spectrum is specific only for ACT. Thus, the strain of N-H group was chosen as the basis for a quantitative calculation. Data from these best spectrums was collected and shown in fig. 6.

Furthermore, the finest IBU spectrum for quantitative measurement was investigated. The spectrum which will be selected should meet with the validation criterion of linearity and specific. The result showed that the spectrum in the area 1847-1758 cm^{-1}, was the most linear toward derivate's absorbance. Moreover, it was also specific, due to only held by IBU, which represented C=O stretching [14]. Thus, this spectrum was then used for calculate the levels of IBU in the sample of combination tablet. For a clear description, the derivate spectrums in this area were shown in fig. 7.

The data of IBU's AUC measurements are listed in table 2. The table shows r value = 0.9992, which proven the good linearity.

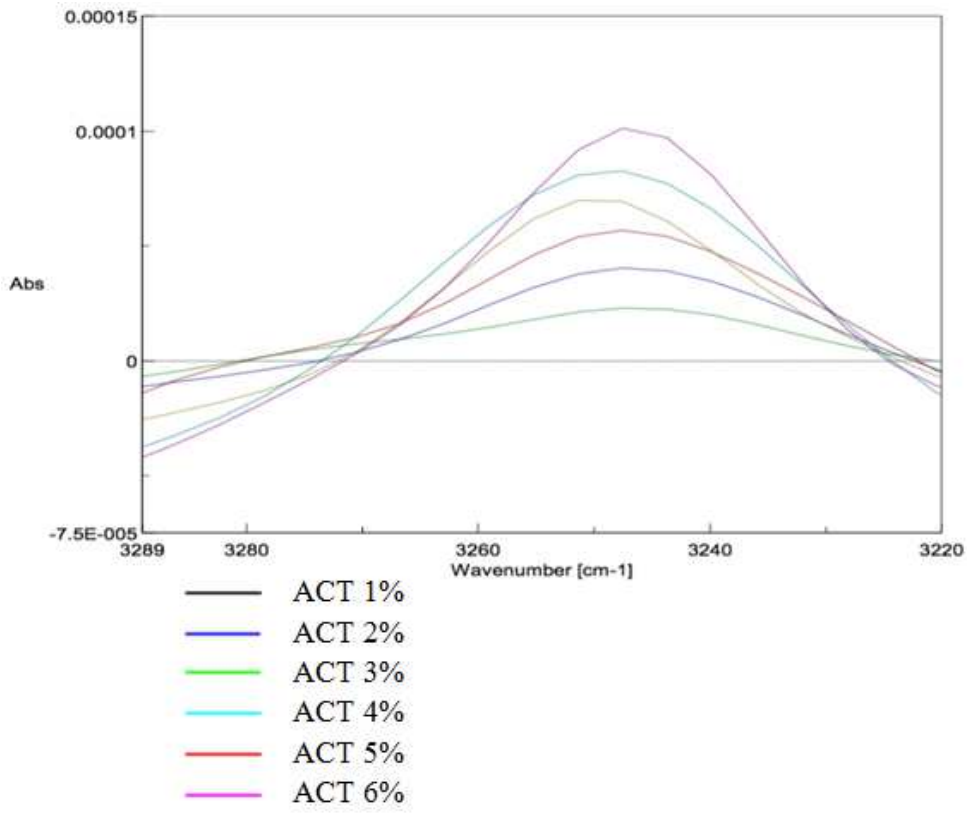

Fig. 6: Derivative absorbance spectra of ACT at 3289–3220 cm^{-1}

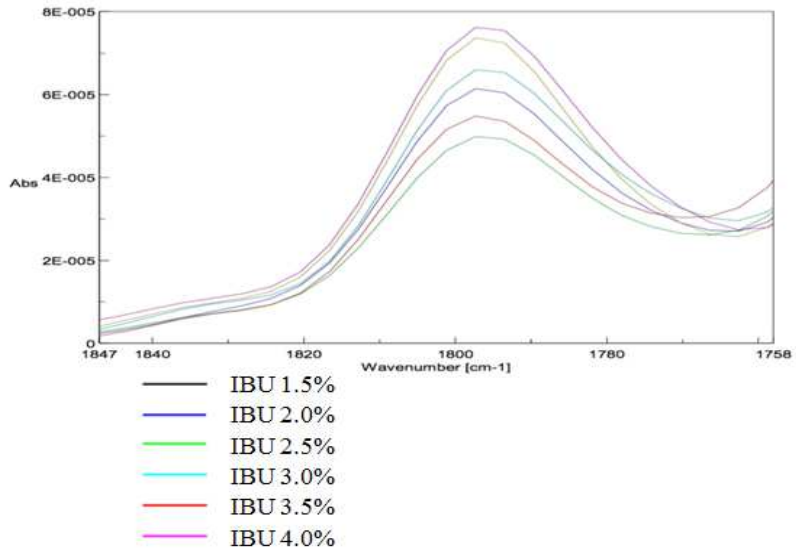

Fig. 7: Derivative absorbance spectrum of IBU at 1847-1758 cm^{-1}

Table 2. IBU concentration versus its AUC of derivative-spectra

Concentration in mixture with KBr (%w/w)	AUC of absorbance-derivative at 1847-1758 cm^{-1}(10^{-3})
1.5	2.2292±0.0071
2.0	2.4296±0.0120
2.5	2.6074±0.0231
3.0	2.8431±0.0222
3.5	3.0351±0.0312
4.0	3.2074±0.0097
r^2	0.9985
Correlation coefficient (r)	0.9992

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

Validation method

Specificity

Specificity test, as the method's ability to analyze accurately, was performed to confirm estimated there are as contamination, degradation products, and the sample matrix. This method uses the specificity test by comparing the absorbance derivative of ACT, IBU, matrix, and tablet simulation.

Derivative absorbance spectrum of the combined ACT, IBU, matrix, and tablet simulation yielded shown in fig. 8. Spectrum A belongs to ACT but not owned by IBU and the matrix. Meanwhile, B is the spectrum which only the spectrum of IBU but not owned by ACT and matrix. Thus, these spectrums can be used to measure the levels of ACT and IBU in tablet dosage combination of the two substances.

Linearity

Linearity is the ability to show the test results directly or through a precise mathematical-transformation, that must be shown the proportional relation between the concentration with the response. Linearity test requires a minimum of five concentrations used, which were plotted to AUC of derivative-absorbance. The data from these experiments are shown in table 3 and 4 for ACT and IBU respectively. Calibration curves yielded from the plotting of concentration to AUC were shown in fig. 9 for ACT and fig. 10 for IBU.

ACT's linearity test

The data listed in table 3 was plotted into the curve which is shown in fig. 9 as follows.

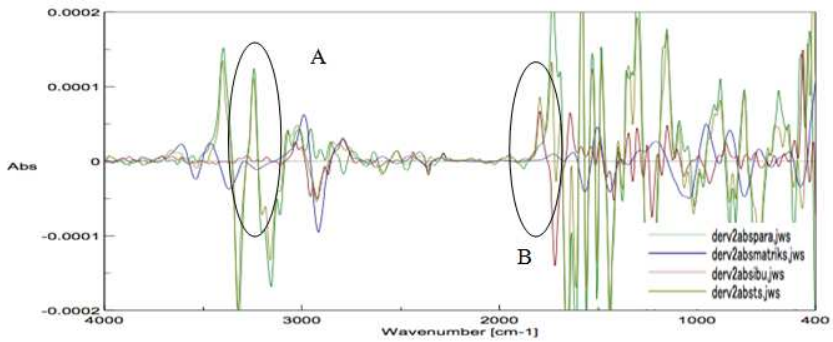

Fig. 8: Specific spectrum of ACT (A) and IBU (B), with matrices as background

Table 3: ACT concentration versus AUC of the derivative spectra

ACT concentration (%w/w)	AUC (10^{-3})
1	0.8205±0.0602
2	1.2397±0.0074
3	1.6242±0.0246
4	2.0456±0.0115
5	2.5350±0.0466
6	2.9083±0.0374

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3.

The regression equation of ACT in the range 1.00% to 6.00%: y = 0.0004 x+0.0004. The coefficient regression was (r) = 0.9994, meanwhile Vxo = 0.0309%. Value of r ≥ 0.999 and Vxo ≤ 2.00% stated that analytical methods had met the requirements of linearity [23-25].

IBU's linearity test

Linearity test for IBU yielded data which is listed in table 4. Then, the calibration of IBU composed from table 4 data is shown in fig. 10.

From the curve, the regression equation of IBU was shown linear within the range of 1.50% to 4.00%: y = 0.0002 x+0.002. The correlation coefficient was (r) = 0.9992, and 0.8063% of Vxo value. Value r ≥ 0.999 and Vxo ≤ 2.00% stated that analytical methods had met the requirements of linearity [23-25].

Accuracy

Accuracy is the degree of closeness between the test results with a validated procedure to correct value. Minimum accuracy determination is used nine times, the concentration of 80%, 100% and 120% respectively of three measurements, as described in table 5 and 6 for ACT and IBU. Accuracy is expressed as a percent recovery's analyte is added [23-25].

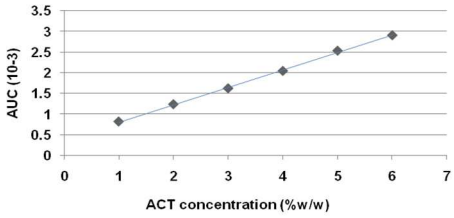

Fig. 9: Calibration curve of ACT

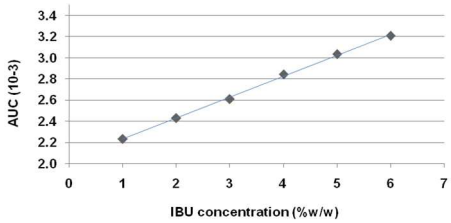

Fig. 10: Calibration curve of IBU

Table 4: IBU concentration versus AUC of the derivative spectra

IBU concentration (%w/w)	AUC (10^{-3})
1.5	2.2291±0.0306
2.0	2.4296±0.0184
2.5	2.6074±0.0258
3.0	2.8431±0.0400
3.5	3.0351±0.0405
4.0	3.2073±0.0414

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

Table 5: Accuration test data of ACT

Concentration (%)	AUC	AUC average	Theoritical AUC	Recovery (%)
80	0.00163	0.00151±	0.00152	100.66
	0.00140	0.00012		
	0.00151			
100	0.00179	0.00179±	0.00180	100.56
	0.00182	0.00004		
	0.00175			
120	0.00210	0.00206±	0.00208	100.97
	0.00205	0.00004		
	0.00203			

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

Table 6: Accuration test data of IBU

Concentration (%)	AUC	AUC average	Theoretical AUC	Recovery (%)
80	0.00235	0.00234±	0.00232	100.86
	0.00238	0.00004		
	0.00230			
100	0.00245	0.00244±	0.00240	98.36
	0.00249	0.00004		
	0.00253			
120	0.00260	0.00251±	0.00248	98.80
	0.00257	0.00002		
	0.00256			

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

Determining the accuracy of ACT tablet simulation performed with the active substance content of 280 mg, 350 mg, and 420 mg; with the number of excipients were adjusted. Next sampled as much as 7.5 mg and then each was mixed with KBr so that its mass to 100 mg. The same procedure was done to IBU with the doses: 160 mg, 200 mg, and 240 mg. The results also have met the acceptance recoveries requirement: 98.00 to 102.00% w/w [23-25].

Precision

Precision test declared the homogeneous of distribution level measurements obtained from multiple samplings under the recommended conditions. Its acceptance criteria are expressed using relative standard deviation. The kind of tests which were performed included:

Repeatability (precision intra-day)

Precision intra-day precision expressed under conditions which at the same time the interval is narrow [23-25]. In the experiment, which yielded data, which is listed in table 7; measurements were taken six times the simulation tablet formulations made with levels of 350 mg ACT and IBU 200 mg, which is equivalent to 100% in one day.

Table 7: Intra-day precision data of standard ACT

Measurement (single)	AUC from test on day-		
	1	**2**	**3**
1	0.00183	0.00178	0.00178
2	0.00179	0.00180	0.00177
3	0.00180	0.00181	0.00183
4	0.00177	0.00173	0.00182
5	0.00180	0.00179	0.00179
6	0.00178	0.00183	0.00181
Average	0.00179	0.00179	0.00180
SD	0.00002	0.00002	0.00004
% RSD	1.15%	0.8 %	1.79%
% Recovery	99.26%	99.49%	99.81%

*AUC: area under the curve

Intra-day precision testing of the standard ACT (table 8) yielded the relative standard deviation (RSD) of 1.83% on the first day; 1.98% on the second day; 1.79% on the third day. The results obtained have met the acceptance criteria of precision value RSD of<2% [23-26].

Intra-day precision testing of raw IBU resulted in RSD of 1.52% on the first day; 1.26% on the second day; 1.34% on the third day. The results obtained have met the acceptance criteria of precision value RSD of<2% [23-26].

Table 8: Intra-day precision data of standard IBU

Measurement (single)	AUC from test on day-		
	1	2	3
1	0.00248	0.00249	0.00246
2	0.00242	0.00244	0.00246
3	0.00246	0.00241	0.00239
4	0.00239	0.00242	0.00242
5	0.00246	0.00240	0.00246
6	0.00248	0.00242	0.00248
Average	0.00245	0.00243	0.00244
SD	0.00002	0.00003	0.00004
% RSD	0.816%	1.12%	1.16%
% Recovery	101.98%	101.29%	101.86%

*AUC: area under the curve

Precision intermediates (inter-day precision)

Precision intermediate shows the variation of testing, for example: different days, analysts, equipment, and so forth. At trial, it carried out in three days with each measurement performed six times respectively, against the tablet simulation. Table 9 shows the result of inter-day precision experiment. Meanwhile, the data of IBU's inter-day precision test is expressed in table 10. Based on the results of inter-day precision test of ACT and IBU in table 9 and 10, the RSD was 0.2767% and 0.3607% respectively. In line with intra-day test results, this parameter also has met the acceptance criteria of precision stated as<2% [23-25].

Table 9: Inter-day trial data of standard ACT

Day-	AUC
1	0.00179±0.0004
2	0.00179±0.0005
3	0.00180±0.0002
Average	0.00179
SD	0.00000
% RSD	0%

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

Table 10: Inter-day trial data of standard IBU

Day-	AUC
1	0.00245±0.00006
2	0.00243±0.00005
3	0.00244±0.00004
Average	0.00244
SD	0.00001
% RSD	0.615%

*AUC: area under the curve, **Each value is represented as a mean±SD, n=3

LOD) and LOQ

The LOD is the lowest concentration of an analyte, which still can be read, represents the sensitivity of the measurement. While the LOQ is the smallest concentration of an analyte in a sample which has been fulfilled the accuracy and precision requirement. Determining LOD and LOQ can be calculated from the linearity data, using *b* as the slope value of calibration curve formula [24].

$S_{y/x} = \left[\frac{\sum(yi-\hat{y}i)^2}{n-2}\right]^{\frac{1}{2}}$

LOD = $\frac{3\,Sy/x}{b}$; LOQ = $\frac{10^{\frac{Sy}{x}}}{b}$

For ACT, the calculation is follows:

$S_{y/x} = \left[\frac{\sum(yi-\hat{y}i)^2}{n-2}\right]^{\frac{1}{2}} = 4.332 \times 10^{-9}$

LOD = $\frac{3\quad /}{} = 3.249 \times 10^{-5}$ %w/w

LOQ = $\frac{10\,Sy/x}{b} = 1.0830 \times 10^{-4}$% w/w

Meanwhile, for IBU the results calculated is shown:

$S_{y/x} = \left[\frac{\sum(yi-\hat{y}i)^2}{n-2}\right]^{\frac{1}{2}} = 4.4348 \times 10^{-8}$

LOD = $\frac{3\,Sy/x}{b} = 6.652 \times 10^{-4}$ % w/w

LOQ = $\frac{10\,Sy/x}{b} = 2.2174 \times 10^{-3}$ % w/w

Using this method, the LOD of ACT was % w/w or mg per 100 mg mixture with KBr. Meanwhile, the LOQ was % w/w or mg ACT per 100 mg mixture with KBr. Afterwards, the LOD of IBU was % w/w. It means that LOD was mg in 100 mg mixture with potassium bromide. The smallest amount of sample IBU which can be measured quantitatively (LOQ) was % w/w or mg of the substance in 100 mg. This LOQ has to appropriate acceptance criteria for accuracy and precision.

Range

The range is the interval between the highest limit and the lower limit of the concentration of an analyte, which can be measured. These parameters be determined in line with precision, accuracy and linearity of the appropriate procedures specified analysis. Based on the linearity test, the concentration range of analysis for ACT was 1.00 to 6.00% w/w. Meanwhile, for IBU, the range was 1.50 to 4.00% w/w.

Review and comparison with other methods

Hence, briefly, the specific spectrums which can be used are the wave numbers 3289-3220 for ACT and 1847-1758 cm-1 for IBU, simultaneously. This method has been evaluated to meet the validation criteria. The parameters checked were: specificity, linearity, accuracy, precision intra-day, inter-day precision. The concentration range of ACT was 1.00 to 6.00% w/w. For IBU; the range was 1.50 to 4.00% w/w. The LOD of ACT is % w/w, and LOQ are % w/w. Currently; LOD and LOQ of IBU were % w/w and % w/w respectively.

Furthermore, parameters of validity such as specificity, accuracy, and precision are comparable and insignificant different from HPLC methods referred [7-12]. The differences are mainly in the range of measurement and the LOD/lOQ. In an example, the method which newest reported by Jahan et al. (2014) is 25–100 µg/ml for paracetamol and 10–40 µg/ml for IBU. Further LOD/lOQ of paracetamol is 2.3 µg/ml/0.213 µg/ml and 7.9/0.711 µg/ml respectively. These values are about 10-2 smaller than the FTIR results, means that the infrared instrument has lower sensitivity. However, paracetamol and IBU in the tablet preparation are relatively used in big enough dose, so this method is considered still usable and appropriate as an alternative. Furthermore, this simultaneous method offers some more advantages practically. These are the easy preparations, fast to conduct, simple of calculation due to few steps of dilution, and free of organic solvent. These advantages will bring to totally cost saving and safely for the environment.

On the other hand, Hoang *et al.* (2014) also reported derivative method of uv spectrophotometry, which showed the calibration graphs in the linear concentration ranges of IBU is 12–32 mg/l. Meanwhile paracetamol (20–40 mg/l). These values are mostly equal to FTIR method recent evaluated. Moreover, this method, as same as to HPLC, has validation parameter values such as accuracy and precision, statistically interchangeable.

Finally, in purpose to proof the suitability, this validated FTIR quantitative method was tried to determine the weight/content uniformity of two branded of ACT-IBU tablets. The results are explained in the next part of the discussion (table 12 and 13).

Determination of levels of ACT and IBU tablet combination

Assay of a combination of ACT and IBU tablet in samples that found from the market was conducted to follow the compendia guidance [5,6] using the validated method. The assay was done simultaneously on two test product's ACT and IBU combination tablet on the market. A total of 20 tablets of each product is weighed and crushed. After that, sampled by the number equal to 3.5 mg ACT, and IBU was 2.0 mg, then was mixed with KBr and measured using FTIR. The experiment yielded data listed in table 12.

Table 12: ACT content in the tablet sample

Tablet product	The average of tablet's weight (mg)	The average of AUC	Tablet's content (mg)	Percentage (%w/w)
A	755.175±11.584	0.00185± 0.00001	362.576	103.59
B	700.425±5.581	0.00186± 0.00003	362.548	103.59

* AUC: area under the curve, **Each value is represented as a mean±SD, n=20

From the assay result of ACT, it can be concluded that both products from the market have to meet the criteria required by the Indonesian Pharmacopoeia [5], levels within the range of 90-110%. These results are listed in table 13.

Table 13: IBU content in the tablet sample

Tablet product	The weight's average (mg)	The average of AUC	Tablet's content (mg)	Percentage (%w/w)
A	755.175±11.584	0.00242± 0.00004	203.836	101.92
B	700.425±5.581	0.00241± 0.00005	201.158	100.58

*AUC: area under the curve, **Each value is represented as a mean±SD, n=20

Based on the data, it can be concluded that both products from the market have to meet the criteria required by the Indonesian Pharmacopoeia: levels IBU should be within the range of 90-110% [5].

Therefore, all the results have proven that validated FTIR method can be used for ACT-IBU quantification in tablet form direct, correct and simultaneously. The most advantages of this method is its simplicity and less costly than other methods compared.

CONCLUSION

FTIR derivative for assay method of ACT and IBU has been validated. The method also has been tried to determine the content of ACT-IBU tablet combination, and showed the appropriate result, successfully. This method is fast, easy, accurate, and free of solvents using. Meanwhile, the sensitivity is lower than HPLC. This method shows the good accuracy, and precision; besides, is safe and friendlier to the environment. In next step, after any comparative test to compendia's, it could be proposed to be the alternative or complementary methods.

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AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declared none

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