Spectrophotometric Determination of Promethazine Hydrochloride and Paracetamol in Pharmaceutical Tablets

Khaleda H. Al-Saidi* and Rana A, Hammza
* Department of Chemistry, College of Science, Al-Nahrain University, Al-Jaderia, Baghdad-Iraq.
*E-mail: Khaleda_alsaidi51@yahoo.com.

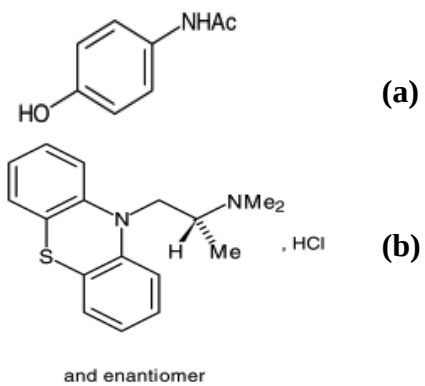
Abstract

Spectrophotometric techniques were developed for the determination of single and binarymixture Promethazine hydrochloride (PMH) and Paracetamol (PCM). Normal and first derivative (^{1}D) used for single drug at λ 249.5 and 243.0 for PMH and 243.5 and 225 for PCM. The simultaneous determination of binary mixture (PMH) and (PCM) were accomplished by first derivative (^{1}D) and second derivative (^{2}D) spectrophotometric technique with applying zero-crossingat valley (V=216.5) and Peak (P=258.8)nm for (PMH) and (V=274.0 and P=299.2 nm for PCM).The correlation coefficient for calibration curves not less than 0.999 and the relative standard deviation not exceed to 0.214. The recovery of individual constituents under establishedconditions inthe ranges from 97.00% to 101.97 %. Linearity is maintained within a wide concentrationrange from 4.00-30.00mg/L for PMH and PCM. Standard addition method used forpharmaceutical tablets. A good accuracy and precision of simultaneous determination of (PCM), and (PMH) were confirmed by statistical analysis. The proposed procedures were successfully applied to the determination of these compounds in different ratio by synthetic mixtures and pharmaceutical tablets without requiring any separation step.

Keywords: Paracetamol; Promethazinehydrochloride; binary mixtures; derivative spectrophotometry; zero-crossing technique.

Introduction

Promethazine hydrochloride has the empirical formula $C_{17}H_{20}N_2S$. HCl and structure as in schem1, the molecular weight is equal to 320.9 g/mol, freely soluble in alcohol and in methylene chloride**,** the action and usehistamine H_1-receptor antagonist; anti-emetic[1]. Several methods used for determination of PMH include, spectrophotometric methods[2], Flow injectionanalysis[3,4], high-performance liquid chromatographic[5], ion-selective electrode[6, 8].



Scheme (1) The structure of, a- Promethazine hydrochloride, b- Paracetamol

Paracetamol (PCM) has the formula $C_8H_9NO_2$, molecular weight 151.2 g/mol and structure as in scheme (1). (PCM) is a white, crystalline powder, sparingly soluble in water (0.1-0.5 g/100mL at 20 ^oC), freely soluble in alcohol, very slightly soluble in ether and in methylene chloride[1]. PCM (acetaminophen) is widely used as an analgesic and as an antipyretic drug. Many assays have been described for PCM including chromatography[9-15], fluorometry[16], colorimetry and UV spectrophotometry[17-20], by enzymatis hydrolysis[21] and various modes of electrochemistry , such the differential pulse voltammetric behavior of some drugs including Paracetamol at various conducting polymers[22], and in a variety of drug formulations containing Paracetamol[23-25]. Although the electrochemical oxidation of Paracetamol at a glassy carbon electrode has[26], differential pulse voltammetry have been reported; for determination of the drug in blood plasma and in a single type of tablet[27], pumice mixed carbon electrodes[28] have been examined and reviewed[29].cyclic voltammetric[30-31].

Derivative spectrophotometric and chemometric methods [32,33], Simultaneous determination using a powder on NIR spectroscopy[34].

In this paper a new spectrophotometric method for simultaneous determination of PCM and PMH hydrochloride using derivative spectrophotometrictechnique[35]was used for quantitative analysis by using first and second order. An attempt was made to find suitable derivatives and wavelength for quantitative analysis for Para and PCM hydrochloride at which both drugs show no interference. As no similar analyses were found in available literature it seems justifiable to develop a simple, quick and easily available spectrophotometric method for drug quality control purposes. This method differ from other it don't need any chemical treatment and both drugs can be determined directly in a single sample without using any separation process.

Experimental

Instruments and Equipments:

Double-beam UV-Visible spectrophoto-meter model (UV-1650 PC) SHIMADZ (Japan), interfaced with computer via a SHIMADZU UV probe data system program (Version 1.10), using 1.00 cm quartz cells, Ultra pure water manufacturing devise, (TORAYPURE), model LV-08 (Japan).

Chemicals:

Standard (PCM) and (PMH) were gift from the State Company of Drug Industries and Medical Appliances S.D.I (IRAQ- Samara), COLDEIN tablet from local market (450.0 mg (PCM) and 5.0 mg (PMH) per tablet) and PCMCETOL tablet (500 mg PCM).All drugs were used as working standards without further purification.

Preparation of stock and working standard solutions:

1-Stock solutions of standard were prepared by dissolving an accurately weighed amount 20 mg of the studied drugs by deionized water in100 ml volumetric flask. The solutions are then made up to the volume with deionized water, to obtain the suitable working standard solutions according to the linear calibration range for each drug.

2- Two series of pure single standards drugs prepared by dilution from stock solutions with the deionized water.

3- Solutions for binary mixtures of standard drugs (PCM) and (PMH) solutions were prepared by two series;
First series of mixture solutions were prepared by using a fixed concentration of (10 mg/L) for (PCM) with different concentrations (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, and 30 mg/L) of (PMH) , second series of mixture contain a fixed concentration (3 mg/L) of (PMH) with different concentration of (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, and 30 mg/L) of (PCM).

4- Standard addition method involves preparing several 10 mL solutions containing the same amount 5mL from 20mg/L drug of tablet solution to determine (PCM), but different amounts of standard (0, 2,8,15,20 and 30) mg/L (PCM), similarly for (PMH).

Preparation of pharmaceutical formulation:

Ten tablets were crushed for each drug, mixed in a mortar and weighted accurately equivalent weight to prepare 450, 500 mg/L from COLDEIN and PARACETOL tablets, respectively, which dissolved by 50 mL deionized water and using ultrasonicator for ١٠min then filtrate and washing the precipitate with deionized water, the filtrate was collected in 100 mL volumetric flaskother solution was prepared by dilution with deionized water.

Results and Discussion

The absorption spectra of the (PMH) and (PCM) were measured from 200-400 nm against deionized water as blank. The wavelength at absorption maximum (λmax) was identified. Fig.(1) show the zero orders (normal spectra) of standard solutions for PMH and PCM. Normal spectra can be used in the determination of single (PMH) and single (PCM) at wavelengths 249.5 and 243.5 nm, respectively.

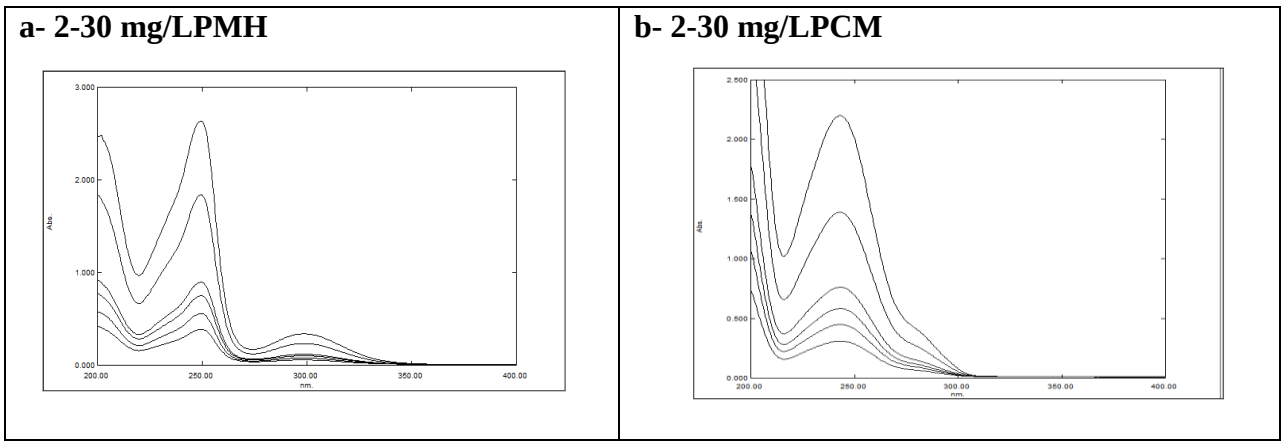


Fig. (1) Normal spectra for a- 2-30 mg/L PMH and b- 2-30 mg/L PCM.

Fig. (2) show first derivative for PMH and PCM, the wavelengths at 243.5 and 225.0 nm were also used to determine single PMH and PCM drug respectively, the results which obtained for each drug were tabulated in Table(1). The calibration curves of normal and ^{1}D for standard solutions (2-30 mg/L) (PMH) and (PCM) were constructed, which regression line gave linear equations with the correlation coefficient and molar absorptivity ε are summarized in Table (1). The results for determination of (PMH) and (PCM) and confidence limits at 95% (t=4.30) are tabulated in Table (2) and (3), respectively. The results for single(PMH)and single (PCM) at which obtained from first derivative were better than the results from normal spectra, where standard deviation not exceed than 0.0010 and 0.0153 and correlation coefficient were 0.99978 and 0.99990 for PMH and PCM, respectively.

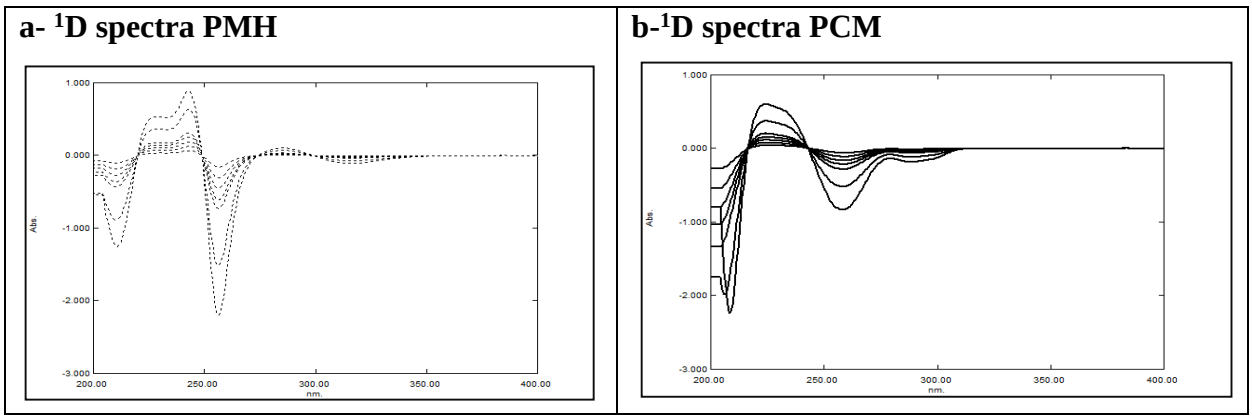


Fig. (2) First derivative spectra: a- PMH, b- PCM for the solutions range (2-30 mg/L).

Table (1)
Thestatistical evolution for the calibration graph for determination of pure PMHand PCM.

Drug	*Concentration range mg/L*	*Method*	*Wavelength*	*Equation*	*r*	*Molar absorptivity*
PMH	2-30	Normal	249.5	Y=0.08709x+0.0400	0.99981	$2.7947x10^4$
PMH	2-30	**^{1}D**	243.0	Y=0.02944x+0.01045	0.99979	---------
PCM	2-30	Normal	243.5	Y=0.07168x+0.01306	0.999565	$1.0838x10^4$
PCM	2-30	**^{1}D**	255.0	Y=0.02030x+0.00596	0.99990	-------

Table (2)
The statistical evolution for determination of standard (PMH) solutions using normal and ^1D spectra at ٢٤٩.5 nm and 243.0nm, respectively.

PMH	PMH. .found*	%Er	Recovery %	RSD%	SD	C.L X±(ts/√N)	PMH. .found*	%Er	Recovery %	RSD%	SD	C.L X±(ts/√N)
	Normal at 249.5 nm						^1D at 243 nm					
4.0	3.973	-0.675	99.30	1.7245	0.0689	3.897±0.1267	3.891	-2.725	97.275	0.025	0.001	3.891±0.00183
6..0	5.936	-1.067	98.93	0.7862	0.0472	5.981±0.086712	6.032	+0.533	100.5	0.0167	0.001	6.032±0.00184
8.0	8.164	+2.05	102.05	1.0489	0.0839	8.072±0.1542	8.138	+1.725	101.73	0.0125	0.001	8.138±0.00184
10.0	9.841	-1.59	98.41	0.7939	0.0794	9.836±0.1459	9.973	-0.27	99.73	0.0058	0.0006	9.973±0.00106
20.0	20.348	+1.74	101.74	0.2753	0.0551	20.262±0.10124	20.368	+1.84	101.8	0.0028	0.0006	20.368±0.00106
30.0	29.798	-0.673	99.33	0.2428	0.0728	29.801±0.1338	29.745	-0.85	99.15	0.0033	0.001	29.746±0.00184

**The average of three measurements and SD not exceed than 0.08 and 0.001 for normal and ^1D respectively*

Table (3)
The statistical evolution for determination of standard (PCM) solutions using normal and ^1D at wavelengths ٢43.50 and 225 nm respectively.

PCM	PCM found*	%Er	Recovery %	RSD%	SD	C.L X±(ts/√N)	PCM .found*	%Er	Recovery %	RSD%	SD	C.L X±(ts/√N)
	Normal at 243.5 nm						^1D at 225.0 nm					
4.0	4.073	+1.825	101.82	0.227	0.0090	4.068±0.0167	4.087	+2.17	102.17	0.025	0.001	4.088±0.00184
6.0	6.082	+1.377	101.37	0.1549	0.0092	6.079±0.017	5.910	-1.40	98.5	0.2546	0.0153	5.9233±0.0281
8.0	8.007	+0.0875	100.09	0.432	0.0345	8.005±0.0635	7.832	-2.10	97.90	0.0191	0.0015	7.834±0.00281
10.0	10.016	+0.16	100.16	0.321	0.0320	10.021±0.059	10.246	+2.46	102.46	0.0416	0.0042	10.245±0.00765
20.0	19.39	-3.05	96.95	1.017	0.2033	19.28±0.3738	19.952	-0.24	99.76	0.0264	0.0053	19.954±0.00973
30.0	30. 36	+1.23	101.23	0.6067	0.182	30.352±0.335	30.003	+0.01	100.01	0.0039	0.0011	30.002±0.00212

**The average of three measurements and SD not exceed than 0.2022 and 0.0153for normal and ^1D respectively.*

Binary Mixture:

Fig. (3a) Show the over lapping of the normal spectra for the two drugs therefore normal spectra cannot be used to determine each of the drug in the mixture. First and second derivative may be used as shown in Fig. (3b and c). Zero crossing method used to determine each drug present in binary mixture at the wavelengths as shown in Fig. (4) and Fig. (5) For PMH and PCM respectively. Calibration curves of ^1D and ^2D at zero crossing for standard solutions of (2-30mg/L) were constructed gave linear equations and the correlation coefficients were listed in Table (4). The results for determination of (PMH) and (PCM) are tabulated in Tables (5, 6) and Tables (7, 8), respectively.

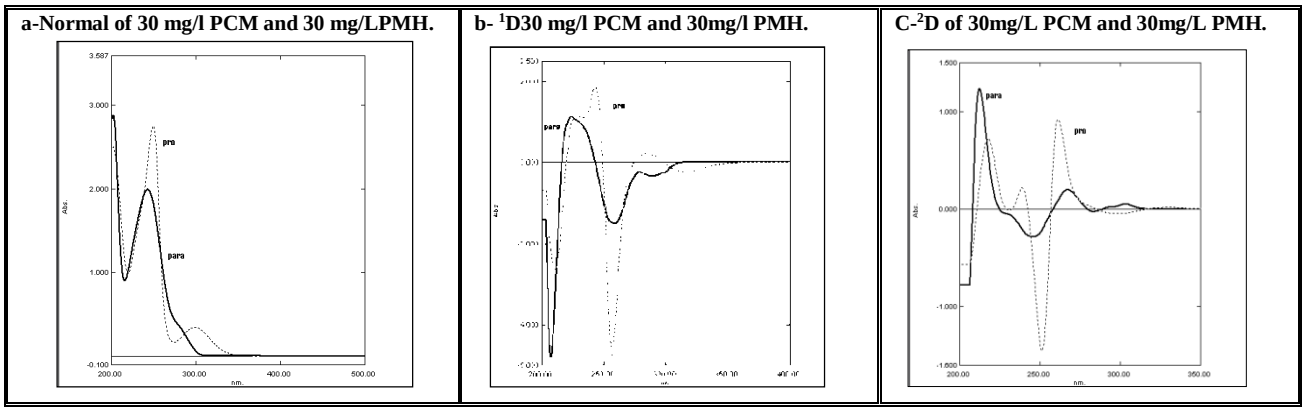
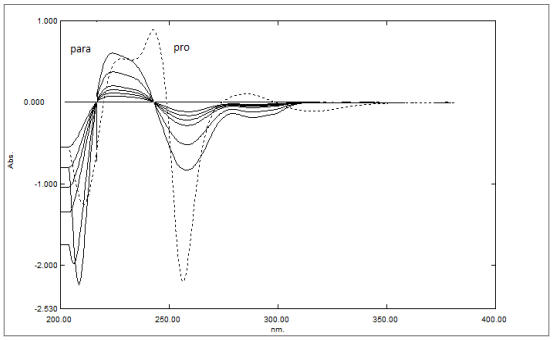


Fig. (3) The spectra of 30 mg/L PCM and 30 mg/L PMH: a- normal spectra, b- ^1D spectra, c- ^2D spectra.

a-^{1}D 30 mg/L PMH + 2-30 mg/L PCM at zero crossing v=216.5nm



b- ^{2}D 30 mg/L PMH + 2-30 mg/L PCM at zero crossing p=258.8 nm

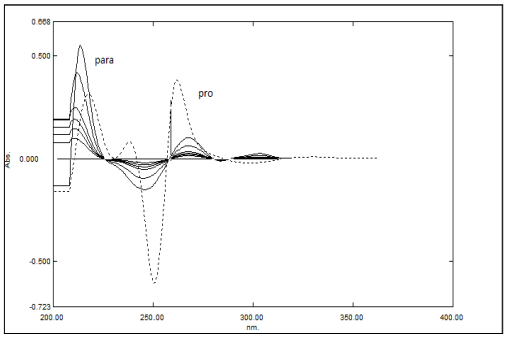
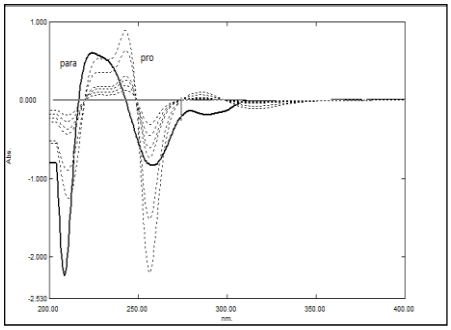


Fig. (4) Zero crossing wavelengths a- ^{1}D at V= 216.5 nm, b-^{2}D at P=258.8 nm for determination of PMH.

a-^{1}D 30 mg/L PCM + 2-30 mg/L PMH at zero crossing at 274 nm



b-^{1}D 30 mg/L PCM + 2-30 mg/L PMH at zero crossing a 299.2 nm

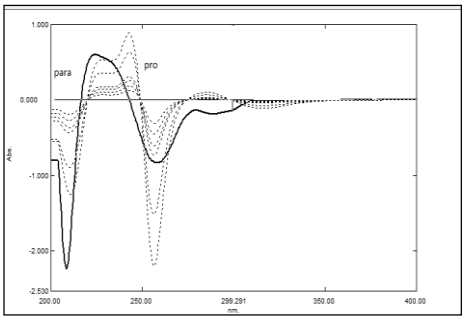


Fig. (5) Zero crossing wavelengths a- ^{1}D at V= 274 nm, b-^{1}D at V=299.2 nm for determination PCM.

Table (4)
The statistical evolution for the calibration graphs for determination of (PMH) and (PCM) using zero crossing method.

Drug	*Concentration range mg/L*	*Method*		*Equation*	*r*
PMH	2-30	^{1}D	V=216.5	Y=-0.02011x-0.00972	0.99978
PMH	2-30	^{2}D	P=258.8	Y=0.00844x+0.00245	0.9996
PCM	2-30	^{1}D	V=274.07	Y=-0.00684x-0.00138	0.99946
PCM	2-30	^{1}D	V=299.20	Y=-0.00457x-0.00026	0.99966

Table (5)
The statistical evolution for determination of standardPMH solutions using first derivative with at zero crossing valley ٢١٦,٥ nm.

Mg/L PMH+PCM	*PMH. mg/L. found**	*Relative error%*	*Recovery %*	*SD*	*C.L X±□ ts□√N□*
2.00+10.00	1.953	-2.35	97.65	0.0288	1.953±0.00106
4.00+10.00	3.942	-1.45	98.55	0.0144	3.942±0.00106
5.00+10.00	4.887	-2.26	97.74	0.0200	4.887±0.00184
10.00+10.00	9.809	-1.91	98.09	0.0058	9.806±0.00106

The average of three measurements and SD not exceed than 0.0288.

Table (6)
The statistical evolution for determination of standard PMH solutions using second derivative at zero crossing at peak 258.8 nm.

Mg/L PMH+PCM	*PMH.mg/L .found**	*Relative error%*	*Recovery %*	*SD*	*C.L*
3.00+1.00	3.029	+0.967	100.97	0.033	3.029±0.00184
3.00+2.00	3.029	+0.967	100.97	0.033	3.029±0.00184
3.00+3.00	3.029	+0.967	100.97	0.033	3.029±0.00184
3.00+4.00	3.029	+0.967	100.97	0.033	3.029±0.00184
3.00+5.00	3.029	+0.967	100.97	0.033	3.029±0.00184
3.00+6.00	2.910	-3.000	97.00	0.510	2.927±0.02808
3.00+7.00	3.029	+0.967	100.97	0.019	3.029±0.001061
3.00+8.00	3.029	+0.967	100.97	0.019	3.029±0.001061
3.00+9.00	3.029	+0.967	100.97	0.019	3.029±0.00106
3.00+10.00	3.029	+0.967	100.97	0.019	3.029±0.00184
1.00+10.00	1.013	+1.300	101.30	0.116	1.014±0.00212
3.00+10.00	2.910	-3.000	97.00	0.333	2.920±0.0184
5.00+10.00	5.044	+0.880	100.88	0.031	5.044±0.00281
6.00+10.00	5.992	-0.130	99.88	0.025	5.993±0.00281
7.00+10.00	7.059	+0.840	101.57	0.014	7.06±0.00184
8.00+10.00	8.126	+1.570	100.84	0.012	8.127±0.00184
10.00+10.00	10.023	+0.230	100.23	0.010	10.024±0.00184
15.00+10.00	15.121	+0.807	100.81	0.013	15.123±0.00368
25.00+10.00	24.604	-1.580	98.42	0.006	24.6037±0.00281
30.00+10.00	30.532	+1.770	101.77	0.007	30.534±0.00368

Table (7)
The statistical evolution for determination of standard PCM solutions using first derivative at peak 274 nm.

PMH + PCM mg/L	*PCM. .found* Mg/L*	*Relative error%*	*Recovery %*	*SD*	*C.L* $X \pm \square ts \square \sqrt{N} \square$
3.00+4.00	3.891	-2.72	97.27	0.1041	3.891±0.0076
3.00+6.00	5.937	-1.05	98.95	0.1018	5.937±0.0112
3.00+7.00	6.814	-2.65	97.34	0.0082	6.814±0.00106
3.00+15.00	14.560	-2.93	97.07	0.0667	14.560±0.01838
3.00+30.00	29.615	-1.28	98.72	0.0033	29.615±0.00184
1.00+10.00	9.737	2.63	97.37	0.0100	9.737±0.00184
3.00+10.00	10.176	1.76	101.76	0.0100	10.176±0.00184
4.00+10.00	9.883	1.17	98.80	0.0208	9.883±0.0038
5.00+10.00	9.883	1.17	98.80	0.0208	9.882±0.0038
8.00+10.00	10. 27	0.027	102.70	0.0577	10.27±0.0106
9.00+10.00	10.27	0.027	102.70	0.0577	10.27±0.0106
10.00+10.00	10.27	0.027	102.70	0.0577	10.27±0.0106

**The average of three measurements and SD not exceed than 0.1041.*

Table (8)
The statistical evolution for determination of standard PCM solutions using first derivative at zero crossing valley 299.2 nm.

Mg/L PMH+PCM	*PCM mg/L. found**	*Relative error%*	*Recovery %*	*SD*	*C.L X±□ts□√N□*
3.00+2.00	2.026	1.15	101.3	0.0500	2.026±0.00184
3.00+4.00	3.994	0.15	99.85	0.0288	3.994±0.00212
3.00+5.00	4.868	2.62	97.36	0.02	4.868±0.00184
3.00+6.00	5.962	0.63	99.37	0.0096	5.962±0.00106
3.00+7.00	6.837	2.33	97.67	0.014	6.837±0.00184
3.00+9.00	8.805	2.16	97.83	0.0064	8.805±0.00106
3.00+20.00	20.394	1.97	101.97	0.0050	20.394±0.00184
3.00+30.00	29.578	1.40	98.59	0.0019	29.578±0.00106
1.00+10.00	10.117	1.17	101.17	0.0100	10.117±0.00184
10.00+10.00	10.117	1.17	101.17	0.0100	10.117±0.00184

**The average of three measurements and SD not exceed than 0.0500.*

First derivative method used to determine PCM in the presence of PMH by using zero crossing method at peak 299.2 and 274.0nmfor the mixtures containing 10%and 90% of PMH. As shown in Tables (7, 8), the standard deviation for each concentration represents an average of three measurements not exceed than 0.1041.

First derivative used to determine PMH in the presence of PCM at 216.5nm for the mixtures containing 25% and 50% of PCM. Second derivative at 258.8 nm for mixtures 0.0%-75.0% of PCM. The standard addition method was used to determine each of drugs in pharmaceutical Tablets.

Analysis of pharmaceutical Tablets:

Accuracy of the proposed method was assisted by determining PMH and PCM solutions using the standard addition method for the above methods and the data obtained for pharmaceutical tablets were listed in Table (9) for COLDEIN and PCMCETAMOL tablets.

Table (9)
Determination of PMH in COLDEIN and PCMCETAMOL tablets using derivative spectrophotometric wavelength.

Conc. Mg/L	*COLDEIN tablet*				*PCMCETAMOL tablet*	
	PMH		*PCM*		*PCM*	
	^{1}D spectra at V 216.5 nm	*^{2}D spectra at P 258.8 nm*	*^{1}D spectra at V 274 nm*	*^{1}D spectra at V 2992. nm*	*^{1}D spectra at V 274 nm*	*^{1}D spectra at V 2992. nm*
20	19.70	20	19.64	19.143	20.32	19.294
RSD%*	0.0577	0.2929	0.0500	0.0050	0.02989	0.0050
RC%	98.51	100	98.20	95.71	101.615	96.47
Equation	Y=0.0006X- 0.0057	Y=-0.0002X- 0.002	Y= -0.0028X- 0.00275	Y=-0.0014X-0 .0134	Y=0.0729X+0.7408	Y=0.0731X+0.7052
Correlation coefficient (R)	0.9997	0.99960	0.99960	0.99965	0.99990	0.99905

Each concentration represents an average of three measurements.

Conclusions

A fast and accurate method for determining Paracetamol and of Promethazine Hydrochloride was developed by using derivative spectrophotometry. The advantage of this method is that both constituents can be determined directly in a single sample without the need to be separated. It was also found that auxiliary drug components had no effect on the results of determination obtained under the established conditions.

References

[1] British pharmacopoeia 2000, CD, ROM.

[2] Theia'a, N. A.; Nief, R. A. and Mona, I. I., "Spectrophotometric Determination of Promethazine hydrochloride via Oxidative Coupling Reaction with Sulfanilic Acid" J. of P.& App.Sci., 2006.

[3] Daniel, D.andGutz, I.G.R, "Flow injection spectroelectroanalytical method for the determination of promethazine hydrochloride in pharmaceutical preparations", Anal. Chim. Acta. Vol. 494, No. 1-2, pp 215-224, 2003

[4] Sultan, S.M.; Hassan, Y.A.M. and Abulkibash, A.M., Talanta, "Chemiluminescence assay of promethazine hydrochloride using acidic permanganate employing flow injection mode operated with syringe and peristaltic pumps " Vol. 59 (6), 1073-1080, 2003.

[5] Huang, M.; Ga o, J.y.; Zhai, Z.g. and Liang, Q.l., "An HPLC-ESI-MS method for simultaneous determination of fourteen metabolites of promethazine and caffeine and its application to pharmacokinetic study of the combination therapy against motion sickness" J. of Pharm. and Bio. Anal.,
Vol 62, 119-128, 2012

[6] Ahmed K. H.; Bahruddin S.; Sulaiman A. and Rohana A., "Ionophore-Based Potentiometric Sensors for the Flow-Injection Ionophore-Based Potentiometric Sensors for the Flow-Injection "Determination of promethazine Hydrochloride in Pharmaceutical Formulations and Human Urine", J. Sensors., Vol. 11, (1), 1028-1042, 2011.

[7] Nabil, S. N. Shahbaz, A. M. and Bashaer, A. A., "Preparation and Potentiometric Study of promethazine Hydrochloride Selective Electrodes and Their Use in Determining Some Drugs", Turk J Chem., Vol. 32, , 539 – 548, 2008.

[8] Khaleda H. A. and Zainab, W. A., "Construction of promethazine Hydrochloride Selective Electrode in a PVC matrix Membrane", J. of AL-Nahrain University- Sci. Vol. 14, (4), 11-17, 2011.

[9] Anuradha S. J.; Savita S Y. and Janhavi R., "Simultaneous determination of Paracetamol and lornoxicam by Rp-Hplc in bulk and tablet formulation", Pharmacie Globale: Int. J. of Comprehensive Pharm., Vol. 2, (9), 1-4, 2011.

[10] DaliborSˇ, I. N.: Petr, S. H.: Sklen, I. M. and Concei, B. S.,"Sequential injection chromatographic determination of Paracetamol, caffeine, and acetylsalicylic acid in pharmaceutical tablets", J. Sep. Sci, V. 27, 529–536, 2004.

[11] Suntornsuk, L., Pipitharome, O., Wilairat, P., "Simultaneous determination of paracetamol and chlorpheniramine maleate by micellarelectrokinetic chromatography", J. of Pharm. and Bio. Anal., Vol. 33, (3), 441-449, 2003.

[12] Sharma, S.; M.C., Sharma1, R. S., Sharma2, A.D.,"High Performance Liquid Chromatographic Assay method for the determination of paracetamol and Caffeine in Tablet Formulation-in vitro dissolution studies" J. of Pharm. Research ,Vol., (5), 1559-1561, 2011.

[13] Maksud, S.M., "HPLC method for selective determination ofaceclofenac, paracetamol and chlorzoxazone in tablets" master thesis, University of Health Science, Al-Ameen College, Bangalore, 2010.

[14] Maitreyi, Z. andAmit, K., "Quantitative Determination of Etoricoxib and paracetamol in Pharmaceutical Dosage Form and in-vitro comparison by Reversed-Phase High Performance Liquid Chromatography (RP-HPLC)" International Journal of Advances in Pharmaceutical Sciences" ,Vol.1,(2), 2011.

[15] Lou, H.g.; Yuan, H.; Ruan, Z.r. and Jiang, B., "Simultaneous determination of paracetamol, pseudoephedrine, dextrophan

and chlorpheniramine in human plasma by liquid chromatography-tandem mass spectrometry" J. of Chrom.,Vol.878, (7-8), 682-688 , 2010.

[16] Li, Li; Lu, Yaxiang; Ding, Yapingand Cheng, Yu.,"Determination of paracetamol Based on its Quenching Effect on the Photoluminescence of CdTe Fluorescence probes" J. of Fluorescence,Vol.22, 2, 591-596, 2012.

[17] Afshari, J.T. and Liu, T.-Z., "Rapid Spectrophotometric Method for the Quantitation of Acetaminophen in Serum", *Analyt. Chim. Acta., Vol. 43*, 165-169, 2001.

[18] Pawar V. T.;Pishawikar S. A and More H. N., "spectrophotometric estimation of aceclofenac and paracetamol from tablet dosage form", J. of Pharm.International Research,Vol. 2, (1), 93-98, 2011.

[19] Mahaprole S. ; Telekone R; Raut R and Damle S, "Simultaneous spectrophotometric determination of drotaverine hydrochloride and paracetamol in tablet" Indian J. of Pharm. Sci. ,Vol.72, (1), 133-136 , 2010.

[20] Das, S., Sharma, S.C., Talwar, S.K. and Sethi, P.D., "Simultaneous Spectrophotometric Determination of Mefenamic Acid and paracetamol in Pharmaceutical Preparations", Analyst, Vol. *114*, 101-103, 1989.

[21] Bramwell, H., Cass, A.E.G., Gibbsm, P.N.B. and Green, M. "Method for Determining paracetamol in Whole Blood by Chronoamperometry following Enzymatis Hydrolysis", J., Analyst, Vol. 115, 185-188, 1990.

[22] Erdogdu, G. and Karagozler, A.E., Talanta, "Investigation and Comparison of the Electrochemical Behavior of Some Organic and Biological Molecules at Various Conducting Polymer Electrodes", *44*, 2011-2018, 1997.

[23] Goyal, R.N.; Gupta, V.K. and Chatterjee, S., "Voltammetric biosensors for the determination of paracetamol at carbon nanotube modified pyrolytic graphite electrode" Sensors & Actuators: B. Chemical, Vol.149,(1), 252-58, 2010.

[24] Fan, Y.; Liu, J.H.; Lu, H.T. and Zhang, Q., "Electrochemical behaviour and voltammetric determination of paracetamol on Nafion/TiO_2-graphene modified glassy carbon electrode", Colloids and Surfaces B: Biointerfaces Vol. 85, (2), 289-292, 2011.

[25] Lau, O.-W., Luk, S.-F. and Cheung, Y.P.M., "Simultaneous Determination of Ascorbic Acid, Caffeine and paracetamol in Drug Formulations by Differential-Pulse Voltammetry Using a Glassy Carbon Electrode", Analyst, Vol. *114*, 1047-1051, 1989.

[26] Sanghavi, B.J.andSrivastava, A.K., "Simultaneous voltammetric determination of acetaminophen, aspirin and caffeine using an in situ surfactant-modified multiwalled carbon nanotube paste electrode ", Electrochemical Acta., Vol. 55,(28), 8638-8648, 2010.

[27] Navarro, I., Gonzalez; Arjona, D., Roldan, E. and Rueda, M., "Determination of Paracetamol in Tablets and Blood Plasma by Differential Pulse Voltammetry"., J. Pharm. Biomed. Anal, Vol. 6, 969-976, 1988.

[28] Wang, C.; Hu, C.X.; Leng, Z.; Yang, G. and Jin, G., "Differential Pulse Voltammetry for Determination of paracetamol at a Pumice Mixed Carbon Electrode", Analyt. Lett., Vol. 34, 2747-2759, 2001.

[29] Ozkan, S.A.; Uslu, B. and Aboul-Enein, H.Y., "Analysis of Pharmaceuticals and Biological Fluids Using Modern Electroanalytical Techniques", Crit. Rev. Analyt. Chem., Vol. 33, 155-181, 2003.

[30] Babaei, A.; Khalilzadeh, B. and Afrasiabi, M.,"A new sensor for the simultaneous determination of paracetamol and mefenamic acid in a pharmaceutical preparation and biological samples using copper(II) doped zeolite modified carbon paste electrode", J. of Appl. Electrochemistry, Vol. 40(8), 1537-1543, 2010.

[31] Kanita T. N. and Duncan T. B., "voltammetric determination of acetaminophen in paracetamol tablets", KMITL Sci. Tech. J., Cyclic, Vol. 5,(3) Jul.-Dec. 2005

٩٧,٠٠ %–١٠١,٩٧%، وان الخطية للمحاليل بين ٢,٠٠–٣٠,٠٠ ملغم/ لتر ان التحليل الاحصائي اثبت الدقة العالية للطريقة وقد طبقت هذه الطريقة بنجاح لنماذج محضرة وبنسب مختلفة، وكذلك على النماذج الدوائية مثل اقراص الكولدين والباراسيتول.

[32] Erk, N., Ozkan, Y.; Banoglu, E.; Ozkan, S.A. and Senturk, Z.," Simultaneous determination of paracetamol and methocarbamol in tablets by ratio spectra derivative spectrophotometry and LC", J. of Pharm. and Bio. Analysis, Vol. 24, (3), 469-475 2001.

[33] Lawan S. and Nongluck R., "Determination of paracetamol and Orphenadrine Citrate in Pharmaceutical Tablets by Modeling of Spectrophotometric Data Using Partial Least-Squares and Artificial Neural Networks", YAKUGAKU ZASSHI, Vol. 127, (10), 1723-1729, 2007.

[34] Ying D, Ying S, Yuqiu R, Yulin R. "Artificial neural network for Simultaneous determination of two components of compound Paracetamol And diphenhydramine hydrochloride powder on NIR spectroscopy", Anal. Chem. Acta., Vol. 528: 55-61, 2005.

[35] El-Sayed, A-A. and El-Salem, N. A., "Recent Development of Derivatives pectrophotometry and Their Analytical Application", Anal. Sci., Vol. 21, 595-614, 2005.

الخلاصة

استخدمت تقنية الاطياف في تعيين كل من هيدروكلوريد البروميثازين والباراستيامول للادوية المنفردة والمزيج الثنائي، وباستخدام الطيف العادي وطيف المشتقة الاولى لتعيين هيدروكلوريد البروميثازين المنفرد في الاطوال الموجية ٢٤٩,٥ و ٢٤٣,٠ نم على التوالي ولتعين الباراستيامول في ٢٤٣,٥ و٢٢٥,٠ نم على التوالي اما المزيج الثنائي فقد استخدمت طريقة التقاطع الصفري لاطياف المشتقة الاولى والثانية لتعيين البروميثازين وفي الاطوال الموجية ٢١٦,٥ و٢٥٨,٨ نم وللمشتقة الاولى لتعيين الباراستيامول في الاطوال الموجية في ٢٧٤,٠ و ٢٩٩,٢ نم. كان معامل الارتباط لمنحنيات المعايرة لايقل عن ٠,٩٩٩٠ ومعدل الانحراف المعياري لايزيد عن ٠,٢١٤ وكذلك نسبة الاسترداد لكل من هيدروكلوريد البروميثازين الباراستيامول بين