Journal of the Iranian Chemical Society (2020) 17:111–118
https://doi.org/10.1007/s13738-019-01758-4

ORIGINAL PAPER

Double injection–single detector flow injection spectrophotometric method for simultaneous determination of ascorbic acid and paracetamol in pharmaceutical formulations

Hunar Yasin Muhammad[1] · **Azad Tawfiq Faizullah**[1]

Received: 6 March 2019 / Accepted: 8 August 2019 / Published online: 16 August 2019

Abstract
A simple and low-cost flow injection spectrophotometric method was proposed for the simultaneous determination of ascorbic acid (AA) and paracetamol (PCM) in pharmaceutical formulations. The present method is based on the reduction of Fe(III) to Fe(II) with AA and PCM in a closed flow system which subsequently combines with the 1,10-phenanthroline to form an orange-coloured complex that is measured at 510 nm. The increase in the absorbance was proportional to the concentration of AA in the range of 0.1–12 µg/ml with a correlation coefficient of 0.9997 and detection limit of 0.31 µg/ml, and to the concentration of PCM in the range of 0.4–24 µg/ml with a correlation coefficient of 0.9999 and detection limit of 0.39 µg/ml. The precision for ten serial estimations of 2 and 7 µg/ml of AA exhibited a relative standard deviation of 3.33% and 2.47% and of 6 and 15 µg/ml of PCM with a relative standard deviation of 3.008% and 2.23%, respectively. The present FI method permits determination of 9 samples per hour with no interference from the common excipients. The developed method was applied to different tablets containing AA and PCM with the recovery of AA from four spiked samples ranged from 95.31 to 104.73%, and of PCM ranged from 95.03 to 104.93%.

Keywords Ascorbic acid · Paracetamol · Double injection–single detector flow injection simultaneous determination · Spectrophotometric determination

Introduction

Ascorbic acid (AA) has an essential role in several natural processes occurring in most vegetables and fruit juices. The basis for its physiological activities and technical applications is the oxidation of ascorbic acid to dehydroascorbic acid. It is used in pharmaceutical products and is also widely used with many functional roles as a food additive [1].

Acetaminophen is known as paracetamol (PCM), and it has good analgesic and strong antipyretic properties. PCM reliefs the mild–moderate pain such as a headache and dental pain, but is of less use in splanchnic pain and inflammatory [2].

AA and PCM together are manipulated in formulations by various manufactories, which combine the relief of dental pain, muscle aches, headaches and fever associated with colds and flu by the action of the PCM and increase the defence towards microorganisms by the support of AA in antibody formation [3].

There are many methods used for the determination of these substances, including spectrophotometric determination of AA [4–9], and several other analytical methods including flow injection analysis [10–19], titrimetric [20–25], electrochemical [26–32], fluorimetric [33–35] and HPLC [36–42] methods.

On the other hand, many spectrophotometric methods were used for the determination of PCM [43–47]. PCM was also determined by FIA techniques with the different detectors, such as a spectrophotometer [48–52], a spectrofluorometer [53, 54], an amperometer [55, 56] and a chemiluminescence meter [57, 58], and several other analytical methods, including titrimetric [59, 60], electrochemical [61–66], fluorimetric [67–69] and HPLC [70–72] methods.

Developing the new methods for the determination of PCM and AA simultaneously or sequentially is highly interested due to the increase in the production and use of

✉ Hunar Yasin Muhammad
Hunar.Muhammad@su.edu.krd

[1] Chemistry Department, College of Science, Salahadin University, Erbil, Iraq

these drugs together. Several simultaneous quantifications of these drugs have developed in the literature such as partial least squares and principal component regression multivariate calibration methods in the UV region [73], voltammetry [74–77] and HPLC [78–80], but there were no published papers for simultaneous determination of AA and PCM by FIA technique up to 2019.

In this work, a new flow injection manifold is developed in which two consecutive injections of the same sample were applied using two sample injectors. Each sample injected was merged with Fe(III) stream. In the first injection, AA rapidly reduces Fe(III) to Fe(II) which merged with 1,10-phenanthroline stream to form orange Fe(II)-1,10-phenanthroline complex (ferroin complex) detected at 510 nm and recorded irrespective of the existence of PCM. In the second injection, both AA and PCM oxidised in a reaction coil with Fe(III) quantitatively proceeded in the water bath at 60 °C, in the presence of 1,10-phenanthroline producing an excessive orange complex that detected at 510 nm. Thus, by providing two peaks in each injection, a novel FI spectrophotometric system was presented and applied to the selective determination of AA and PCM consecutively in the different tablets.

Experimental

Apparatus

The spectral measurements were taken on a (CECIL CE3021, England) UV/Vis spectrophotometer. The schematic design of the FI system used in this modified method includes a multichannel peristaltic pump (DESAGA Heidelberg, England) provided with silicone pump tubes (0.8 mm id.) used to deliver the flow streams. A six-way injection valve (Rheodyne, USA, with variable loop volumes), PTFE tubes, Y-pieces and mixing coils (0.8 mm id.) in different lengths were used to connect and mix varying flow streams. The three-way Hamilton plug valve selects the sample zone pathway. The coloured products formed were monitored spectrophotometrically using JENWAY 6300 spectrophotometer equipped with a flow cells (Sterna micro-flow cell, 100 µl and 1.0 cm path length) and connected to a recorder (type PM 8251A PHILIPS—one line recorder).

Reagents

All reagents were of analytical grade, and distilled water (DW) was used for the preparation of their working solutions. The stock solution of $FeCl_3$ (BDH 60%) was daily prepared in a standardised HCl (PROLAB 37%), and 1,10-phenanthroline (PanReac 99%) was prepared freshly daily by dissolving it in distilled water and kept in a dark container.

Standard and sample solutions

A stock solution of 1000 µg/ml of standard AA and PCM (Awamedica Swedish Expertise and Quality, Erbil, Iraq) was prepared daily by dissolving 0.1 g of each analyte in DW and then completed in an ambient volumetric flask to 100 ml with DW. The working solutions were prepared by simple dilution of appropriate amounts of both drugs standard solutions and kept protected from light.

Sample solutions of different tablets, purchased from local drug stores (Table 1), were prepared by weighing ten tablets of the commercial sample and then crushed and mixed. A stock solution was prepared accurately by dissolving the average weight of each tablet in distilled water inside a beaker, shaking it mechanically for 15 min, and then filtered. The residue was washed with DW three times, and then the filtrate was diluted to the mark with DW. The injection sample solutions were prepared from the stock solution by appropriate dilutions.

Recommended procedure

The flow injection arrangement shown in Fig. 1 was used for simultaneous determination of AA and PCM from two injections of the same sample with different pathways in a two-step consecutive procedure. A series of critical chemical operations were executed instantly inside the FI manifold including reduction of Fe(III) to Fe(II) by the effect of AA and PCM followed by reaction with 1,10-phenanthroline to form a coloured complex. Mixing, heating and spectrophotometric determinations were processed simultaneously inside this manifold.

Table 1 Tablet samples analysed by the present methods

Sample no.	Name	Manufacture—country	PCM (mg/tablet)	AA (mg/tablet)
1	Apotel C (effervescent)	UNI-PHARMA—Greece	500	300
2	Doliprane (effervescent)	SANOFI—France	500	150
3	FLU-OUT	SDI—Iraq	500	100
4	FLU-OUT	SDI—Iraq	350	100

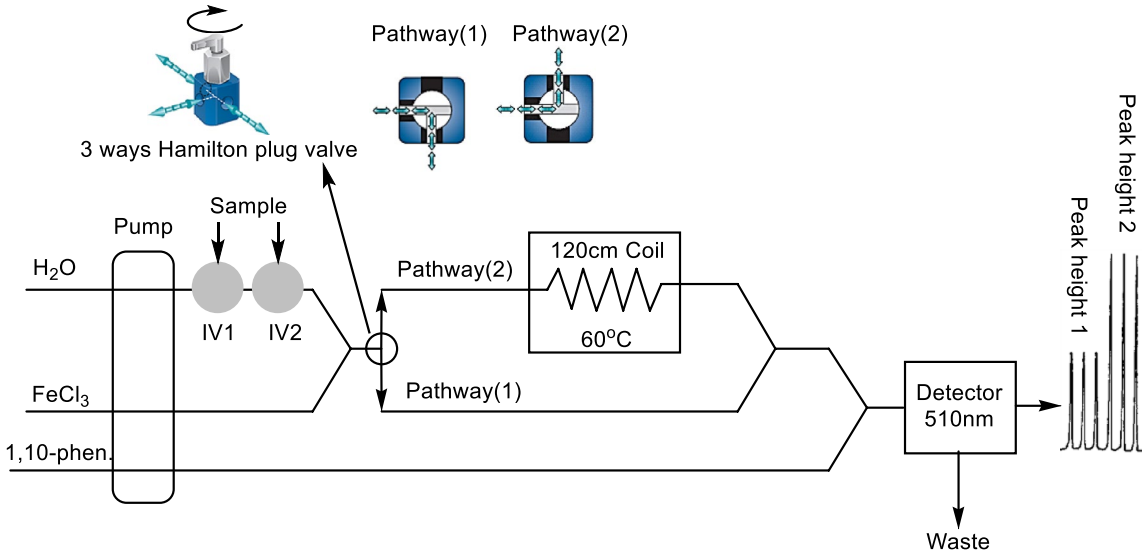

Fig. 1 FI manifold used for simultaneous determination of AA and PCM

Water carrier, $FeCl_3$ (1.5×10^{-3} M) in HCl (5×10^{-3} M) and 1,10-phenanthroline (3×10^{-3} M) solutions were propelled at flow rates of 1.5 ml/min using the multichannel peristaltic pump, and waste output in the system was 4.4 ml/min. In the first step, aliquot volumes (125 µl) of the sample solutions containing (AA + PCM) are loaded into the injection loops of the IV-1 and IV-2 valves. The injection valve IV-1 is rotated to the injection position, while the injection valve IV-2 is kept at the load position. The sample solution is injected into a water stream, merged with Fe(III) which reduced to Fe(II) by the effect of AA in the pathway(1) and then merged with 1,10-phenanthroline line to produce orange ferroin complex, and its absorbance was continuously recorded at a wavelength of 510 nm (peak height 1). This measures the AA concentration only. A calibration graph was constructed for this determination by plotting peak heights against AA concentrations. In the second step, the stream direction is changed to the pathway(2) via a three-way Hamilton plug valve, then the IV-2 valve is rotated to the injection position, and the time between these two injections depends on the height of the peak which recorded after first injection. As a result, the sample solution is injected to a water stream and merged with Fe(III), and then Fe(II) was produced by the effect of AA and PCM in a mixing coil placed inside a water bath at 60 °C. This temperature is found necessary to activate the redox process. Eventually, complex formation reaction takes place when the formed Fe(II) is coupled with 1,10-phenanthroline to produce an orange-coloured complex. The absorbance of the product formed was continuously recorded at a wavelength of 510 nm that is responsible for AA and PCM concentrations (peak height 2). The concentration of the PCM was determined by plotting (peak height 2–peak height 1) in the PCM-constructed calibration graph.

Results and discussion

AA is found to be oxidised alone with Fe(III) in the pathway(1), forming an active Fe(II) product which is combined with 1,10-phenanthroline producing a new orange product according to the redox complex formation reaction illustrated in Fig. 2, which absorbs strongly at 510 nm. There is a direct relation between absorbance and AA concentration and can be determined because PCM does not react with Fe(III) according to the conditions of pathway(1).

When the sample zone was altered to the pathway(2), AA produced a signal with the same intensity as in the pathway(1). PCM is oxidised to N-acetylquinoneimine with Fe(III) by heating, forming an orange product in the presence of 1,10-phenanthroline in Fig. 2. The amount of orange complex produced is proportional to the concentration of AA and PCM which absorbs strongly at 510 nm. Therefore, the PCM concentration is measured by subtracting peak intensity in the pathway(1) from peak intensity in the pathway(2).

Effect of chemical parameters

The effects of the concentrations of $FeCl_3$, HCl and 1,10-phenanthroline on the coloured intensity (as peak heights) were examined. The results are demonstrated in Figs. 3, 4 and 5. The concentration ranges and the optimum concentrations are shown in Table 2.

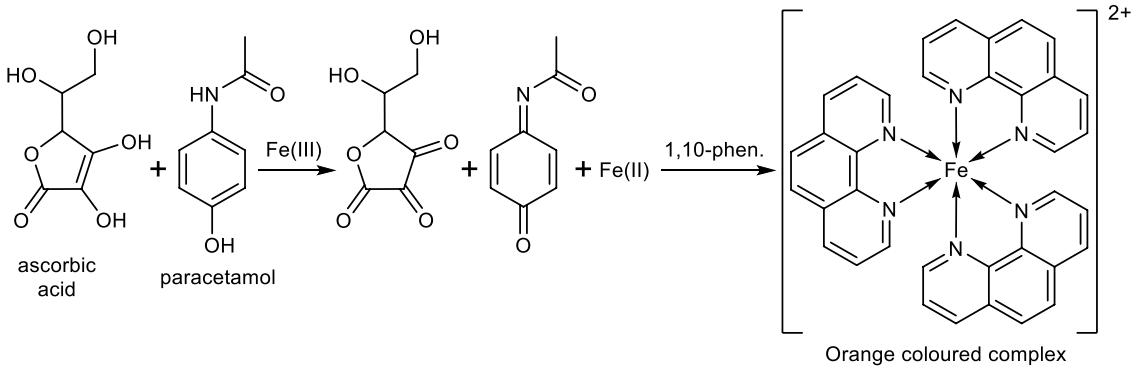

Fig. 2 Reaction mechanisms

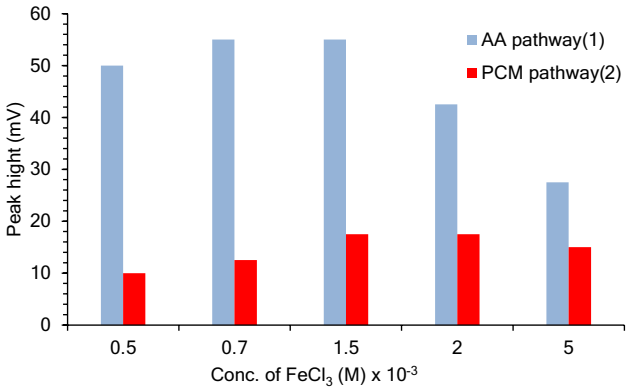

Fig. 3 Effect of $FeCl_3$ concentration on the peak height

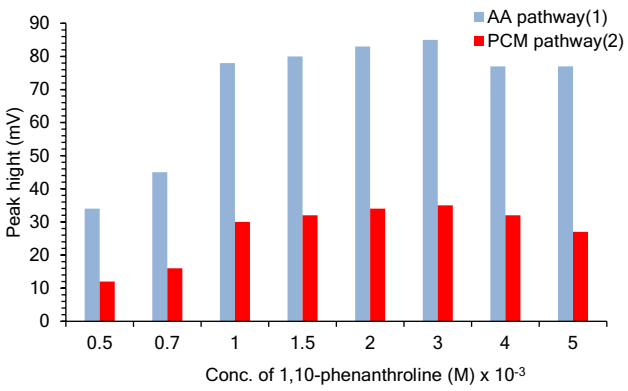

Fig. 5 Effect of 1,10-phenanthroline concentration on the peak height

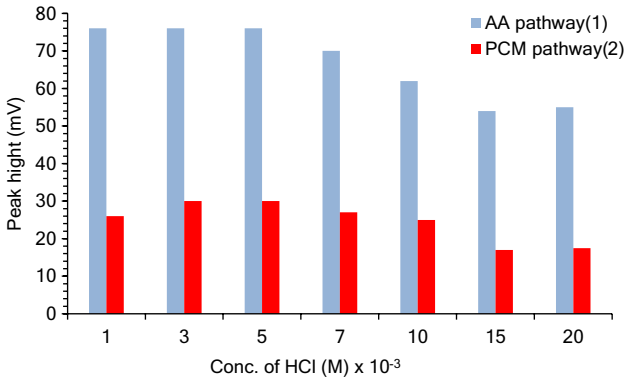

Fig. 4 Effect of HCl concentration on the peak height

Effect of physical parameters

The influence of each physical parameters was studied by obtaining the identical peak heights for AA in both pathways (1) and (2) and no signal for PCM in the pathway(1) in addition to highest peak achievement.

A combined streams flow rate was studied from 1.0 to 5 ml/min under optimum chemical conditions. Increasing flow rate led to falling in the peak heights as shown in Fig. 6, but a flow rate of 1.5 ml/min was chosen for the procedure, because there was no any signal corresponding to the presence of PCM in the pathway(1), and AA has the same peak intensity in both pathways. Figure 7 shows the effect of increasing lengths of mixing coil on the reaction lines of $FeCl_3$ with AA and PCM from the pathway(1) and pathway(2), respectively. Figure 8 shows the effect of introducing the mixing coil into the coloured complex formation line between produced Fe(II) and 1,10-phenanthroline. The effect of temperature as shown in Fig. 9 was studied in the second step procedure by placing the 120-cm reaction coil [pathway(2)] in a water bath at different temperature ranges 25–85 °C with constant flow rate 1.5 ml/min. The influence of the sample volume was studied by double injection of different sample volumes for both steps of procedure as shown in Fig. 10. The ranges and optimum concentrations of all physical parameters are shown in Table 2.

Table 2 Studied range and optimum chemical and physical parameters

Parameters	Ranges		Optimum value
	From	To	
$FeCl_3$ concentration (M)	0.5×10^{-3}	5×10^{-3}	1.5×10^{-3}
HCl concentration (M)	1×10^{-3}	20×10^{-3}	5×10^{-3}
1,10-phenanthroline concentration (M)	0.5×10^{-3}	5×10^{-3}	3×10^{-3}
Flow rate (ml/min)	1	5	1.5
Mixing coil for (analyte and $FeCl_3$) from pathway(1) (cm)	Without coil	120	No need
Mixing coil for (analyte and $FeCl_3$) from pathway(2) (cm)	20	160	120
mixing coil length in the coloured complex formation line (cm)	Without coil	60	No need
Temperature (°C)	25	85	60
Sample volume (µl)	60	200	125

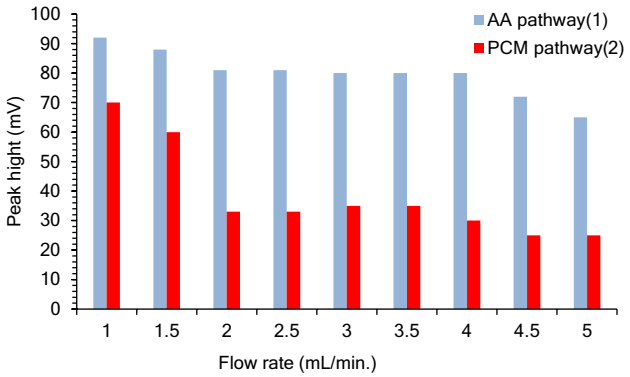

Fig. 6 Effect of flow rate on the peak height

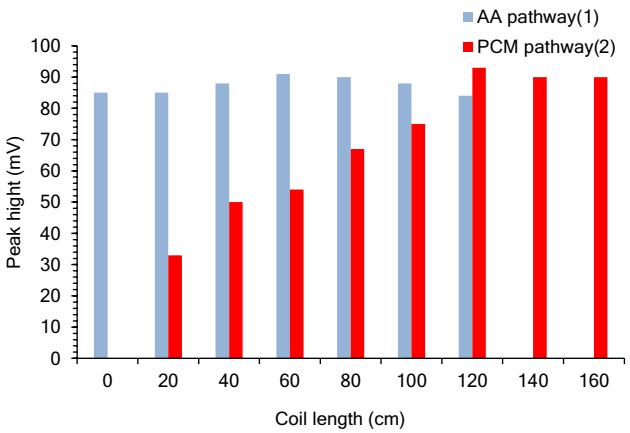

Fig. 7 Effect of mixing coil length in the reaction lines of $FeCl_3$ with AA and PCM from the pathway(1) and pathway(2) on the peak height

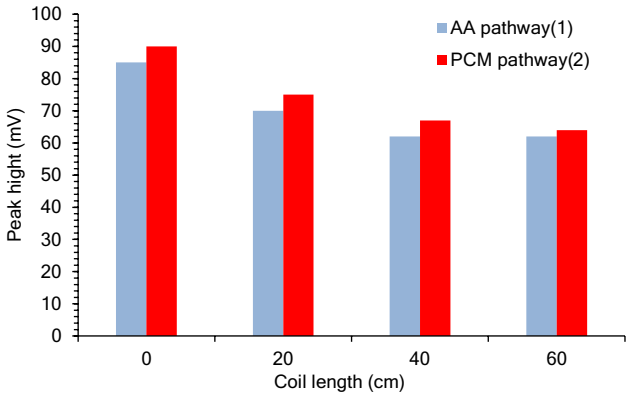

Fig. 8 Effect of mixing coil length in the coloured complex formation line between produced Fe(II) and 1,10-phenanthroline on the peak height

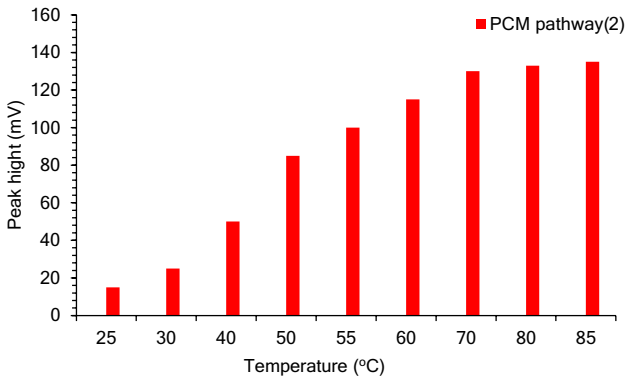

Fig. 9 Effect of temperature on the peak height

Effect of interferences

For the determination of 4 µg/ml AA and 10 µg/ml PCM, a study of interfering effects of some usual excipients has been performed, and the results obtained are shown in Table 3. It was ascertained that drug excipients from the various tablets did not interfere. Thus, the present method has an appropriate indicating assay for the analysis of AA and PCM in tablets in the presence of different excipients found in formulations. In addition, a large amount of excipient separately or collectively is tolerated, because those exhibited an error not exceeding ± 5% in the determination of 4 µg/ml AA and 10 µg/ml PCM.

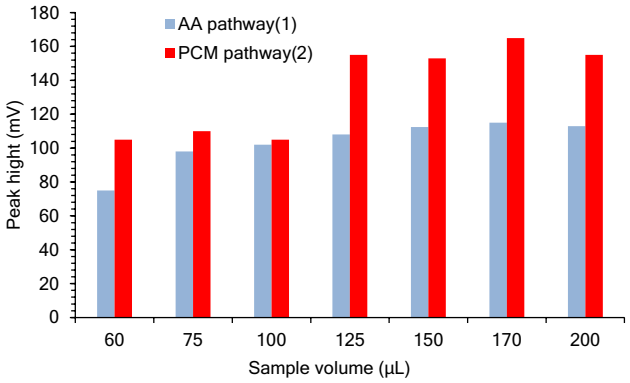

Fig. 10 Effect of sample volume on the peak height

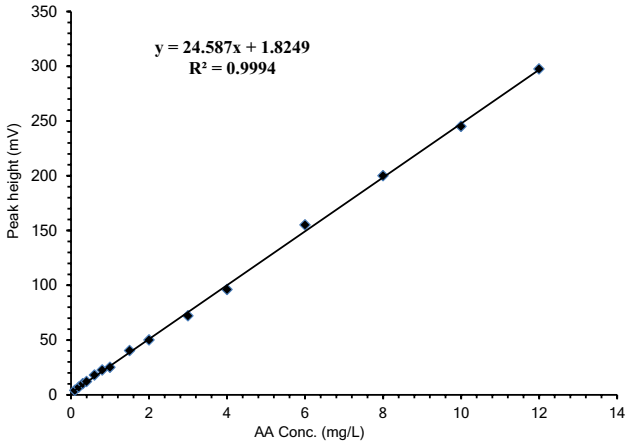

Fig. 11 Calibration graph for the determination of AA

Calibration graphs

Under optimised operating conditions mentioned in Table 2 and by injecting 0.1–12 µg/ml AA and 0.4–24 µg/ml PCM standard solutions into the FI spectrophotometric system shown in Fig. 1, calibration graphs were constructed. Good linearity was obtained between absorption peak heights and analyte concentrations with good correlation coefficients as shown in Figs. 11 and 12. The statistical variables including low LOD and LOQ for both analyte determinations are illustrated in Table 4.

Accuracy and precision

Ten replications for two different concentrations of AA and PCM in the linear ranges were measured and determined by the recommended procedure for checking the accuracy and precision of the method by performing relative error (*%E*) and relative standard deviation (RSD). The results tabulated in Table 5 indicate that the method is accurate and precise.

Application

Four different local commercial pharmaceutical tablets containing these analytes were quantified to evaluate the developed procedure, using the redox complex formation reaction and FI spectrophotometric method for their simultaneous determinations. The absorption signals for each pharmaceutical sample are obtained with triplicate analysis. The precision was studied and found to be less

Table 3 Effect of interference on the determination of 4 µg/ml AA & 10 µg/ml PCM

Excipients	Using AA 4 µg/ml			Using PCM 10 µg/ml		
	Fold added	AA determined (µg/ml ± SD)	*%E*	Fold added	PCM determined (µg/ml ± SD)	*%E*
$NaHCO_3$	22.5	3.98 ± 0.15	−0.51	6	9.83 ± 0.09	−1.68
Na_2CO_3	22.5	3.85 ± 0.14	−3.73	6	10.34 ± 0.04	3.42
$MgSO_4$	22.5	4.07 ± 0.08	1.85	6	10.11 ± 0.09	1.1
Na-saccharinate	22.5	4.19 ± 0.04	4.9	6	10.25 ± 0.04	2.49
Citric acid	22.5	4.19 ± 0.11	4.9	6	9.83 ± 0.09	−1.68
Disodium citrate	22.5	4.07 ± 0.08	1.85	4	9.64 ± 0.18	−3.55
Adipic acid	20	4.19 ± 0.08	4.9	6	10.48 ± 0.37	4.82
Povidone	22.5	4.17 ± 0.06	4.39	6	10.39 ± 0.09	3.89
Sorbitol	22.5	4.15 ± 0.08	3.89	6	10.25 ± 0.04	2.49
Lactose	22.5	4.07 ± 0.04	1.85	5	9.73 ± 0.09	−2.61
Starch	22.5	4.17 ± 0.1	4.39	5	9.73 ± 0.0	−2.61
Chlorpheniramine malate	22.5	4.07 ± 0.03	1.85	6	10.32 ± 0.15	3.27
All above	2	3.98 ± 0.2	−0.51	0.5	10.08 ± 0.08	0.79

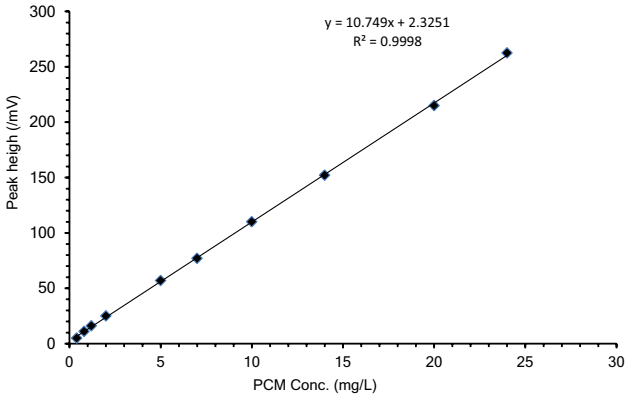

Fig. 12 Calibration graph for the determination of PCM

Table 4 Analytical characteristic for calibration curves

	AA	PCM
No. of measurements	15	10
Linear range (µg/ml)	0.1–12	0.4–24
Correlation coefficient (R)	0.9997	0.9999
LOD (µg/ml)	0.31	0.39
LOQ (µg/ml)	0.94	1.2

Table 5 Accuracy and precision of the method

Analytes	Concentrations (µg/ml ± SD)		*%E*	RSD ($n=10$)
	Standard solution	Determined by the proposed method		
AA	2	1.97 ± 1.67	− 1.42	3.33
	7	7.02 ± 4.31	0.32	2.47
PCM	6	6.09 ± 2.04	1.52	3.008
	15	15.13 ± 3.68	0.89	2.23

than 2.29% (RSD) for AA and 5.29% for PCM; also by using prepared amounts as a theoretical value, the recovery percentages were calculated.

Also, the certified reference materials of AA and PCM spiked with the appropriate amounts were directly analysed for applying the developed method. The recovery percentages obtained for the sample analysis are within the range of 95.31–104.73% and 95.03–104.93% for AA and PCM, respectively. The results are shown in Table 6.

Conclusion

The proposed method is novel because in the literature currently, there are no proposed FI spectrophotometric methods for the determination of these drugs in the binary mixture.

The optimisation of the chemical and physical parameters allowed linear calibration curves for the determination of AA and PCM easily in different samples based on the different rates of their reactions with Fe(III) with the low limit of detection 0.31 µg/ml and 0.39 µg/ml for AA and PCM, respectively, and a good recovery percentage attainment for the spiked sample analysis.

The results obtained show that the double injection of the same sample solution and a single spectrophotometric detector flow injection system are found to be proper for simple, selective, sensitive, low-cost, accurate and precise quantification. The method can be developed from semi-automated to fully automated by some manufacturers which they needed for quality control of the drugs.

Table 6 Application of the proposed method for the determination of AA and PCM in different tablets

Sample	Prepared amount (µg/ml)		Added (µg/ml)		AA determination			PCM determination		
	AA	PCM	AA	PCM	Found AA (µg/ml ± SD)	*%R*	RSD ($n=3$)	Found PCM (µg/ml ± SD)	*%R*	RSD ($n=3$)
1	3	5	–	–	2.83 ± 0.05	94.23	1.79	5.3 ± 0.08	106.07	1.65
2	3	10	–	–	2.98 ± 0.03	99.2	1.11	9.77 ± 0.51	97.69	5.29
3	3	15	–	–	2.89 ± 0.06	96,49	2.29	18.32 ± 0.3	122.18	1.67
4	3	10.5	–	–	2.72 ± 0.05	90.62	1.86	10.63 ± 0.3	101.3	2.88
1	3	5	1	2	3.8 ± 0.05	99.56	1.33	7.66 ± 0.15	104.93	1.98
2	3	10	1	2	3.88 ± 0.15	97.84	4.04	11.56 ± 0.37	98.28	3.21
3	3	15	1	2	4.07 ± 0.04	104.73	0.99	19.32 ± 0.18	95.03	0.96
4	3	10.5	1	2	3.54 ± 0.03	95.31	0.93	12.62 ± 0.28	99.85	2.21

References

1. A. Selimović, M. Salkić, A. Selimović, Int. J. Basic Appl. Sci. **11**, 106 (2011)
2. H. Lullman, H. Lutz, M. Klaus, B. Detlef, *Color Atlas of Pharmacology*, 3rd edn. (Thieme, Stuttgard, 2005), p. 198
3. H.R. Zare, B. Moradiyan, Z. Shekari, A. Benvidi, Measurement **90**, 510 (2016)
4. S.P. Arya, M. Mahajan, P. Jain, Indian J. Chem. **38**, 1303 (1999)
5. S.H. Davies, S.J. Masten, Anal. Chim. Acta **248**, 225 (1991)
6. X. Gu, C. Chen, T. Zhou, Fresenius J. Anal. Chem. **355**, 94 (1996)
7. K. Güçlü, K. Sözgen, E. Tütem, M. Özyürek, R. Apak, Talanta **65**, 1226 (2005)
8. S.S. Hassan, M.A. El Fattah, M. Zaki, Fresenius' Zeitschrift für analytische Chemie **277**, 369 (1975)
9. H.-H. Shieh, T.R. Sweet, Anal. Biochem. **96**, 1 (1979)
10. A. Jain, A. Chaurasia, K.K. Verma, Talanta **42**, 779 (1995)
11. A. Molina-Dıaz, I. Ortega-Carmona, M. Pascual-Reguera, Talanta **47**, 531 (1998)
12. A.V. Pereira, O. Fatibello-Filho, Talanta **47**, 11 (1998)
13. D.G. Themelis, P.D. Tzanavaras, F.S. Kika, Talanta **55**, 127 (2001)
14. M. Yebra, R. Cespon, A. Moreno-Cid, Anal. Chim. Acta **448**, 157 (2001)
15. M. Noroozifar, M. Khorasani-Motlagh, Talanta **61**, 173 (2003)
16. M.R. Rama, A.R. Medina, A.M. Dıaz, Microchem. J. **78**, 157 (2004)
17. A.B. Vishnikin, T.Y. Svinarenko, H. Sklenářová, P. Solich, Y.R. Bazel, V. Andruch, Talanta **80**, 1838 (2010)
18. L. Kukoc-Modun, M. Biocic, N. Radić, Talanta **96**, 174 (2012)
19. R. Hassan, A. Faizullah, J. Iran. Chem. Soc. **8**, 662 (2011)
20. G.G. Rao, G.S. Sastry, Anal. Chim. Acta **56**, 325 (1971)
21. M. Barakat, S. Shehab, N. Darwish, E. El-Zoheiry, Anal. Biochem. **53**, 245 (1973)
22. D.E. Hughes, J. Pharm. Sci. **72**, 126 (1983)
23. K.G. Kumar, P. Indrasenan, Talanta **37**, 269 (1990)
24. S.M. Sultan, Talanta **40**, 593 (1993)
25. B. Vahid, *J. Chem. Soc. Pak.* **34**, 1510–1512 (2012)
26. M. Koupparis, T. Hadjiioannou, Anal. Chim. Acta **94**, 367 (1977)
27. J.C.B. Fernandes, L. Rover Jr., L.T. Kubota, G.D. Oliveira Neto, J. Braz. Chem. Soc. **11**, 182 (2000)
28. R. Thangamuthu, S.S. Kumar, K.C. Pillai, Sens. Actuators B Chem. **120**, 745 (2007)
29. M. Motshakeri, J. Travas-Sejdic, A.R.J. Phillips, P.A. Kilmartin, Electrochim. Acta **265**, 184 (2018)
30. M. Doulache, M. Trari, B. Saidat, J. Chem. Sci. **130**, 110 (2018)
31. A.A. Hathoot, K.M. Hassan, W.A. Essa, M. Abdel-Azzem, J. Iran. Chem. Soc. **14**, 1789 (2017)
32. K.M. Hassan, *J. Iran. Chem. Soc.* **15**, 1007–1014 (2018)
33. T. Maki, N. Soh, K. Nakano, T. Imato, Talanta **85**, 1730 (2011)
34. Y. Matsuoka, M. Yamato, T. Yamasaki, F. Mito, K.-I. Yamada, Free Radic. Biol. Med. **53**, 2112 (2012)
35. G. Xue, Z. Yue, Z. Bing, T. Yiwei, L. Xiuying, L. Jianrong, J. Lumin. **180**, 146 (2016)
36. X. Li, A.A. Franke, J. Chromatogr. B **877**, 853 (2009)
37. M. Ciulu, S. Solinas, I. Floris, A. Panzanelli, M.I. Pilo, P.C. Piu, N. Spano, G. Sanna, Talanta **83**, 924 (2011)
38. R. Kanďár, P. Drábková, R. Hampl, J. Chromatogr. B **879**, 2834 (2011)
39. R. Ferin, M.L. Pavão, J. Baptista, Clin. Biochem. **46**, 665 (2013)
40. R. Zuo, S. Zhou, Y. Zuo, Y. Deng, Food Chem. **182**, 242 (2015)
41. T.Z. Attia, Spectrochim. Acta Part A Mol. Biomol. Spectrosc. **169**, 82 (2016)
42. F. Turak, R. GŘzel, E. Dinš, J. Food Drug Anal. **25**, 285 (2017)
43. J.T. Afshari, T.-Z. Liu, Anal. Chim. Acta **443**, 165 (2001)
44. Z.A. ALOthman, M.A. Abdalla, Arab. J. Chem. **4**, 239 (2011)
45. H. Filik, M. Hayvali, E. Kilic, Anal. Chim. Acta **535**, 177 (2005)
46. F.A. Mohamed, M.A. AbdAllah, S.M. Shammat, Talanta **44**, 61 (1997)
47. P. Nagaraja, K.S. Murthy, K. Rangappa, J. Pharm. Biomed. Anal. **17**, 501 (1998)
48. Z. Bouhsain, S. Garrigues, A. Morales-Rubio, M. de la Guardia, Anal. Chim. Acta **330**, 59 (1996)
49. A.R. Medina, M.F. de Córdova, A.M. Dıaz, Anal. Chim. Acta **394**, 149 (1999)
50. A. Criado, S. Cárdenas, M. Gallego, M. Valcárcel, Talanta **53**, 417 (2000)
51. M. Knochen, J. Giglio, B.F. Reis, J. Pharm. Biomed. Anal. **33**, 191 (2003)
52. A.F. Lavorante, C.K. Pires, B.F. Reis, J. Pharm. Biomed. Anal. **42**, 423 (2006)
53. J.M. Calatayud, C.G. Benito, Anal. Chim. Acta **231**, 259 (1990)
54. J.M. Pulgarín, L.G. Bermejo, Anal. Chim. Acta **333**, 59 (1996)
55. V.A. Pedrosa, D. Lowinsohn, M. Bertotti, Electroanal. Int. J. Devoted Fundam. Pract. Asp. Electroanal. **18**, 931 (2006)
56. Z. Xu, Q. Yue, Z. Zhuang, D. Xiao, Microchim. Acta **164**, 387 (2009)
57. G.G. Oliveira, B.C. Janegitz, M.B. Batistão, F.H. Salami, O. Fatibello-Filho, O.D. Leite, Quim. Nova **32**, 1755 (2009)
58. W. Ruengsitagoon, S. Liawruangrath, A. Townshend, Talanta **69**, 976 (2006)
59. K.G. Kumar, R. Letha, J. Pharm. Biomed. Anal. **15**, 1725 (1997)
60. G. Burgot, F. Auffret, J.-L. Burgot, Anal. Chim. Acta **343**, 125 (1997)
61. A.K. Baytak, S. Duzmen, T. Teker, M. Aslanoglu, Mater. Sci. Eng. C **57**, 164 (2015)
62. L. Ahmadpour-Mobarakeh, A. Nezamzadeh-Ejhieh, Mater. Sci. Eng. C **49**, 493 (2015)
63. S.H. Lee, J.H. Lee, V.-K. Tran, E. Ko, C.H. Park, W.S. Chung, G.H. Seong, Sens. Actuators B Chem. **232**, 514 (2016)
64. F. Cao, Q. Dong, C. Li, J. Chen, X. Ma, Y. Huang, D. Song, C. Ji, Y. Lei, Sens. Actuators B Chem. **256**, 143 (2018)
65. Y. Xu, W. Lei, J. Su, J. Hu, X. Yu, T. Zhou, Y. Yang, D. Mandler, Q. Hao, Electrochim. Acta **259**, 994 (2018)
66. B. Habibi, M. Jahanbakhshi, M. Abazari, J. Iran. Chem. Soc. **11**, 511 (2014)
67. M.A. Oliva, R.A. Olsina, A.N. Masi, Talanta **66**, 229 (2005)
68. E. Llorent-Martínez, D. Šatínský, P. Solich, P. Ortega-Barrales, A. Molina-Díaz, J. Pharm. Biomed. Anal. **45**, 318 (2007)
69. H. Montaseri, P.B. Forbes, Mater. Today Commun. **17**, 480 (2018)
70. M. Locatelli, R. Cifelli, C. Di Legge, R.C. Barbacane, N. Costa, M. Fresta, C. Celia, C. Capolupo, L. Di Marzio, J. Chromatogr. A **1388**, 79 (2015)
71. M.-H. Langlois, A. Vekris, C. Bousses, E. Mordelet, N. Buhannic, C. Séguard, P.-O. Couraud, B.B. Weksler, K.G. Petry, K. Gaudin, J. Chromatogr. B **988**, 20 (2015)
72. N.W. Ali, M. Gamal, M. Abdelkawy, Arab. J. Chem. **10**, S1868 (2017)
73. H. Khajehsharifi, Z. Eskandari, A. Asadipour, Drug Test. Anal. **2**, 162 (2010)
74. S. Sharifian, A. Nezamzadeh-Ejhieh, Mater. Sci. Eng. C **58**, 510 (2016)
75. M. Taei, M.S. Jamshidi, Microchem. J. **130**, 108 (2017)
76. C. Li, J. Xu, Y. Wu, Y. Zhang, C. Zhang, W. Lei, Q. Hao, J. Electroanal. Chem. **824**, 52 (2018)
77. N.H. Phong, T.T.T. Toan, M.X. Tinh, T.N. Tuyen, T.X. Mau, D.Q. Khieu, J. Nanomater. **2018**, 1–15 (2018)
78. M. Gioia, P. Andreatta, S. Boschetti, R. Gatti, J. Pharm. Biomed. Anal. **48**, 331 (2008)
79. B. Tsvetkova, I. Pencheva, P. Peikov, Afr. J. Pharm. Pharmacol. **6**, 1332 (2012)
80. F. Ibrahim, N. El-Enany, R.N. El-Shaheny, I.E. Mikhail, Anal. Sci. **31**, 943 (2015)