Asian Journal of Chemistry Vol. 19, No. 6 (2007), 4533-4546

Simultaneous Spectrophotometric Determination of Paracetamol and *p*-Aminophenol by H-point Standard Addition Method and Partial Least Squares Regression

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Two new, simple, inexpensive and sensitive methods for the simultaneous spectrophotometric determination of paracetamol (PAR) and *p*-aminophenol (PAP) by H-point standard addition method (HPSAM) and partial least squares (PLS) calibration is described. The methods were based on the difference in the rate of reduction of iron(III) with PAR and PAP in the presence of 2,2'-bipyridine (Bpy) and subsequent complex formation between resulted Fe(II) and 2,2′-bipyridine. The coloured complex of $[Fe(Bpy)_3]^{2+}$ resulted can be monitored at 520 nm. The results showed that the simultaneous determination of PAR and PAP could be performed in their concentration ranges of 0.4-70.0 and 0.03-8.0 μg mL^{-1} for HPASM, 2.0-100.0 and 0.2-10.0 μg mL^{-1} for PLS method, respectively. The total relative standard error for applying the PLS method on 10 synthetic samples in the concentration ranges of 4.0-28.0 μg mL^{-1} of PAR and 0.5-6.0 μg mL^{-1} of PAP was 3.79. The proposed methods were successfully applied to the simultaneous determination of PAR and PAP in several commercially available PAR formulations and satisfactory results were obtained.

Key Words: Paracetamol, *p*-Aminophenol, Simultaneous determination, HPSAM, PLS.

INTRODUCTION

Paracetamol (N-acetyl-4-aminophenol, acetaminophen) is an extensively administered antipyretic analgesic for treating the symptoms of different painful processes. It belongs to the mild analgesics group of drugs in the analgesic-antipyretics subgroup[1]. The most common dosage forms

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for paracetamol (PAR) are tablets. *p*-Aminophenol (PAP) is a synthetic non-opiate, which produces analgesia and antipyresis by a mechanism similar to that of salicylates. Under abnormal conditions such as heat, pH, *etc.*, PAR degrades slowly forming a mixture of contaminants such as acetic acid and PAP. PAP is the hydrolytic product of acetaminophen and is reported to have significant nephrotoxicity and teratogenic effects and has been detected in acetaminophen as an impurity or synthetic intermediate[2].

Determination of PAR as an analgesic agent and PAP as hydrolytic product of PAR is very important. Some numerous methods such as spectrophotometry[3-8], spectrofluorimetry[9], liquid chromatography[7,10-15] and electroanalytical techniques[8,16] have been used for their quantification individually or with other compounds in drug products. A large number of publications (more than thousand) have been published and presented on PAR quantification that shows the importance of this compound. There are still attempts to develop some simple and accurate methods for PAR measurement individually in drug formulations and its simultaneous determination with other compounds.

Multivariate calibration methods are being successfully applied to the multicomponents kinetic determination to overcome some of the drawbacks of classical methods. Recently, soft algorithms such as principle component regression (PCR), partial least squares (PLS) and artificial neural network (ANN), which avoid the colinearity problems, have been used for simultaneous determination of the analytes having the same chemical properties that cannot be resolved with common methods[17-20]. Numerical methods based on the mathematical resolution of multivariate signals, such as UV-Visible spectroscopic data, have been shown to allow the resolution of complex mixtures with high speed and acceptable accuracy and precision. Among them, the partial least-squares regression with a single dependent variable (PLS-1) has found important application in pharmaceutical analysis[21]. PLS is capable of being a full-spectrum method and it therefore enjoys the signal averaging advantages of other full-spectrum methods, such as PCR and classical least squares (CLS).

H-point standard addition method (HPSAM) is a modification of the standard addition method that transforms the incorrigible error resulting from the presence of a direct interference in the determination of an analyte into a constant systematic error[22-25]. This error can be evaluated and eliminated. By using this method, it is possible to measure two and even three species that exist together within the mixture that cannot be measured simultaneously with common standard addition methods. This method can also be applied to kinetic data for the simultaneous determination of binary mixtures or the calculation of analyte concentration completely free from bias error[25,26].

Recently, Karimi *et al.*[27] reported a kinetic-spectrophotometric method for the simultaneous determination of hydrazine and its derivatives using PCR and PLS models. The method was based on the difference observe in the rate of reduction of Fe(III) with hydrazine (HZ), thiosemicarbazide (TSCZ) and phenylhydrazine (PHZ) in the presence of the reagent 2,2'-bipyridine (Bpy). The aim of this work was to evaluate the possibility of using HPSAM and PLS method and above complex system (Fe(III)/Bpy) in the presence of PAR and PAP as reducing agents for their simultaneous determination. The difference observed in the rate of reduction of Fe(III) by PAR and PAP and then complex formation between resulted Fe(II) and 2,2'-bipyridine (Bpy) with maximum absorbance in the wavelength of 520 nm was the basis of the both methods.

EXPERIMENTAL

A GBC UV-Visible Cintra 6 Spectrophotometer model, attached to a Pentium (IV) computer, with 1 cm glass cells was used for recording the kinetic spectrophotometric data. The Metrohm 781 pH-meter was used to adjust pH of the buffered solutions. PLS analysis was performed using PLS toolbox in MATLAB 7.0 program. All chemicals were of analytical reagent grade and the solutions were prepared with double distilled water. The stock solution of PAR (2000 μg mL^{-1}) was prepared in a 100 mL volumetric flask by dissolving 0.2 g of paracetamol (purchased as analytical grade from Darou Pakhsh Co., Tehran, Iran) in water and diluting with water to the mark. The stock solution of *p*-aminophenol (1000 μg mL^{-1}) was prepared in a 100 mL flask by dissolving 0.1 g of PAP (Fluka) in water and diluting with 0.01 M HCl to the mark. These solutions (PAR and PAP) are fairly stable at least for a month in refrigerator. PAR solution in water (not in acidic medium) is stable for few days in refrigerator. So, it was preferred to prepare its stock solution in acidic medium. The stock solution of 0.05 M Fe(III) was prepared in a 100 mL volumetric flask by dissolving 2.43 g ammonium ferric sulfate in water and diluting to the mark with water. The stock solution of 0.05 M 2,2'-bipyridine (Bpy) was prepared by dissolving 0.784 g of Bpy (Merck) in alcohol and diluting to 100 mL volumetric flask with water. Phosphate buffer solution (1.0 M, pH 2.0) was prepared by using phosphoric acid and KOH solutions and adjusting its pH with a pH meter.

Recommended procedure: The Fe(III)/Bpy complex solution as oxidizing agent in both proposed methods was prepared daily in a 100 mL volumetric flask by the addition of 10.0 mL Bpy solution (0.05 M) and 10.0 mL Fe(III) solution (0.05 M) and then 10.0 mL of buffer solution (pH 2.0) (for HPSAM) or 10.0 mL Bpy solution (0.05 M) and 20.0 mL Fe(III) solution (0.05 M) and then 10.0 mL of buffer solution (pH 2.0) (for PLS

analysis) and diluting with water to the mark. After thermostating this solution at 25°C for 15 min, 2.4 mL of the solution was transferred into a glass cell of the spectrophotometer and the absorbance of this solution was zeroed against air before injecting the analyte(s). Then, 100 µL of solution containing PAR or PAP or mixture of them in the range of the analyte(s) determination was injected with a 100 microliter syringe into the cell. The absorbance changes *vs.* time were recorded at 520 nm at the time intervals of 2.0 s.

Simultaneous determination of PAR and PAP by HPSAM was performed by measuring the absorbance of the solution at 150 and 300 s for each sample. Synthetic samples containing different concentration ratios of PAR and PAP were prepared and standard addition of PAR were made. The concentration ranges for PAR and PAP for the construction of HPSAM calibration graphs were 0.4-70.0 and 0.03-8.0 µg mL^{-1}, respectively.

Simultaneous determination of PAR and PAP with PLS method was performed by recording the absorbance spectra for each solution from 0.0 to 300 s. The concentration ranges for PAR and PAP in PLS method in the optimized conditions were 2.0-100.0 and 0.2-10.0 µg mL^{-1}, respectively.

RESULTS AND DISCUSSION

The Fe(III)-2,2'-bipyridine (Bpy) system allows the spectrophotometric determination of a reducing agent, A_{red}, as follows[27,28]:

$$n[Fe(Bpy)_3]^{3+} + A_{red} \rightarrow n[Fe(Bpy)_3]^{2+} + A_{ox}$$

The reaction is complete with the formation of an equivalent amount of $[Fe(Bpy)_3]^{2+}$ with respect to the *n*-electron reductant, A_{red}. The reduction of $[Fe(Bpy)_3]^{3+}$ to complex of $[Fe(Bpy)_3]^{2+}$ (with λ_{max} = 520 nm) is completed in the presence of suitable reducing agents such as PAR and PAP in few minutes. The reduction rate of $[Fe(Bpy)_3]^{3+}$ with PAR and PAP was different. The difference provided the possibility of resolving their mixtures using HPSAM and PLS method. Characteristics of calibration graphs of PAR and PAP are given in Table-1.

TABLE-1
CHARACTERISTIC OF CALIBRATION GRAPHS FOR THE DETERMINATION OF PAR AND PAP

Parameter	PAR		PAP	
	HPSAM	PLS	HPSAM	PLS
Slope	0.0223	0.0110	0.1848	0.1719
Intercept	0.0991	0.0980	0.0626	0.0237
Correlation coefficient (n = 12)	0.9991	0.9994	0.9994	0.9983
Linear range (µg mL^{-1})	0.4-70.0	2.0-100.0	0.03-8.0	0.2-10.0
Detection limit (µg mL^{-1})	0.0580	0.2590	0.0150	0.0440

A series of experiments were conducted to establish the optimum analytical to achieve maximum sensitivity in the simultaneous determination of PAR and PAP. The experimental parameters, such as reagents concentration, temperature and pH of solutions were optimized. Optimization process gave similar results for both individual analytes and mixture of two analytes.

Effect of Fe(III) and Bpy concentrations: The effect of Fe(III) and Bpy concentrations, in the ranges of 5.0×10^{-4}– 2.0×10^{-2} M were studied. At a constant concentration of Bpy equal to 5.0×10^{-3} M, Fe(III) concentration was varied in above-mentioned range. With an increase in Fe(III) concentration, the reaction rate and absorbance increase up to 5.0×10^{-3} M (for HPSAM) and 1.0×10^{-2} M (for PLS) for both PAR and PAP, but at the higher concentrations of Fe(III), a decrease in reaction rate and amount of absorbance was observed. So, concentrations of 5.0×10^{-3} and 1.0×10^{-2} M Fe(III) were selected as the optimum concentrations for HPSAM and PLS method, respectively. The effect of Bpy concentration on the reaction rate and absorbance of PAR and PAP at constant concentration of Fe(III) (1.0×10^{-2} M) was also studied. The increase of Bpy concentration up to 5.0×10^{-3} M, causes an increase in the reaction rate and absorbance of 1.0×10^{-2} M. But at higher concentrations of Bpy, a decrease in reaction rate and amount of absorbance was observed. Thus, for simultaneous determination of PAR and PAP by both HPSAM and PLS method, it was preferred to choose 5.0×10^{-3} M Bpy as the optimum concentration for further studies.

Effect of pH: The effect of pH over the ranges of 1.0 to 7.0 on the reaction rate of two compounds with Fe(III) in the presence of Bpy was studied. For both of PAR and PAP, pH 2.0 has maximum absorbance, but at above pH 2.0, the absorbance and reaction rate decrease. Thus, pH 2.0 was chosen as an optimized pH value.

Effect of temperature: The effect of temperature on the absorbance of PAR and PAP with Fe(III) in the presence of Bpy was studied in the range of 20-70°C. An increase in the temperature caused an increase in the reaction rates of both two analytes. However, for the sake of simplicity and better control of the temperature effects on the precision of determinations, 25°C was chosen as the optimum temperature.

Absorbance-time behaviour: Under the optimized conditions, reactions of PAR and PAP with Fe(III)-Bpy system showed the different kinetic behaviours (Fig. 1). This difference in reaction rates allows designing multivariate method of PLS and HPSAM to determine simultaneously PAR and PAP.

H-Point standard addition method (HPSAM): For the selection of appropriate times for applying HPSAM, the following principles were followed. Consider an unknown sample containing an analyte X and an

interference Y. In this special system, either PAR or PAP can be considered as the analyte and the other one as the interferent. For the cases in which the reaction X and Y occurs in a different kinetic way and also it depends on time, the determination of the concentration of X by HPSAM under these conditions requires the selection of two times, t_1 and t_2, at which the interferent species, Y, should have the same absorbance[25]. In addition, the slope difference of the two straight lines obtained at t_1 and t_2 must be as large as possible in order to get good accuracy. As shown previously by Compains-Falco *et al.*[29], higher the value of the slope increment, the smaller the error for the analyte concentrations. For this reason, the time pairs of 150 and 300 s that gave the best accuracy, the lowest error and the shortest analysis time were used. As mentioned before, the reaction of PAP was completed at 60.0 s, while the reaction of PAR was relatively slow.

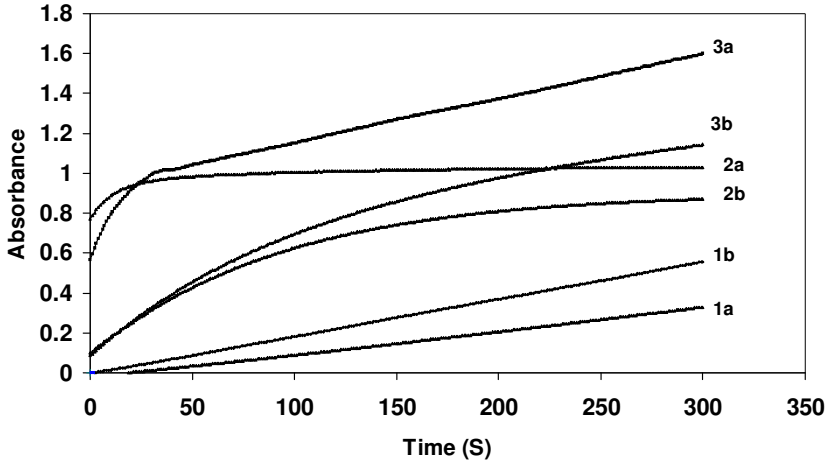

Fig. 1. Absorbance changes of Fe(III)/Bpy complex *vs.* time in the reaction with: 20 μg mL^{-1} of PAR (1a), 5.0 μg mL^{-1} of PAP (2a) and mixture of them (3a) for HPSAM and 20 μg mL^{-1} of PAR (1b), 5.0 μg mL^{-1} of PAP (2b) and mixture of them (3b) for PLS method. HPSAM conditions: 5.0×10^{-3} M Fe(III), 5.0×10^{-3} M of Bpy, pH 2.0, 25°C. PLS conditions: 1.0×10^{-2} M Fe(III), 5.0×10^{-3} M of Bpy, pH 2.0, 25.0°C

By plotting the analytical signal *vs.* the added Y concentration in selected time pairs, two straight lines are obtained that have a common point with coordinates H ($-C_H$, A_H) where C_H is the unknown X concentration and A_H the analytical signal due to the Y species.

At t_1 and t_2 the absorbances of X will be b_i and A_i, while those of Y will be b and A'. For X species we can say:

$$A_i = b_i + m_i t_j \quad (1)$$

for $t_1 \leq t_j \leq t_2$ and i = 0,1,2,…,n
and for Y:

$$A' = b + mt_j \text{ and } m = 0 \quad (2)$$

where the subscripts i and j are the different solutions for n additions of X concentration prepared to apply the HPSAM and for a time comprised in the range of t_1 to t_2, respectively.

According to the HPSAM theory, for binary mixture of PAR-PAP, the resulting absorbance of the reaction of them with Fe(III)/Bpy complex in acidic media are measured at 520 nm at times of 150 and 300 s. The following equations show the relation between them:

$$A_{150} = b_0 + b + M_{150}Ci \quad (3)$$

$$A_{300} = A_0 + A' + M_{300}Ci \quad (4)$$

From the reason that A_{150} is the same as A_{300} at the point H and PAP not to evolve over time (then A' = b), the coordinates of H will be

$$b_0 + b + M_{150}(-C_H) = A_0 + A' + M_{300}(-C_H) \quad (5)$$

Hence,

$$-C_H = [(A' - b) + (A_0 - b_0)]/(M_{150} - M_{300}) \quad (6)$$

$$A' = b$$

$$-C_H = (A_0 - b_0)/(M_{150} - M_{300}) \quad (7)$$

which is equivalent to the existing $C_{PAR}(= b_0/M_{150} = A_0/M_{300})$.

Substituation of C_{PAP} into eqns. 1 and 2 yields $A_H = b$ and the overall equation for the absorbance at H-point simplifies to

$$A' = b = A_H = A_{PAP} \quad (8)$$

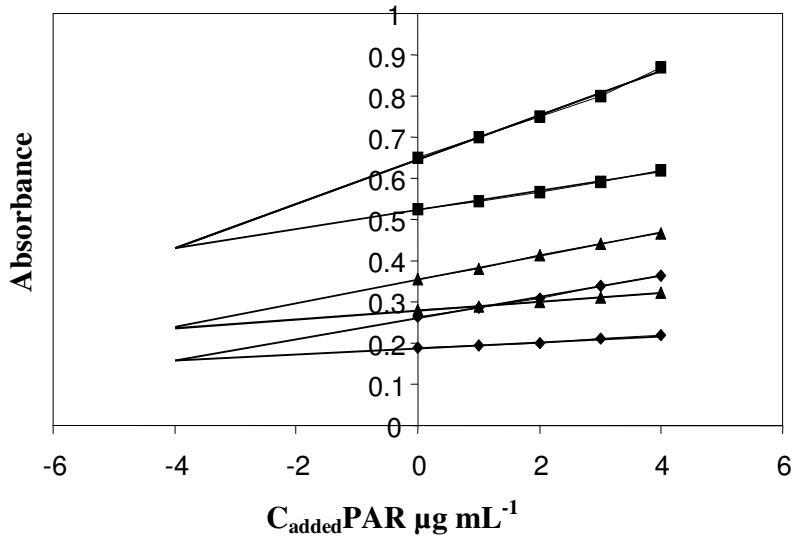

Fig. 2. Plot of H-point standard addition method for fixed PAR (4.0 µg mL^{-1}) and 0.5 (◆), 1.0 (▲) and 2.0 µg mL^{-1} (■) of PAP.

In this special system, PAR can be considered as the analyte and PAP as the interferant. The concentration of PAP was calculated in each test solution by the calibration method with a single standard and ordinate value of the A_H. Fig. 2 shows the plot of HPSAM for fixed PAR (4.0 μg mL^{-1}) and different concentrations of PAP. The results of several experiments for the analysis of PAR and PAP mixtures in different concentration ratios are shown in Table-2.

TABLE-2
RESULTS OF SEVERAL EXPRIMENTS FOR THE ANALYSIS OF PAR AND PAP MIXTURES IN DIFFERENT COCENTRATION RATIOS (T = 25ºC)

A-C equation	r	Taken (μg mL^{-1})		Found (μg mL^{-1})	
		PAR	PAP	PAR	PAP
A_{300} = 0.0275Ci + 0.8357	0.9889	3.50	3.50	3.79	3.62
A_{150} = 0.0122Ci + 0.7776	0.9810				
A_{300} = 0.0229Ci + 0.2640	0.9988	5.00	0.50	5.04	0.46
A_{150} = 0.0086Ci + 0.1918	0.9995				
A_{300} = 0.0224Ci + 0.2388	0.9952	4.00	0.50	3.95	0.47
A_{150} = 0.0073Ci + 0.1792	0.9910				
A_{300} = 0.0293Ci + 0.4528	0.9966	5.00	1.25	5.15	1.29
A_{150} = 0.0121Ci + 0.3641	0.9956				
A_{300} = 0.0226Ci + 0.5178	0.9994	8.00	1.50	7.99	1.49
A_{150} = 0.0102Ci + 0.4187	0.9969				
A_{300} = 0.0251Ci + 0.3515	0.9984	10.00	0.20	10.40	0.15
A_{150} = 0.0098Ci + 0.1929	0.9967				

Partial least squares (PLS) method: The first step in the simultaneous determination of species by PLS methodology involves constructing the calibration matrix for the binary mixture of PAR and PAP. A synthetic set of 35 solutions of mixture of PAR and PAP were randomly prepared. The concentration ranges used were 4.0-28.0, 0.5-6.0 μg mL^{-1} for PAR and PAP, respectively. From the series, 25 solutions (Table-3) were chosen for the calibration set and the other 10 solutions were used as prediction set. Changes in the absorbance of the solutions were recorded during a time period of 300 s.

To select the number of factors in the PLS algorithm, a cross-validation method leaving out one sample at a time[30], was employed and the prediction residual sum of squares (PRESS) was calculated and drawn against the number of factors. Fig. 3 shows the plot of PRESS against the number of factors for each individual component. The optimal number of factors yielding the smallest error (PRESS) was obtained as 3 for PAR and

TABLE -3
RESULTS OF FOUR REPLICATE EXPRIMENTS FOR THE ANALYSIS OF PAR AND PAP MIXTURES (T =25ºC)

A-C equation	r	Taken (μg mL^{-1})		Found (μg mL^{-1})	
		PAR	PAP	PAR	PAP
$A_{300} = 0.0225\ C_i + 0.5152$	0.9995	8.00	1.50	7.920	1.480
$A_{150} = 0.0102\ C_i + 0.4178$	0.9967				
$A_{300} = 0.0226\ C_i + 0.5178$	0.9994	8.00	1.50	7.990	1.490
$A_{150} = 0.0102\ C_i + 0.4187$	0.9969				
$A_{300} = 0.0226\ C_i + 0.5149$	0.9991	8.00	1.50	7.960	1.470
$A_{150} = 0.0103\ C_i + 0.4170$	0.9970				
$A_{300} = 0.0222\ C_i + 0.5192$	0.9982	8.00	1.50	7.920	1.520
$A_{150} = 0.0100\ C_i + 0.4226$	0.9970				
Mean				7.950	1.490
Standard deviation				0.034	0.022
RSD (%)				0.430	1.480

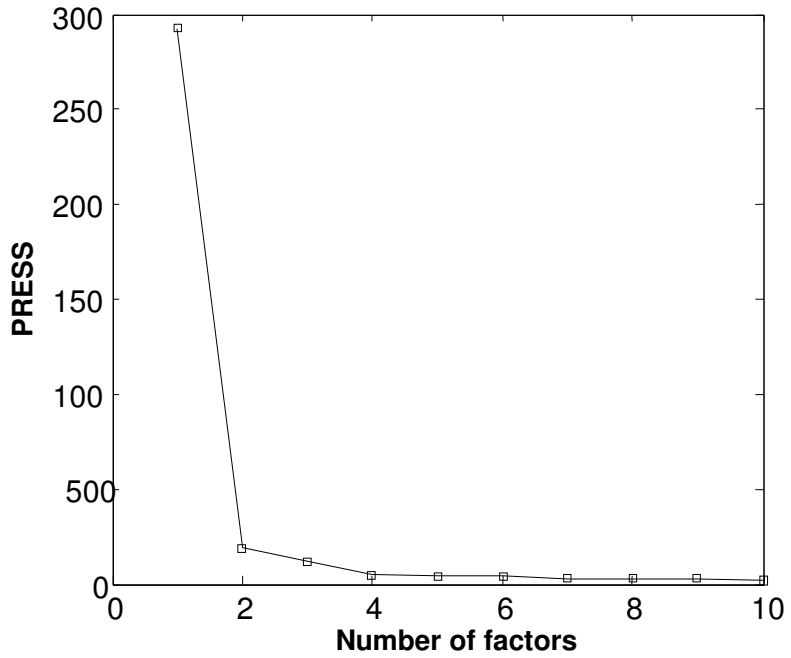

Fig. 3. Plot of PRESS against the number of factors for mixture of PAR and PAP

PAP. The validation step of PLS methodology was carried out by running PLS on the prediction set. The results are shown in Table-5. The obtained results are quite acceptable for both analytes. The prediction error of a

TABLE -4
VALUES OF THE PAR AND PAP COCENTRATIONS USED AS CALIBRATION AND PREDICTION SOLUTION IN μg mL^{-1}

Sample no.	Calibration set		Prediction set	
	PAR	PAP	PAR	PAP
1	4.0	0.5	6.0	1.0
2	4.0	1.0	9.0	0.6
3	4.0	2.0	10.0	3.4
4	4.0	4.0	9.0	4.4
5	4.0	6.0	15.0	5.0
6	6.0	0.5	19.0	3.2
7	6.0	1.0	21.2	2.8
8	6.0	2.0	24.4	1.4
9	6.0	4.0	20.0	2.0
10	6.0	6.0	28.0	5.0
11	8.0	0.5	–	–
12	8.0	1.0	–	–
13	8.0	2.0	–	–
14	8.0	4.0	–	–
15	8.0	6.0	–	–
16	12.0	0.5	–	–
17	12.0	1.0	–	–
18	12.0	2.0	–	–
19	12.0	4.0	–	–
20	12.0	6.0	–	–
21	15.0	0.5	–	–
22	15.0	1.0	–	–
23	15.0	2.0	–	–
24	15.0	4.0	–	–
25	15.0	6.0	–	–

single component in the mixture is calculated as the relative standard error (RSE) of predicted concentration:

$$RSE(\%) = 100 \times \left(\frac{\sum_{j=1}^{N} (\hat{C}_j - C_j)^2}{\sum_{j=1}^{N} (C_j)^2} \right)^{1/2} \quad (9)$$

where N is the number of samples, C_i the concentration of the component in the ith mixture and $\hat{C}_i$ the estimated concentration. The total prediction error of N samples is calculated as follows:

$$RSE_t(\%) = 100 \times \left(\frac{\sum_{i=1}^{M}\sum_{j=1}^{N}(\hat{C}_{ij} - C_{ij})^2}{\sum_{i=1}^{M}\sum_{j=1}^{N}(C_{ij})^2} \right)^{1/2} \quad (10)$$

where C_{ij} is the concentration of the ith component in the jth sample and $\hat{C}_{ij}$ is the estimated concentration.

TABLE-5
COMPOSITION OF PREDICTION SET, THEIR PREDICTION BY PLS AND STATISTICAL PARAMETERS FOR THE SYSTEM

Sample	Synthetic (μg mL^{-1})		Prediction (μg mL^{-1})		Recovery (%)	
	PAR	PAP	PAR	PAP	PAR	PAP
1	6.0	1.0	6.90	0.99	115.0	99.0
2	9.0	0.6	9.35	0.57	103.9	95.0
3	10.0	3.4	10.80	3.31	108.0	97.4
4	9.0	4.4	8.60	4.35	95.6	98.9
5	15.0	5.0	15.80	5.09	105.3	101.8
6	19.0	3.2	18.70	3.40	98.4	106.3
7	21.2	2.8	21.40	2.96	100.9	105.7
8	24.4	1.4	24.60	1.42	100.8	101.4
9	20.0	2.0	20.20	1.94	101.0	97.0
10	28.0	5.0	26.60	4.97	95.0	99.4
Mean recovery					102.4	100.2
RSE (%) single					3.8	2.9
RSE (%) total					3.79	

Accuracy and precision of the method: Under the optimum conditions, the simultaneous determination of several synthetic mixed samples with different concentrations of PAR and PAP were analyzed by HPSAM and PLS method. Table-2 shows, the accuracy of the results is satisfactory when the concentrations ratio of PAR and PAP varied from 50:1 to 1:1.

To check the reproducibility of the method, five replicates were performed and the relative standard deviation (RSD) was obtained for binary mixtures. As Table-3 shows, the precision of the results is satisfactory.

Interference studies: In order to assess the possible analytical applications of the proposed methods, the effect of common excipients used in pharmaceutical preparations and various co-existing compounds at different concentrations on the absorbance of synthetic sample solutions containing mixture of 10.0 and 3.0 μg mL^{-1} of PAR and PAP, respectively,

were studied. The undissolved material was filtered before measurement. The recovery results are given in Table-6. No interference was observed from any of the excipients tested and only co-existing compounds of ascorbic acid, salicylic acid because of their reducing properties appeared to interfere in this method. The interference of ascorbic acid was eliminated when the synthetic sample solution was measured after ≥ 1 h.

TABLE-6
RECOVERY OF 10.0 μg mL^{-1} PAR AND 3.0 μg mL^{-1} PAP FROM SOLUTION WITH VARIOUS ADDITIVES USED AS EXCIPIENTS

Additive	Conc. of additive (μg mL^{-1})	Recovery (%)			
		HPSAM		PLS	
		PAR	PAP	PAR	PAP
Glucose	250.0	94.4	99.1	103.8	96.8
Ascorbic acid	20.0	170.0	180.8	139.0	134.6
Tartaric acid	100.0	97.4	102.2	104.8	99.9
Methocarbamol	200.0	97.0	102.3	98.0	100.1
Phenacetin	50.0	102.6	102.0	97.2	98.1
Salicylic acid	20.0	116.0	115.8	113.6	116.1
Caffeine	200.0	94.5	99.4	93.0	100.5

TABLE-7
RESULTS OF DETERMINATION OF PAR AND PAP QUANTIFICATION OF PAR AND PAP IN PHARMACEUTICAL SAMPLES

Sample	Nominal (μg mL^{-1})		Spiked (μg mL^{-1})		Found* (μg mL^{-1})				Recovery (%)			
					HPSAM		PLS		HPSAM		PLS	
	PAR	PAP	PAR	PAP	PAR	PAP	PAR	PAP	PAR	PAP	PAR	PAP
1[a]	5.0	–	8.0	1.0	12.98	0.99	13.41	1.01	99.8	99.0	105.1	101.0
2[a]	5.0	–	12.0	1.0	17.09	0.96	17.62	0.92	100.8	96.0	105.2	92.0
3[a]	5.0	–	17.0	1.0	22.08	0.96	22.44	1.01	100.5	96.0	102.6	101.0
1[b]	5.0	–	9.0	1.0	13.97	0.98	13.99	0.94	99.7	98.0	99.89	94.0
2[b]	5.0	–	10.0	1.0	15.09	0.99	15.25	0.91	100.9	99.0	102.5	91.0
RSE (%)									0.59	2.76	3.45	6.08

[a]Acetaminophen tablet (325 mg per tablet); Jalinous Lab., Tehran, Iran.
[b]Adult cold tablet (325 mg per tablet); Dr. Abidi Co., Tehran, Iran.
*Mean value (n = 3).

Application of the method: The proposed methods were applied to the determination of PAR and PAP in several commercially available PAR formulations including tablets prepared from several manufacturers. Ten tablets of each sample were accurately weighed and their solutions were prepared by dissolving them in water and filtering the solutions. The prepared solutions containing aliquot amounts of PAR and PAP (spiked in the solutions) were analyzed (n = 3). The quantitative results of this analysis are summarized in Table-7. The good agreement between these results and the nominal values labeled indicates the successful applicability of HPSAM and PLS for the simultaneous determination of PAR and PAP in pharmaceutical samples.

Conclusion

In this work it is shown that the application of HPSAM and PLS can be well adopted for simultaneous determination of PAR and PAP. The HPSAM and PLS model are suitable for simultaneous kinetic determination of PAR and PAP, but the PLS method was more rapid than HPSAM. In addition, HPSAM can be used in the complex samples with matrix effect because standard addition method has capability of removing these effects. Therefore, in the mixtures with matrix effects, HPSAM is preferred. But in the mixtures without these effects, PLS is better than HPSAM because of rapidly.

Both methods are cheaper than chromatographic methods, furthermore, in these methods, no toxic organic solvents are required. In other words, they belong to green chemistry. The proposed methods as new, inexpensive and sensitive methods offers good selectivity, accuracy and precision that can be applied for a wide range of PAR and PAP concentrations.

ACKNOWLEDGEMENT

The authors wish to express their gratitude to the Islamic Azad University of Yazd for the support of this work.

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(*Received*: 17 June 2006; *Accepted*: 21 April 2007) AJC-5590