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Simultaneous determination of potassium guaiacolsulfonate, guaifenesin, diphenhydramine HCl and carbetapentane citrate in syrups by using HPLC-DAD coupled with partial least squares multivariate calibration

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ABSTRACT

A simple and rapid analytical procedure was proposed for the determination of chromatographic peaks by means of partial least squares multivariate calibration (PLS) of high-performance liquid chromatography with diode array detection (HPLC-DAD). The method is exemplified with analysis of quaternary mixtures of potassium guaiacolsulfonate (PG), guaifenesin (GU), diphenhydramine HCI (DP) and carbetapentane citrate (CP) in syrup preparations. In this method, the area does not need to be directly measured and predictions are more accurate. Though the chromatographic and spectral peaks of the analytes were heavily overlapped and interferents coeluted with the compounds studied, good recoveries of analytes could be obtained with HPLC-DAD coupled with PLS calibration. This method was tested by analyzing the synthetic mixture of PG, GU, DP and CP. As a comparison method, a classsical HPLC method was used. The proposed methods were applied to syrups samples containing four drugs and the obtained results were statistically compared with each other. Finally, the main advantage of HPLC-PLS method over the classical HPLC method tried to emphasized as the using of simple mobile phase, shorter analysis time and no use of internal standard and gradient elution.

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1. Introduction

Potassium guaiacolsulfonate (PG) and guaifenesin (GU) are expectorants which help loosen mucus. Diphenhydramine HCI (DP) is a first generation antihistamine mainly used to treat allergies and may act as an antiemetic, sedative and hypnotic. Carbetapentane citrate (CP) has atropine-like and local anaesthetic actions and effectively suppresses acute cough due to common upper respiratory infections. The combination of PG, GU, DP and CP is used to treat a cough caused by the common cold, infections or allergies.

Several methods are used for determination of these compounds singly or in combination with other drugs. But, no analytical method has been reported for the simultaneous determination of these compounds in their multicomponent mixture. A few analytical method has been reported for the determination of PG in pharmaceutical preparations by HPLC [1] and spectrophotometry [2]. GU has been recently determined by HPLC [3], micellar chromatography [4], liquid chromatography–tandem mass spectrometry [5], gas chromatography [6], principal component regression method (PCR) [7], ridge regression spectrophotometry [8] and other analytical techniques [9,10]. Various recent methods including the use of liquid chromatography and HPLC [11], spectrophotometry [12], flow injection [13], electrophoresis [14] and partial least squares (PLS)-principal component regressions [15–18] have been used for the determination of DP in pharmaceutical preparations and biological fluids. CP has been determined in some mixtures by colorimetry [19], by potentiometry [20] and by flow injection [21].

Chromatographic techniques are among the most powerful tools available for qualitative and quantitative determination of various components of a mixture. But in chromatographic analyses, poor chromatographic resolutions or partially separated peaks often occur, especially in the analysis of complex matrices. This problem becomes more important when the analyte is at a concentration level near the detection limit. Traditionally, this type of problem has been solved by modifying the experimental conditions by trial and error until the aforesaid errors are minimized. Thus, different mobile or stationary phases (columns) or even working techniques (e.g. isocratic, gradient elution), which are time-consuming and involve the consumption of expensive solvents, are tested. Nevertheless, complex multicomponent mixtures can in many cases be qualitatively and quantitatively resolved by means of chemometrics. Depending on their nature, data can be arranged in a two-way structure (a table or matrix), as in the case of collecting the absorbance spectra for many samples, or in a three-way structure, e.g. in HPLC-DAD, where spectra are recorded at

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several retention times for each sample. Such data arrangements in three- or higher way arrays can be handled using multi-way methods of analysis. In these cases, a number of chemometric methods which do not require complete separation of the analytes for the analysis of overlapping chromatographic peaks have been suggested. Examples of these methods are partial least squares and principal component regression (PLS-PCR) [22–25], cross-section technique linked PLS (CS-PLS) [26], two way, unfolded three-way and three mode PLS [27], artificial neural network (ANN) [28], second order calibration methods [29–32], principal component analysis (PCA) [33], multivariate curve resolution alternating least squares (MCR-ALS) [34], target factor analysis (TFA) [35].

We recently reported the simultaneous determination of mixtures of some components in pharmaceutical and food products by PLS-2 calibration method using UV-VIS spectrophotometer [36–41]. In this paper, PLS-2 calibration is employed to determine the concentration of PG, GU, DP and CP in syrup preparations from HPLC-DAD data. A simple mobile phase consisting of water and acetonitrile (ACN) was used. Though heavily overlapped chromatographic peaks of the analytes and interferences were obtained and the spectra of these species were also overlapped, the powerful PLS algorithm can resolve the overlapped peaks into corresponding chromatographic, spectral and concentration profiles even in the presence of interferences.

Table 1
PG, GU, DP and CP concentrations in calibration set.

Sample	PG ($\mu g\,mL^{-1}$)	GU ($\mu g\,mL^{-1}$)	DP ($\mu g\,mL^{-1}$)	CP ($\mu g\,mL^{-1}$)
1	1300	900	120	100
2	1300	700	80	140
3	1100	700	160	80
4	1100	1100	100	140
5	1500	800	160	100
6	1200	1100	120	80
7	1500	900	100	80
8	1300	800	100	120
9	1200	800	140	140
10	1200	1000	160	120
11	1400	1100	140	100
12	1500	1000	120	140
13	1400	900	160	140
14	1300	1100	160	60
15	1500	1100	80	120
16	1500	700	140	60
17	1100	1000	80	100
18	1400	700	120	120
19	1100	900	140	120
20	1300	1000	140	80
21	1400	1000	100	60
22	1400	800	80	80
23	1200	700	100	100
24	1100	800	120	60
25	1200	900	80	60

2. Experimental

2.1. Chemicals

PG, GU, DP and CP were obtained from Zeytas Pharmaceutical Ltd., Turkey. Analytical reagent-grade chemicals and milli-Q water were used. Stock solutions of PG (10,000 $\mu g\,mL^{-1}$), GU (10,000 $\mu g\,mL^{-1}$), DP (1000 $\mu g\,mL^{-1}$) and CP (1000 $\mu g\,mL^{-1}$) were prepared in water. Standard solutions and mixtures of drugs were freshly prepared by appropriate dilution of stock solutions with mobile phase water/ACN (60:40, v/v).

The "Gayaben®" commercial syrup samples containing 133 mg of PG, 100 mg of GU, 10 mg of DP and 8.3 mg of CP in 5 mL syrup formulation was acquired from Turkey pharmacies.

2.2. Chromatography conditions

The mobile phase, under isocratic conditions, was water/ACN (60:40, v/v). This mobile phase composition was used to reduce the time of analysis and avoid too much dispersion of peaks. Chromatographic analysis were performed using a Shimadzu LC-MS system consisting of LC-20 AD pump unit. C_{18} (150 mm × 4.6 mm) RP column was used. The flow rate was set at 0.8 mL min^{-1} and 5 μL of the solution was injected. UV detection was performed using a Model SPD-M 20. Photodiode array detector-UV spectra were collected in the range of 190–300 nm. The digital resolution was 0.64 s in time and 1.2 nm in wavelength. For all analysis, the data matrix for each individual run was set at 371 points in the time direction and 92 points in the wavelength direction.

2.3. Procedure

2.3.1. Calibration and validation sets

Mixtures with varying concentrations of PG, GU, DP and CP were analyzed by HPLC-DAD, and calibration and prediction data sets were constructed. A 25 set was built according to multilevel multifactor design [42] for calibration with PLS-2 (Table 1). The levels correspond to values in the range of 1100–1500 $\mu g\,mL^{-1}$ for PG, 700–1100 $\mu g\,mL^{-1}$ for GU, 80–160 $\mu g\,mL^{-1}$ for DP and 60–140 $\mu g\,mL^{-1}$ for CP. Duplicate analysis was performed for each sample, and HPLC-DAD was measured in random order according to the sample number. The validation set was prepared with three different levels of PG, GU, DP and CP in same conditions for calibration solutions. Three groups of all samples were prepared and analyzed in three times a day and four consecutive weeks. This procedure allowed us to assess intra- and inter-day assay accuracy and precision.

PLS-2 model was applied to HPLC-DAD data for determination of studied components.

2.3.2. Syrup samples

A volume of the syrup equivalent to 13.3 mg of PG, 10 mg of GU, 1 mg of DP and 0.83 mg of CP was diluted to 10 mL with water/ACN (60:40, v/v). Samples were homogenized, filtered through 0.45 μm membranes and injected into the chromatographic system. The studied components were determined as described in Calibration and test sets.

2.3.3. Classical HPLC

The determination of the contents of PG, GU, DP and CP in syrup preparations was also verified by classical HPLC at 200 nm with a stationary phase in the apparatus and software section. GU, DP and CP were determined with mobile phase of the pH 3 phosphate buffer containing 0.2% triethylamine and ACN (70:30, v/v). For determination of PG, mobile phase compositon was changed as a pH 3 phosphate buffer/ACN (90:10, v/v). The flow rate was 1 mL min^{-1}.

3. Method

The calibration involves the record of a series of detector responses (usually absorbance of compounds for HPLC) and related concentrations with them. A model is then built which can be subsequently used to predict concentrations of unknown compounds. Calibration can be performed in various modes namely: univariate; two-way PLS; three-way unfolded PLS; and three-mode PLS. In this work, three-way unfolded PLS was used. The raw data for all methods stored as a three-way tensor $\underline{\mathbf{Z}}$ of dimensions $M \times I \times J$ (M = number of training samples, I = number of elution time data points, J = number of digitized wavelengths) which can be rearranged to meet the dimensional demands of each method. Fol-

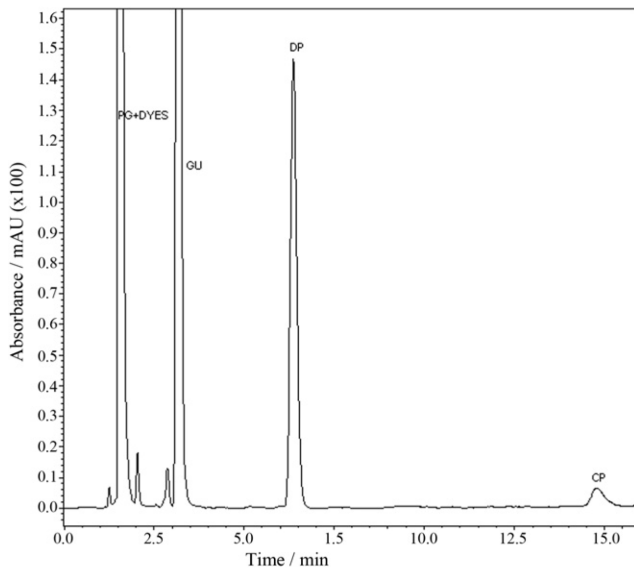

Fig. 1. Chromatographic separation of syrup samples by using classical HPLC method in pH 3 phosphate buffer that contains 0.2% triethylamine and ACN (70:30, v/v).

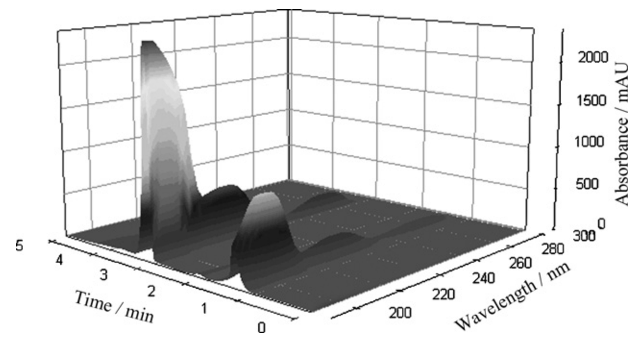

Fig. 2. Three-dimensional plot of quaternary mixture of 1300 μg mL^{-1} of PG, 1000 μg mL^{-1} of GU, 100 μg mL^{-1} of DP and 80 μg mL^{-1} of CP when the chromatographic separation is performed in 5 min and recorded with a diode array detector in the region of 190–300 nm.

lowing PLS decomposition, the resultant scores, $\boldsymbol{t}$ (correspond to elution profiles) and loadings, $\boldsymbol{p}$ (correspond to spectral profiles), are extracted for PLS.

In unfolded three-way PLS calibration, tensor $\underline{\boldsymbol{Z}}$ is unfolded into a 2D $\boldsymbol{X}$ matrix. To do this, the rows of $\underline{\boldsymbol{Z}}$ are concatenated to give a row vector, so that the resultant two-way $\boldsymbol{X}$ matrix now has dimensions $M \times IJ$. For three way-unfolded PLS, this matrix was used as the data block [27].

All calculations were performed in Matlab 7 using a software provided by PLS-Toolbox 5.2.

4. Results and discussion

4.1. Method development

In this study firstly, several mobile phase systems were tested to determine PG, GU, DP and CP by classical HPLC method. Using the pH 3 phosphate buffer that containing 0.2% triethylamine and ACN (70:30, v/v) as a mobile phase, PG, GU, DP and CP were well separated. But in syrup samples as shown in Fig. 1, the peak of PG was not separated from two dye additives. Separation of PG from these dye additives could be accomplished by performing a second injection with the new pH 3 phosphate buffer/ACN (90:10, v/v) ratio mobile phase system. In this situation, the complete quantitative analysis of the analytes can be performed by two separate injections or gradient elution with long elution time. Instead of these two alternatives we tried to analyse this syrup preparation by PLS-2 multivariate calibration method coupled with HPLC-DAD detection which has some advantages such as; solvent and time savings, and accordingly reduction of both the cost per analysis

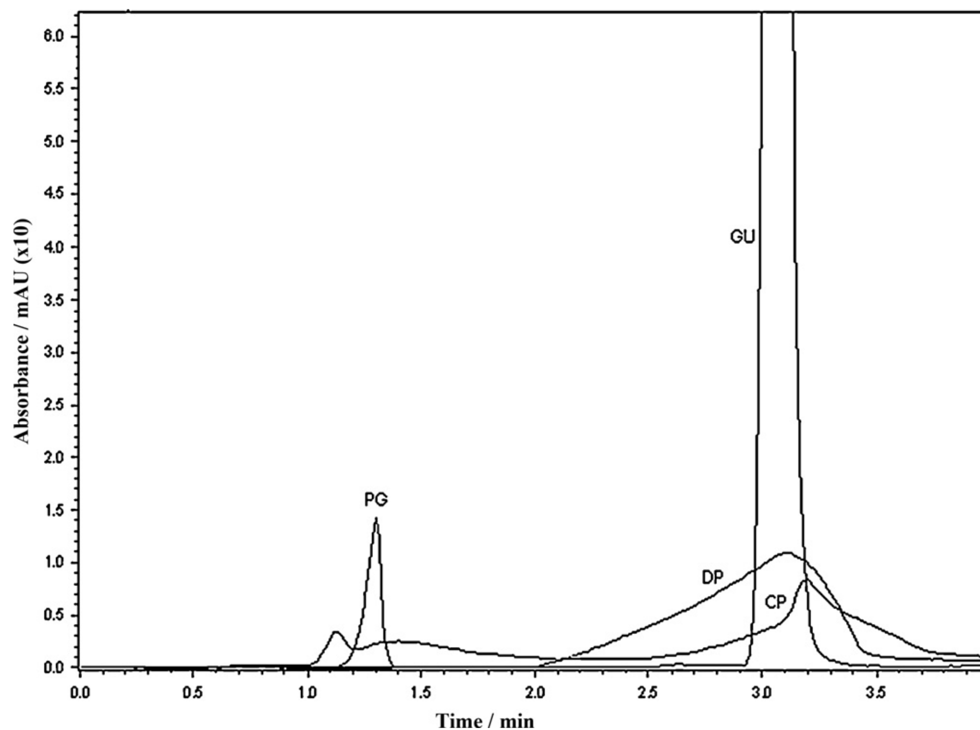

Fig. 3. Time profiles of the four drugs were recorded at the corresponding wavelength for each compound (i.e. PG: 279 nm, GU: 275 nm, DP: 225 nm and CP: 208 nm) in mobile phase.

Table 2
Optimum number of factors and calibration statistical parameters when applying PLS-2.

Statistical parameter[a]	PG	GU	DP	CP
Factors	5	5	5	5
RMSD	22.6	12.9	4.2	4.9
REP%	1.7	1.4	3.4	4.9
R^2	0.9745	0.9917	0.9780	0.9725

[a] x RMSD $= [1/m\sum_1^m (c_{act} - c_{pred})^2]^{1/2}$; %REP $= 100/\bar{c}[1/m\sum_1^m (c_{act} - c_{pred})^2]^{1/2}$ and $R^2 = 1 - (\sum_1^m (c_{act} - c_{pred})^2 / \sum_1^m (c_{act} - \bar{c})^2)$ $\bar{c}$ is the avarage component concentration in the m mixtures.

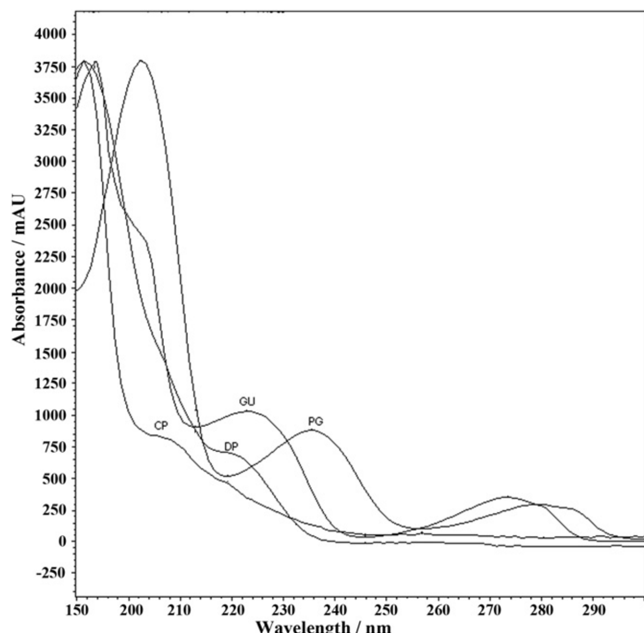

Fig. 4. Spectral profiles of the four drugs in mobile phase.

and environmental impact. In this method, simple mobile phase of water/ACN was used. In order to determine the best ratio to be used, three different ratio of water/ACN were tested such as 50:50, 60:40 and 70:30 (v/v). It has been shown that with 50:50 ratio, the chromatographic and spectral peaks of the mixture of four drugs were overlapped, apparently only two chromatographic peaks could be observed, with 60:40 ratio, three chromatographic peaks could be observed and with 70:30 ratio, still three chromatographic peaks could be observed with long elution time. Taking into account the elution time and the peak profile, water/ACN ratio of 60:40 was chosen.

4.2. HPLC-DAD analysis

The DAD allows the collection of the full spectral data at rates of up to several scans per second. With the data it is possible to construct three-dimensional plots of absorbance, wavelength and time. A typical 3D spectrochromatogram of the mixture of 1300 μg mL^{-1} of PG, 1000 μg mL^{-1} of GU, 100 μg mL^{-1} of DP and 80 μg mL^{-1} of CP using simple mobile phase water/ACN (60:40, v/v) is shown in Fig. 2. Figs. 3 and 4 also show both the time and spectral profiles of the four drugs at the same concentration in Fig. 2. Time elution profiles were recorded at the corresponding wavelength for each compound (i.e. PG: 279 nm, GU: 275 nm, DP: 225 nm and CP: 208 nm). As can be observed, because of the highly overlapping peaks, conventional measures of the different analytical signals (area or height of chromatographic peak) cannot be realized. For this reason, PLS-2 was utilized in order to resolve the quaternary mixture as an appropriate way.

In the simultaneous determination of PG, GU, DP and CP, the response data were taken over an elution time range of 1.05–5.00 min (Δt = 1/93.8 min) and wavelength range of 190–300 nm ($\Delta\lambda$ = 1.2 nm), the recorded data were combined into a 371 × 92 × 25 data array, where the number 25 corresponds to 25 calibration samples in the prediction set (Table 1). The unfolded three way data matrix was then decomposed with PLS-2. Usual statistical parameters giving an indication of the quality of fit of all the data are the root-mean square difference (RMSD), relative error of prediction (REP%), and square of the correlation coefficient (R^2). The obtained values for the present calibration and optimum number of factors are summarized in Table 2. The number of factors has been determined by cross-validation and no preprocessing has been applied.

4.3. Method validation

In order to test the prediction and accuracy performance of the proposed method intra-day (one day operation under the same conditions) and inter-day (four different days) variations using three different concentration levels were used. Results were summarized in Table 3. The values of the root mean square difference (RMSD) and the relative error of prediction (REP) for each component were included in order to give an indication the average error in the analysis. Good prediction results were obtained. RMSD and REP of intra-day for PG 49.1 and 3.8, for GU 14.4 and 1.5, for DP 8.4 and 7.6, for CP 8.1 and 8.5 were found, respectively. RMSD and REP of intra-day for PG 49.1 and 3.8, for GU 14.4 and 1.5, for DP 8.4 and 7.6, for CP 8.1 and 8.5 were found, respectively.

The limit of detections and quantitations were determined as 3.1 and 9.4; 1.9 and 5.9; 0.3 and 0.9; 0.2 and 0.6 μg mL^{-1} for PG, GU, DP and CP, respectively.

Table 3
Intra- and inter-day precision and accuracy of assay for PG, GU, DP and CP by using PLS-2.

	PG (μg/mL)			GU (μg/mL)			DP (μg/mL)			CP (μg/mL)		
Intra-assay	1200.0	1300.0	1400.0	1100.0	1000.0	900.0	80.0	100.0	120.0	60.0	80.0	100.0
	1250.2	1338.9	1428.1	1087.1	996.0	904.0	86.8	104.8	117.4	63.9	84.5	93.6
	1248.6	1331.9	1420.4	1105.0	997.7	897.7	87.1	105.2	117.8	63.4	83.9	96.7
	1252.9	1334.5	1422.2	1095.4	998.6	905.9	86.4	105.9	118.3	64.4	84.8	94.9
RMSD		38.2			5.7			5.1			4.3	
REP%		2.9			0.6			5.1			5.4	
Recovery%		102.8			99.9			103.3			101.4	
Inter-assay	1257.2	1321.9	1384.0	1105.0	998.6	897.7	86.4	104.8	118.3	65.1	86.7	96.7
	1239.9	1342.2	1440.5	1111.9	1010.8	915.2	83.9	104.2	120.4	62.9	83.9	92.2
	1248.6	1331.9	1420.4	1069.2	979.5	903.9	87.5	105.3	116.1	64.3	82.8	94.4
	1251.9	1329.5	1438.1	1090.5	993.6	906.9	85.2	106.1	117.5	63.4	85.8	93.6
RMSD		38.5			13.2			4.6			5.0	
REP%		3.0			1.3			4.6			6.3	
Recovery%		102.7			99.8			103.0			101.2	

Table 4
Comparison of results in two method analysis of commercial formulation "Gayaben®".

$n_1 = n_2 = 5$	PG ($\mu g\,mL^{-1}$)		GU ($\mu g\,mL^{-1}$)		DP ($\mu g\,mL^{-1}$)		CP ($\mu g\,mL^{-1}$)	
	PLS-2	Classical HPLC	PLS-2	Classical HPLC	PLS-2	Classical HPLC	PLS-2	Classical HPLC
Mean ± SD[a]	26.50 ± 1.10	27.60 ± 0.50	20.10 ± 0.56	20.60 ± 0.35	2.09 ± 0.10	1.99 ± 0.09	1.690 ± 0.007	1.750 ± 0.003
Recovery%	99.6	103.8	100.5	103.0	104.5	99.5	101.8	105.4
t test of significance	2.04		1.82		1.67		1.76	
F test of significance	4.93		2.56		1.23		5.44	
	$t_8^{0.05} = 2.31$				$F_{4.4}^{0.05} = 6.39$			

[a] SD: standard deviation.

The solution of PG, GU, DP and CP were stable for at least 24 h when kept at room temperature.

4.4. Application of syrup samples

The proposed method was also applied to the determination of PG, GU, DP and CP in syrup samples, as it was described in Section 2. This method was also compared with classical HPLC method. The assay results obtained by both methods were statistically compared at the %95 level. The calculated *F*-values and *t*-values were found to be less than the critical values at 95% confidence level (6.39 and 2.31, respectively). So as shown in Table 4, there was no significant differences between the mean values and precisions of the data obtained by two methods.

5. Conclusions

In this paper, PLS-2 calibration method has been applied for the HPLC-DAD determination of PG, GU, DP and CP in syrup samples. For the determination of analytes in syrup samples with heavily overlapped peaks and interferences, the PLS-2 can provide satisfactory concentration estimates. In the present work, simple and low cost mobile phase and short analysis time have been used. This method, which did not require complete separation of the analytes, demonstrated good accuracy and recoveries, and is free from interferences, can be used as an alternative method in routine analysis. Without the need to use internal standards and gradient elution, the proposed method allows an easy and fast determination of PG, GU, DP and CP in syrup samples.

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References

[1] S. Wongiel, A. Hymete, A.I.M. Mohammed, Ethiop. Pharm. J. 26 (2008) 39–48.
[2] A.A.M. Wahbi, M.M. Bedair, S.S. Elomar, Anal. Lett. 22 (1989) 885–896.
[3] M.R. Louhaichi, S. Jebali, M.H. Loueslati, N. Adhoum, L. Monser, Talanta 78 (2009).
[4] N.L. Denola, N.S. Quiming, Y. Saito, A.P. Catabay, K. Jinno, J. Liq. Chromatogr. Related Technol. 32 (2009) 1407–1422.
[5] T.H. Eichhold, D.L. McCauley-Myers, D.A. Khambe, G.A. Thompson, S.H. Hoke, J. Pharm. Biomed. Anal. 43 (2) (2007) 586–600.
[6] T. Harsono, M. Yuwono, G. Indrayanto, J. AOAC Int. 88 (2005) 1093–1098.
[7] L.Q. Zhang, X.H. Wu, X. Tang, X.L. Zhu, W.T. Su, Spectrosc. Spectral Anal. 22 (2002) 427–429.
[8] L.Q. Zhang, X. Tang, X.L. Zhu, J. Wuhan Univ. Technol. Mater. Sci. Ed. 16 (2001) 79–82.
[9] K.M. Emara, H.M. Abdel-Wadood, M.F. Bakr, B. Pharm. Sci. 31 (2008) 183–195.
[10] I. Tapsoba, J.E. Belgaied, K. Boujlel, J. Pharm. Biomed. Anal. 38 (2005) 162–165.
[11] U. Doge, K. Eger, Pharmazie 62 (2007) 174–178.
[12] W.S. Hassan, M.M. El-Henawee, A.A. Gouda, Spectrochim. Acta A 69 (2008) 245–255.
[13] C.Z. Zhao, X.L. Chai, S.C. Tao, M.H. Li, K. Jiao, Anal. Sci. 24 (2008) 535–538.
[14] M.E. Capella-Peiro, A. Bossi, J. Esteve-Romero, Anal. Biochem. 352 (2006) 41–49.
[15] A. El-Gindy, S. Emara, M.K. Mesbah, G.M. Hadad, Anal. Lett. 39 (2006) 2699–2723.
[16] A. El-Gindy, S. Emara, A. Mostafa, J. Pharm. Biomed. Anal. 41 (2006) 421–430.
[17] Y. Dou, Y. Sun, Y.Q. Ren, Y.L. Ren, Anal. Chim. Acta 528 (2005) 55–61.
[18] H.C. Goicoechea, A.C. Olivieri, Anal. Chim. Acta 453 (2002) 289–300.
[19] K. Weclawska, A. Regosz, Pharmazie 42 (1987) 483–484.
[20] H. Hopkala, L. Przyborowski, J. Flieger, Anal. Lett. 27 (1994) 2223–2238.
[21] H.Z. Zhang, F. Nie, J.R. Lu, Spectrochim. Acta A 72 (2009) 858–862.
[22] A.G. Frenich, M.M. Galera, J.L.M. Vidal, M.D.G. Garcia, J. Chromatogr. A 727 (1996) 27–38.
[23] P. Parrilla, M.M. Galera, A.G. Frenich, J.L.M. Vidal, J. Liq. Chromatogr. Related Technol. 20 (1997) 425–442.
[24] M.M. Galera, A.G. Frenich, J.L.M. Vidal, J. Liq. Chromatogr. Related Technol. 23 (2000) 1187–1202.
[25] Y.Z. Zhou, X.X. Liu, X.H. Zheng, J.B. Zheng, Chromatographia 66 (2007) 635–637.
[26] A.G. Frenich, J.L.M. Vidal, M.M. Galera, Anal. Chem. 71 (1999) 4844–4850.
[27] K.D. Zissis, R.G. Brereton, S. Dunkerley, R.E.A. Escott, Anal. Chim. Acta 384 (1999) 71–81.
[28] A.G. Frenich, M.M. Galera, M.D.G. Garcia, J.L.M. Vidal, M. Catasus, L. Marti, M.V. Merderos, J. Liq. Chromatogr. Related Technol. 24 (2001) 651–668.
[29] E. Comas, R.A. Gimeno, J. Ferre, R.M. Marce, F. Borrull, F.X. Rius, J. Chromatogr. A 1035 (2004) 195–202.
[30] Y. Zhang, H.L. Wu, Y.J. Ding, A.L. Xia, H. Cui, R.Q. Yu, J. Chromatogr. B 840 (2006) 116–123.
[31] Y. Zhang, H.L. Wu, A.L. Xia, Q.J. Han, H. Cui, R.Q. Yu, Talanta 72 (2007) 926–931.
[32] M.J. Culzoni, A.V. Schenone, N.E. Llamas, M. Garrido, M.S.D. Nezio, B.S.F. Band, H.C. Goicoechea, J. Chromatogr. A 1216 (2009) 7063–7070.
[33] K. Wiberg, M. Andersson, A. Hagman, S.P. Jacobsson, J. Chromatogr. A 1029 (2004) 13–20.
[34] M.J.R. Cuesta, R. Boque, F.X. Rius, J.L.M. Vidal, A.G. Frenich, Chemometr. Intell. Lab. Syst. 77 (2005) 251–260.
[35] S.E.G. Porter, D.R. Stoll, C. Paek, S.C. Rutan, P.W. Carr, J. Chromatogr. A 1137 (2006) 163–172.
[36] O. Aksu, A. Bozdogan, G. Kunt, Anal. Lett. 31 (1998) 859–866.
[37] O. Aksu, A. Bozdogan, G. Kunt, Anal. Lett. 39 (2006) 751–761.
[38] O.A. Dönmez, A. Bozdogan, G. Kunt, Monatshefte für Chemie 137 (2006) 1163–1168.
[39] O.A. Dönmez, A. Bozdogan, G. Kunt, Rev. Anal. Chem. 26 (2007) 209–217.
[40] O.A. Dönmez, A. Bozdogan, G. Kunt, Y. Div, Chem. Anal. (Warsaw) 52 (2007) 135–140.
[41] O.A. Dönmez, A. Bozdogan, G. Kunt, Y. Div, J. Anal. Chem. 65 (2010) 30–35.
[42] R.G. Brereton, Analyst 122 (1997) 1521–1529.