International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304
Vol.7, No.2, pp 349-353, 2014-2015

Development Method for Determination of Ternary Mixture of Paracetamol, Ibuprofen and Caffeine in Tablet Dosage Form Using Zero-crossing Derivative Spectrophotometric

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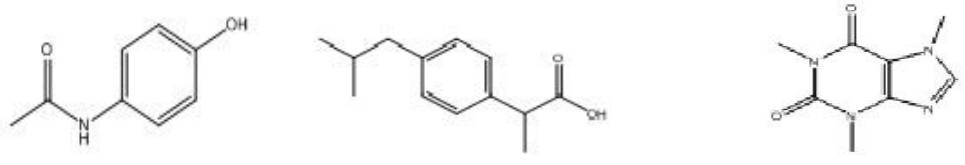
Abstract: A derivative spectrophotometric method was developed for the assay of ternary mixtures of paracetamol, ibuprofen and caffeine. The aim of this work is to find the best orde to determine this ternary mixtures in tablet dosage form using phosphat buffer pH 7.2 as solvent. The method is based on measurements at zero-crossing wavelengths. The concentration of the other components are then determined from their respective calibration curves treated similarly. The described method was applied for the determination of these combination in commercial tablet. This study showed that paracetamol and ibuprofen were measured best on their first derivative while caffeine in third derivative. The result obtained were accurate and precise.
Keyword: Paracetamol, Ibuprofen, Caffeine, Derivative spectrophotometric, Zero-crossing, Ternary mixture, First derivative, Third derivative.

Introduction

Paracetamol (PAR) is an effective alternative to aspirin as an analgesic–antipyretic agent; however, its anti-inflammatory effects are much weaker. Ibuprofen (IBU), the most commonly used NSAID in the U.S., was the first member of the propionic acid class of NSAIDs to come into general use, and it is available without a prescription in the U.S. Caffeine **(**CAF), a mild stimulant, is the most widely used psychoactive drug in the world[1]. This combination is used for moderate pain in case of headaches. The chemical structure of PAR, IBU and CAF were in Fig.1.

Resolving the overlapped spectra of multicomponent mixtures dosage forms whether ternary or more as mixtures was rather a difficult task[2]. Derivative spectrophotometry, a well established analytical technique which is frequently used in the contemporary analysis of drugs in mixtures when the spectral classic bands of components are overlapped. Zero-crossing derivative methods are simple, fast and precise and it could be applied to resolve ternary mixtures[3].

To the best our knowledge, double divisor-ratio spectra method had applied for quantification ternary mixtures of PAR, IBU and CAF in ethanol and Briton Robbinson buffer pH 11[4]. While, chemometric method also reported for quantification the same drug in methanol:HCl 0,1N (3:1)[5]. Despite of used methanol as a solvent, phosphat buffer pH 7.2 also could be a solvent to PAR and IBU[6]. The aim of this work is to developed a spectrophotometric method for determination of this ternary mixture in tablet dosage form using phosphat buffer pH 7.2 as solvent.



a **b** **c**

Fig 1. Chemical structure of (a) PAR, (b) IBU, (c) CAF

Experimental

Apparatus

The spectrophotometric measurements were carried out on a Shimadzu UV-1800 spectrophotometer. The absorption spectra were measured using 1 cm quartz cells. For the derivative method, the absorption spectra were recorded on the same spectrophotometer, with 1 cm quartz cells and supported with UV-Probe 2.34 software.

Materials and reagents

All material and reagents were analytical reagent grade. Paracetamol, ibuprofen and caffeine were purchased from National Agency of Drugs and Foods Control Indonesia and Fluka Sigma Aldrich.

Preparation of standard solutions

Stock solutions containing 25 µg/mL PAR, 25 µg/mL IBU and 25 µg/mL CAF were prepared in phosphat buffer pH 7.2. Further dilutions were done using phosphat buffer pH 7.2 as described under construction of calibration graphs.

Construction of calibration graphs

Different aliquouts of the standard solution of PAR, IBU and CAF, was transferred into 50 ml volumetrric flask. The solutions were then completed to the volume with phosphat buffer pH 7.2, so the final concentration for PAR were 2.5; 5.0; 7.5; 10; 12.5; 15.0 µg/mL, IBU were 1.5; 3.0; 4.5; 6.0; 7.5; 9.0 µg/mL and CAF were 0.4; 0.8; 1.2; 1.6; 2.0; 2.4. The absorption spectrum of each solution was recorded within the wavelength range 200-400 nm and stored.

Assay of tablet formulation by derivative spectrophotometry

Twenty commercial tablets which contained 350 mg PAR, 200 mg IBU and 50 mg CAF were weighed accurately. A powder quantity equivalent to 100 mg paracetamol was accurately weighed and transferred to volumetric flask of 250 ml capacity. One hundred ml phosphat buffer pH 7.2 was transferred to this volumetric flask and sonicated 15 minutes. The flask was shaken and volume was made up to the mark with phosphat buffer pH 7.2. The above solution was filtered through whatman filter paper no. 42. The solution was made up to the mark with phosphat buffer pH 7.2 to give a solution containing 10 µg/mL, 5.71 µg/mL and 1.43 µg/mL paracetamol, ibuprofen and caffeine respectively. The resulting solution was analyzed by proposed method. The quantitation was carried out by keeping these values to the straight line equation of calibration curve.

Method validation

The proposed method has been extensively validated in terms of linearity, accuracy, precision. The accuracy of the method was determined by calculating recovery of PAR, IBU and CAF by the standard addition method.

Result and Discussion

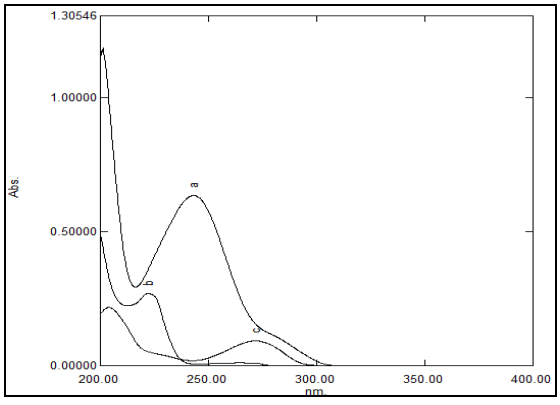


Fig. 2. Absorption spectra of (a) 10 µg/mL PAR, (b) 6 µg/mL IBU, (c) 1.6 µg/mL CAF.

The absorption spectra of three components are strongly overlapped (Fig. 2) that was sufficiently enough to demonstrate the resolving power of the proposed method.

In this respect, different solutions of PAR, IBU and CAF were prepared in the concentration ranges stated in construction of calibration graph. The absorption spectra of these concentrations were recorded and stored.

For the determination of PAR, the first derivative the stored spectra of standard solutions of PAR, IBU and CAF and a solution of their mixture were calculated with Δλ 4 nm and scalling factor 1 (Fig. 3). From this figure, PAR can be determined in this mixture by measuring the amplitude at 271.2 nm where there is no contribution from IBU and CAF (zero-crossing point of IBU and CAF).

For the determination of IBU, the first derivative the stored spectra of standard solutions of PAR, IBU and CAF and a solution of their mixture were calculated with Δλ 16 nm and scalling factor 1 (Fig. 4). From this figure, IBU can be determined in this mixture by measuring the amplitude at 242.4 nm where there is no contribution from PAR and CAF (zero-crossing point of PAR and CAF).

For the determination of CAF, the third derivative the stored spectra of standard solutions of PAR, IBU and CAF and a solution of their mixture were calculated with Δλ 16 nm and scalling factor 100 (Fig. 5). From this figure, CAF can be determined in this mixture by measuring the amplitude at 302.4 nm where there is no contribution from PAR and IBU (zero-crossing point of PAR and IBU).

The wavelengths 271.2 nm, 242.4 nm and 302.4 nm in each condition were selected for analysis of PAR, IBU and CAF respectively.

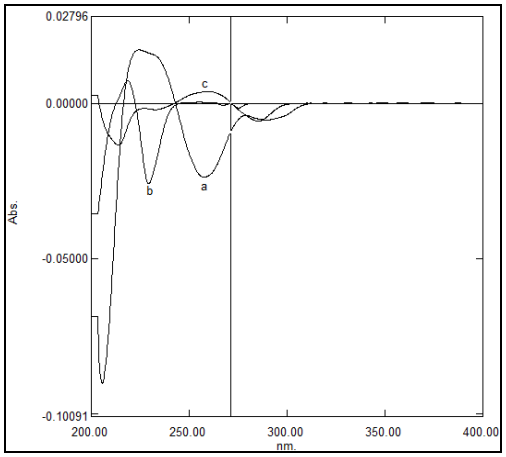


Fig. 3. First derivative spectra were calculated with Δλ 4 nm and scalling factor 1 of (a) 10 µg/mL PAR, (b) 6 µg/mL IBU, (c) 1.6 µg/mL CAF.

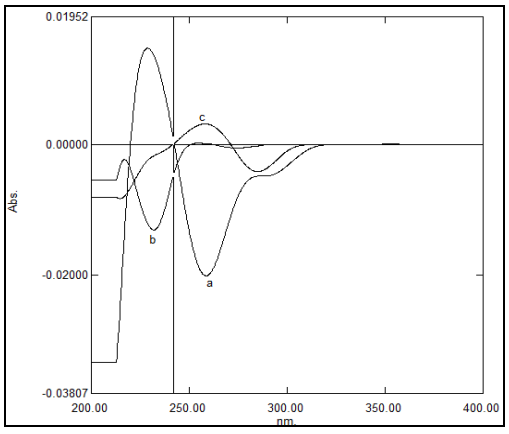


Fig. 4. First derivative spectra were calculated with Δλ 16 nm and scalling factor 1 of (a) 10 µg/mL PAR, (b) 6 µg/mL IBU, (c) 1.6 µg/mL CAF.

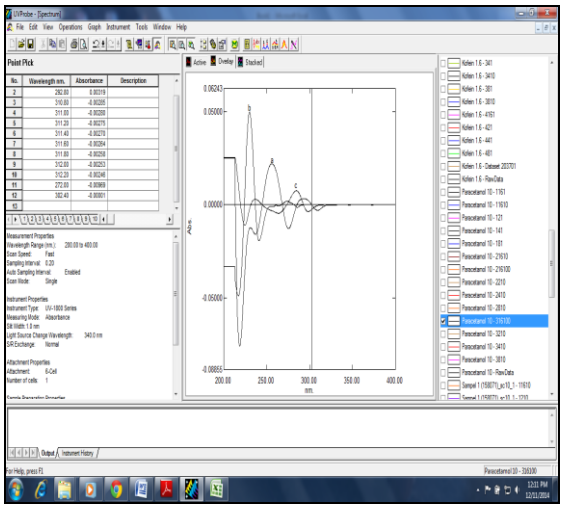


Fig. 5. Third derivative spectra were calculated with Δλ 16 nm and scalling factor 100 of (a) 10 µg/mL PAR, (b) 6 µg/mL IBU, (c) 1.6 µg/mL CAF.

Method validation

The linearity of the proposed method was evaluated for each drug by analyzing different concentration of each PAR, IBU and CAF, within the concentration range in construction calibration graph. The assay was performed according to the previously stated conditions. A straight line was obtained in each case. Analysis of these graphs showed excellent linearity of the calibration graph and agreement to Beer's law.

Table 1. Validation parameters for derivative spectrophotometry

Parameters	Paracetamol	Ibuprofen	Caffeine
Corr. Coeff (r)	-0.99999	-0.99998	-0.99980
Slope	-9.14857×10^{-4}	-0.00072	-0.00163
Intercept	2.857×10^{-6}	0.00002	-0.00002
Accuration	101%	102%	101%
LOD	-0.07680	-0.07270	-0.05729
LOQ	-0.25601	-0.24235	-0.19096

As shown in table 1, the value of the intercept are so small that they do not significantly differ from zero, so the proposed method is free from error in the procedure. The resulting mixtures were asssayed according to the above stated procedure and the results were calculated as the percentage of analyte recovered. LOD and LOQ values were indicated that the method shows high sensitivity. The good recovery values assure the high accuracy of the proposed method.

Application of the method in commercial tablet

The proposed method was applied for the determination of PAR, IBU and CAF in their combined commercial tablet and the result are shown in table 2.

Table 2. Result of quantification of PAR, IBU and CAF in marketed formulation by derivative spectrophotometry method

Drug	Label claim (mg/tablet)	Amount Found (mg/tablet)	Precision (%RSD)
Paracetamol	350	322	1.6
Ibuprofen	200	212	1.9
Caffeine	50	50	1.6

Conclusion

The proposed method provides a simple and accurate quantitative analysis for the determination of PAR, IBU and CAF as a ternary mixture. The proposed method is simple as there is no need for solvent extraction and direct as it estimates each component independent of the other, and also the method is rapid, low cost and harmless to the environment. So it could be applied in quality control laboratories.

References

1. Brunton, L., Parker, K.L, Blumenthal, D.K, Buxton, L.O., Goodman and Gillman's Manual of Pharmacology and Therapeutics, Mc. Graw Hill Company, 2008, 396, 445, 451.
2. Blanco, C.C., Campaña, A. M. G., and Barrero, F. A., Derivative Spectrophotometric Resolution of Mixtures of the Food Colourants Tartrazine, Amaranth and Curcumin in a Micellar Medium, Talanta, 1996, 43: 1019.
3. Kazemipour, M. and Mehdi, A., Derivative Spectrophotometry for Simultaneous Analysis of Chlorpheniramine Maleate, Phenylephrine HCl, and Phenylpropanolamine HCl in Ternary Mixtures and Pharmaceutical Dosage Forms, Iranian Journal of Pharmaceutical Research, 2004, 3: 152.
4. Hajian, R., and Afshari, N, The Spectrophotometric Multicomponent Analysis of Ternary Mixture of Ibuprofen, Caffeine and Paracetamol by The Combination of Double Divisor-Ratio Spectra Derivative and H-Point Standard Addition Method, E-Journal of Chemistry, 2012, 9(3): 1154-1155.
5. Khoshayand, M. R., Abdollahi, M. H., Shariatpanahi, A., Saadatfard, A., Mohammadi, Simultaneous spectrophotometric determination of paracetamol, ibuprofen and caffeine in pharmaceuticals by chemometric methods, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2007, 70(3): Abstract.
6. Hoang, V.D., Dong, T.H.L., Nguyen, H.T. and Hue, M.T.N. UV Spectrophotometric Simultaneous Determination of Paracetamol and Ibuprofen in Combined Tablets by Derivative and Wavelet Transforms, Scientific World Journal, 2014: 4.

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