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Research Article

SIMULTANEOUS SPECTROPHOTOMETRIC DETERMINATION OF PARACETAMOL, PROPYPHENAZONE AND CAFFEINE BY USING ABSORPTION RATIO METHOD

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ABSTRACT

The Absorption Ratio method involves measuring the absorbance at two wavelengths, namely the iso-absorptive point and the maximum wavelength. Its method could be an option in determining the level of a drug. The aim of this study was to determine whether the absorption ratio method can be used to determine the levels of paracetamol (PCT), propyphenazone (PRO) and caffeine (CAF) in tablet form. The absorption ratio method was used to determine the levels of the mixed drug compound without the separation stage and using the maximum wavelength and iso-absorptive point. The result of the study showed that the absorption ratio method used to solve multicomponent problems in tablet form can be performed and satisfy the validation requirements of the method according to international Conference on Harmonization Q2 (R1) (ICH) guidelines. The absorption ratio method was a simple and accurate to be used determine PCT, PRO, CAF in tablet form.

Keywords : Paracetamol, Propyphenazone, caffeine, absorption ratio

Article Info: Received: 17 Aug, 2018; Review Completed: 09 Sept, 2018; Accepted: 10 Oct, 2018; Available online: 20 Oct, 2018



Cite this article as:

FP. Ainil *, DLP. Effendy, MS. Siti, Simultaneous Spectrophotometric Determination of Paracetamol, Propyphenazone And Caffeine By Using Absorption Ratio Method, Asian Journal of Pharmaceutical research and Development. 2018;6 (5):05-08

DOI: <http://dx.doi.org/10.22270/ajprd.v6i5.412>

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INTRODUCTION

Paracetamol is 4- hydroxyacetanilide, which is used as an antipyretic and analgesic, it is commonly used in multi ingredient preparation for migration, headache, antipyretic action¹. PCT alone can be combined with other drugs such as PRO and CAF, then analyzed using spectrophotometry, HPLC, TLC, HPTLC, LC-MS, FT-IR^{2,3}, PRO is 1.5 dimethyl-2-phenyl-4-prophan-2-ylpyrazol-3-one used as analgesic. PCT and PRO are drugs that are widely used to help reduce pain (analgesics) and fever (antipyretics), whereas CAF is often combined with paracetamol and PRO to strengthen its analgesic effect⁴.

The absorbance ratio method is a method for simultaneous of two or three components depending upon the property that the ratio of

absorbances⁵, absorption ratio method is used for the ratio of the absorption at two elected wavelength one of which is the iso absorptive point and λ_{max} from each substances⁶⁻⁷. Its method could be an option in determining the level of a drug. It is necessary to conduct research that the absorption ratio method can be used to determine the levels of paracetamol (PCT), propyphenazone (PRO) and caffeine (CAF) in tablet form

MATERIAL AND METHODS

Materials

Pure drug samples of PCT, PRO and CAF were provided by Anqiu Lu'an Pharmaceutical Co Ltd, Shandong Xinhua Pharmaceutical Co Ltd and PT Kimia Farma. Tablet P (PT. Konimex), All other chemicals and reagents used were for analytical grade.

Apparatus and conditions

In this study shimdzu UV-1800 double beam spectrophotometry was used. Absorption in each substance in the double divisor then overlaid, the absorption was recorded at a wavelength of 200-400 nm using a 1 cm cuvette using UV-probe software.

Preparation of standard stock solution

Weight accurately about 50 mg of standard PCT, 50 mg of standard PRO and 50 mg of standard CAF, transferred into a 100 ml volumetric with solvent mixtur of phosphate buffer pH 7.2 and methanol (70:30), prepared concentration of 3-10.5 µg/ml solution for

paracetamol, 5-17.5 µg/ml for propyphenazone and 4.5-13 µg/ml for caffeine.

Divisor of PCT, PRO, KOF absorption spectrum in a double divisor

The division of the PCT spectrum was divided by PRO 10 µg/ml spectrum and KOF spectrum 8.5 µg/ml. The distribution of PRO spectrum is divided by PCT spectrum 6 µg/ml and KOF spectrum 8.5 µg/ml. The KOF spectrum division is divided by the 6 µg/ml PCT spectrum and the PRO 10 µg/ml spectrum. Divided using UV-probe software. The spectrum double divisor of PCT , PRO, CAF sohwn in Fig. 1-3, Overlay spectrum PCT, PRO, CAF sown in Fig. 4

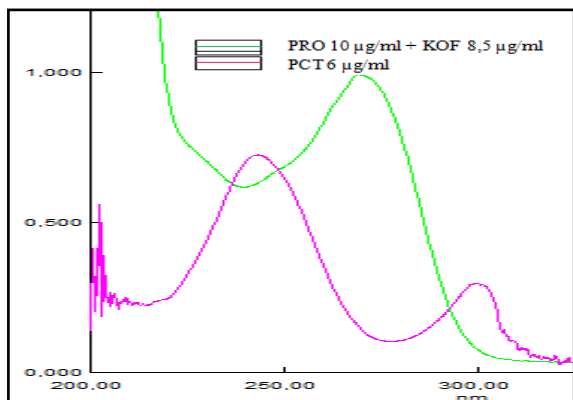


Fig. 2: Spectrum double divisor PRO

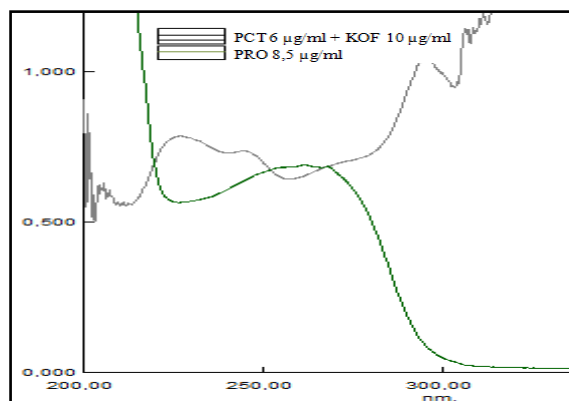


Fig. 1: Spectrum double divisor PCT

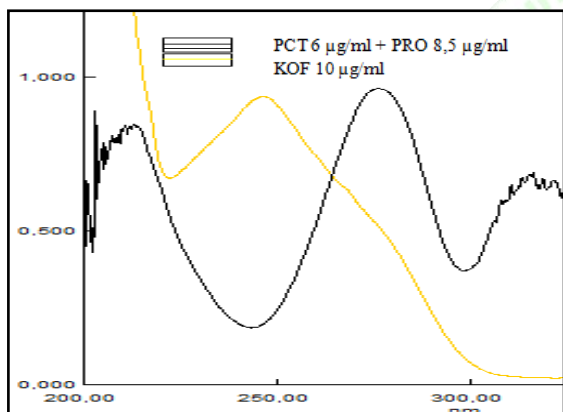


Fig. 3: Spectrum double divisor KOF

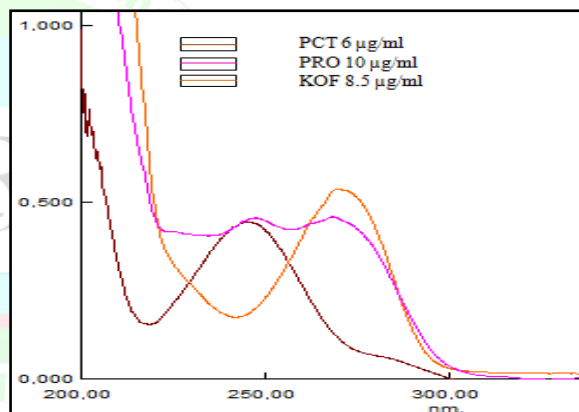


Fig. 4: Overlay spectra PCT, PRO, KOF

The maximum absorption (λmax) of PCT was found at 245 nm and iso-absorptive point at 248.6 nm, the maximum absorption of PRO was found at 265 nm and iso-absorptive point at 268.2 nm, and maximum absorption of KOF 273 nm and iso-absorptive point at 264.2 nm. Absorption and absorptivity for a series of standard solutions were recorded at selected wavelength.

Preparation of sample solution

Take 20 tablets and crush the tablets, take equivalent weight 350 mg PCT, 150 mg PRO and 50 mg CAF in 50 mlvolumetric flask to this add 25 ml of solvent, sonicate for 15 min, filtered the solution with Whatman® filter paper No. 42

Methodology

Absorption ratio method uses maximum absorption and iso-absorptive point from PCT, PRO and KOF. The concentration of three drugs in the mixture can be calculating by using the formula :

$$Ca_{(PCT)} : \frac{Q_{m1} - Q_{PRO}}{Q_{PCT} - Q_{PRO}} \times \frac{A}{a_{PCT1}}$$

$$Cb_{(PRO)} : \frac{Q_{m2} - Q_{KOF}}{Q_{PRO} - Q_{KOF}} \times \frac{A}{a_{PRO1}}$$

$$Cc_{(KOF)} : \frac{Q_{m3} - Q_{PCT}}{Q_{KOF} - Q_{PCT}} \times \frac{A}{a_{KOF1}}$$

Where; Qm1 = A2/A1, Qm2 = A3/A2, Qm3= A4/A3, QPCT = aPCT2/aPCT1, QPRO = aPRO2/aPRO1, QKOF = aKOF2/aKOF1. aPCT1= absorptivity of PCT at 248.6 nm, aPRO1= absorptivity of PRO at 248.6 nm, aPCT2= absorptivity of PCT at 245 nm, aPRO2= absorptivity of PRO at 245 nm. aPRO1= absorptivity of PRO at 268.2 nm, aKOF1= absorptivity of KOF at 268.2 nm, aPRO2=

absorptivity of PRO at 265 nm, aKOF2= absorptivity of KOF at 265 nm. aKOF1= absorptivity of KOF at 264.2 nm, aPCT1= absorptivity of PCT at 264.2 nm, aPCT1= absorptivity of PCT at 264.2 nm, aKOF2= absorptivity of KOF at 273 nm, aPCT2= absorptivity of PCT at 273 nm (RA 3 camp)⁸.

RESULT AND DISCUSSION

In this study, the first step to determine the absorbance ratio was the validation of the analysis method. Validation of developed method was carried out as per ICH guideline. Parameters such as linearity, accuracy, precision, LOD and LOQ were taken up as tests for analytical method validation.

Linearity

Linearity was evaluated by preparing different concentration in the range of 3-10.5 µg/ml for PCT, 5-17.5 µg/ml for PRO and 4.5-13 µg/ml for KOF and

absorption was measured. Each measured was carried out in triplicate.

Accuracy

Accuracy (% recovery), The recovery experiments were carried out in triplicate, by analyzing the sample first with different concentrations.

Precision

The precision of the instrument was checked by repeated scanning and measurement of absorbance of solution (n=3) for PCT, PRO, KOF.

Limit of detection (LOD) and limit of quantitation (LOQ)

They were calculated as $3.3 \sigma/S$ and $10 \sigma/S$ respectively. Where σ is the standard deviation of the response (y-intercept) and S, is the mean of the slope of calibration plot. The results of data calculation from the analysis method can be seen in Table.1

Table: 1

No	Parameter	PCT		PRO		CAF	
		λ 245 nm	λ 248.6 nm	λ 265 nm	λ 268.2 nm	λ 273 nm	λ 264.2 nm
1.	Linearity (R^2)	0.9979	0.9981	0.9983	0.9986	0.9986	0.9974
2.	Accuracy (%)	100.4	100.5	101.8	99.96	100.2	100.1
3.	Precision(%RSD)	0.319	0.844	1.955	0.310	0.513	0.277
4.	LOD (µg/ml)	0.8276	1.4206	1.2375	1.1795	0.8730	1.2130
5.	LOQ (µg/ml)	2.5080	4.3051	3.7500	3.5745	2.6455	3.6758

The calculation value of the method validation can be seen in Table 1. The results of the validation show that the accuracy value found using the absorbance ratio method according to the method validation requirements

is 98-102%⁹, and the precision parameter, the RSD value obtained is < 2%¹⁰. The result of data analysis for tablet formulation can be seen in Table 2.

Table: 2

Formulation	Substance	Wavelength (nm)	Absorption Ratio Method (%)	
Tablet P	PCT	Maximum	245	100.47
		iso-absorptive	248.6	100.58
	PRO	Maximum	265	101.86
		iso-absorptive	268.2	99.96
	KOF	Maximum	273	100.22
		iso-absorptive	264.2	100.16

The results of the study showed that the levels produced by the absorbance ratio method on the determination of PCT, PRO, KOF levels in P tablets, the resulting levels meet the specified requirements, where the levels of substances are in the range 90-110%.

CONCLUSION

The method that used in this study was simple, accurate and suitable for the analysis of PCT, PRO and CAF, the absorption ratio method was a cheaper method and

doesn't require sophisticated instrumentation. This method could be applied to the analysis of quality control drugs in the laboratory for the quality control process.

ACKNOWLEDGEMENT

The authors are grateful to Anqiu Lu'an Pharmaceutical Co Ltd, Shandong Xinhua Pharmaceutical Co Ltd and PT. Kimia Farma to provide standard PCT, PRO and CAF in this study.

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