FABAD J. Pharm. Sci., 50, 2, 371-384, 2025
Doi: 10.55262/fabadeczacilik.1664557
RESEARCH ARTICLE

Quantitative Estimation of Dexketoprofen and Paracetamol in Effervescent Tablets by Chemometrics-Assisted Spectrophotometry

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SUMMARY

Dexketoprofen (DEX) and paracetamol (PAR), a common drug pair in multimodal analgesia, exhibit overlapping absorbance spectra, making conventional UV-Vis spectroscopy unsuitable for their simultaneous quantification. The objective of this work was to develop and validate chemometrics-assisted spectrophotometric methods for the simultaneous quantification of these drugs in effervescent tablet formulations, despite their overlapping spectra. UV-Vis spectrophotometry was combined with Principal Component Regression (PCR) and Partial Least Squares (PLS) regression to develop predictive models. A calibration set of 25 binary mixtures, with concentration ranges of 3–18 µg/mL for DEX and 5–25 µg/mL for PAR, was used to develop the chemometric models. The models were built using the concentration data set and the spectral data between 220 and 320 nm (Δλ=0.1 nm). The accuracy and precision of the proposed chemometric methods were assessed by analyzing a set of independent test samples as well as intra-day and inter-day samples. The PCR and PLS models provided accurate and precise quantification, with mean recovery values and relative standard deviations within acceptable limits. Commercial effervescent tablet samples were analyzed to evaluate the applicability, and assay results showed good agreement with label claims. The proposed PCR and PLS methods offer reliable and cost-effective alternatives to HPLC for the simultaneous analysis of DEX and PAR in pharmaceutical formulations. These methods are suitable for routine quality control, reducing analysis time and solvent consumption.

Key Words: *Dexketoprofen, paracetamol, PCR, PLS, UV-Vis spectroscopy*

Kemometri Destekli Spektrofotometri ile Efervesan Tabletlerdeki Deksketoprofen ve Parasetamolün Kantitatif Tayini

ÖZ

Deksketoprofen (DEX) ve parasetamol (PAR), multimodal analjezide yaygın olarak kullanılan iki ilaçtır. Ancak, UV bölgesinde örtüşen spektrumları nedeniyle geleneksel UV-GB spektroskopisi ile bu bileşiklerin eş zamanlı kantitatif tayini mümkün değildir. Bu çalışmanın amacı, spektral örtüşmeye rağmen DEX ve PAR etken maddelerinin aynı anda analizini sağlayan kemometri destekli spektrofotometrik yöntemler geliştirmek, valide etmek ve bu yöntemleri efervesan tablet formülasyonlarının analizine uygulamaktır. Bu doğrultuda, birincil bileşen regresyonu (PCR) ve kısmi en küçük kareler (PLS) regresyonu modellerinin UV-GB spektroskopisi ile beraber kullanılımlı iki farklı miktar tayini yöntemi geliştirilmiştir. Modellerin oluşturulması için 3-18 µg/mL DEX ve 5-25 µg/mL PAR konsantrasyon aralığında hazırlanan 25 adet ikili karışımdan oluşan bir kalibrasyon seti hazırlanmıştır. Bu setin 220–320 nm (Δλ = 0.1 nm) arasındaki spektral verileri ve konsantrasyon değerleri arasındaki ilişki PCR ve PLS yöntemleri ile modellenmiştir. Önerilen kemometrik yöntemlerin doğruluğu ve kesinliği, bağımsız test örnekleri ile birlikte gün içi ve günler arası analizlerle değerlendirilmiştir. PCR ve PLS modelleri, kabul edilebilir sınırlar içinde geri kazanım yüzdeleri ve bağıl standart sapma değerleriyle doğru ve hassas sonuçlar vermiştir. Geliştirilen ve valide edilen bu yöntemler, ticari efervesan tablet örneklerinin analizine uygulanmış ve elde edilen sonuçlar, etiket değerleriyle büyük ölçüde uyumlu bulunmuştur. Geliştirilen PCR ve PLS yöntemlerinin, HPLC'ye maliyet açısından avantajlı, güvenilir bir alternatif sunarak rutin kalite kontrol analizleri için uygun olduğu belirlenmiştir. Bu yöntemler, rutin kalite kontrol için uygun olup, analiz süresini ve solvent tüketimini azaltır.

Anahtar Kelimeler: *Deksketoprofen, parasetamol, PCR, PLS, UV-GB spektroskopisi*

Received: 25.03.2025
Revised: 5.06.2025
Accepted: 7.07.2025

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INTRODUCTION

Multimodal analgesia, the simultaneous use of multiple analgesic drugs with different mechanisms of action, is a pharmacologic approach designed to provide superior pain control with reduced side effects (O'Neill & Lirk, 2022; Yerebakan et al., 2024). Dexketoprofen (DEX), the active enantiomer of ketoprofen, is a non-steroidal anti-inflammatory drug prescribed for short-term treatment of moderate pain, particularly musculoskeletal pain, dental pain, and dysmenorrhea (Kuczyńska et al., 2022). Paracetamol (PAR) is one of the most popular and widely used drugs in pain management. It has a central analgesic effect and is primarily used for treating headaches, minor aches, and moderate pain (Ayoub, 2021). As these drugs reduce pain through different mechanisms, they are a common pair in multimodal pain strategies. Combining DEX and PAR leads to more effective analgesia while lowering the required doses of each drug and reducing side effects. This has led to the development of pharmaceutical formulations containing DEX and PAR for acute pain management, including musculoskeletal and post-operative pain, and for arthritis (López Navarro et al., 2019). Additionally, this combination has been used for the treatment of post-COVID-19 symptoms, including myalgia and headache (Medhat et al., 2024).

Developing new and effective analytical methods is crucial to ensure the quality, efficacy, and safety of drugs and pharmaceutical dosage forms. UV-Vis spectrophotometry offers several advantages as an analytical technique, including simplicity, accessibility, minimal sample preparation, and rapid analysis. The simplicity and low-cost equipment of spectrophotometry make it the method of choice for many laboratories. However, classical spectrophotometric methods may fail when analyzing dosage forms containing more than one active ingredient with overlapping spectra, such as DEX and PAR. In these cases, the researchers choose high-performance liquid chromatography (HPLC), despite the disadvantages, which include high costs, extensive maintenance, time-consuming procedures, higher solvent use, and less environmentally friendly operations. A literature review shows that the simultaneous determination of DEX and PAR has primarily been conducted using HPLC (Medhat et al., 2024; Mulla et al., 2011; Pokharkar et al., 2011; Rao et al., 2011).

On the other hand, there are less labor-intensive and more feasible options to overcome these challenges, such as chemometrics-assisted UV-Vis spectrophotometry. Chemometric methods allow the extraction of relevant information from complex datasets, including overlapping spectral data. Principal component regression (PCR) and partial least squares (PLS) are multivariate chemometric techniques commonly used in combination drug analysis to handle complex, multicomponent systems. Chemometric techniques, especially PCR and PLS, play an essential role in overcoming the challenges of analyzing combination drugs with overlapping spectral data. These methods provide the accuracy needed for quality control in the pharmaceutical industry, ensuring safe and effective medications reach the market.

PCR and PLS are well-established tools in pharmaceutical analysis and they are extensively documented in the chemometric literature for their high predictive power, robustness to noise, and flexibility in handling collinear and overlapping data. Recent studies continue to demonstrate their effectiveness in the quantification of multicomponent mixtures in both pharmaceutical and biological matrices (Aktas & Sahin, 2021; Çolak, 2024; Demirkaya Miloğlu & Karagöl, 2023; Ertokus, 2022; Gandhi et al., 2021; Michael et al., 2024; Pekcan, 2024; Sayed et al., 2021; Sebaiy et al., 2023). These methods not only improve analytical sensitivity and selectivity but also streamline method development by reducing reliance on expensive instrumentation and solvent-intensive protocols.

To date, the only spectrophotometric quantification study reported in the literature for this combination (Kothapalli et al., 2011) employed classical

spectrophotometric methods, specifically the simultaneous equation method and the Q-absorbance ratio method. In these approaches, concentrations are determined by solving simultaneous equations derived from absorptivity coefficients at selected wavelengths. While these methods are simple, rapid, and cost-effective, they depend heavily on the careful selection of wavelengths, such as isosbestic points or regions with significant absorbance differences, which limits their applicability. These univariate techniques are generally effective when spectral overlap between analytes is minimal or well-characterized, but tend to be less reliable in cases of substantial spectral overlap and often result in lower sensitivity and selectivity.

In contrast, chemometrics-assisted methods, such as PCR and PLS, utilize the full spectral dataset to model latent variables that correlate with analyte concentrations. These multivariate approaches do not require prior selection of discrete wavelengths and can accurately resolve overlapping spectra without physical separation of analytes. As a result, they offer improved sensitivity, robustness, and analytical performance, particularly in complex mixtures or formulations.

In this work, two chemometrics-assisted spectrophotometric methods were developed to simultaneously quantify PAR and DEX in spite of their overlapping spectra. PCR and PLS methods were developed and validated by employing training and test sets containing both drugs in their linear concentration range. Intra-day and inter-day measurements were also performed for the validation of the analytical methods. Finally, the chemometric methods were applied to the quantitative estimation of PAR and DEX in effervescent tablet samples.

MATERIAL AND METHODS

Instruments and Software

A Shimadzu UV-2550 double-beam UV-VIS spectrophotometer (Kyoto, Japan) with UVProbe Software (Shimadzu, Kyoto, Japan) was used to record absorption spectra of samples. A quartz cuvette with a 1 cm light path was used, and the slit width was set to 2 nm. Spectra were recorded over the wavelength range of 200–340 nm with an increment of 0.05 nm. The spectra were transferred to an Excel sheet as column vectors. Absorbance data between 220 and 320 nm ($\Delta\lambda$=0.1 nm), along with the nominal concentration data, were used to model and validate the PCR and PLS methods using MATLAB software (MathWorks, USA).

Chemicals and reagents

The standard materials of paracetamol and dexketoprofen trometamol were kindly gifted by a national pharmaceutical manufacturer Deva (Tekirdağ, Türkiye). Methanol of analytical grade supplied by Carlo Erba (Milan, Italy). The commercial sample, as an effervescent tablet preparation, was procured from a local pharmacy. It was produced by Neutec Pharmaceuticals, with a label claim of 50 mg DEX and 300 mg PAR per effervescent tablet.

Standard solutions

Individual stock solutions of PAR and DEX were prepared by dissolving 10 mg standard paracetamol and 14.8 mg standard dexketoprofen trometamol (equivalent to dexketoprofen) in 100 mL methanol. A calibration set of 25 solutions (planned by 5^2 a factorial design, 5 levels and 2 analytes) was prepared by mixing appropriate amounts of stock solutions and diluting them in methanol. The working concentration ranges were 3-18 µg/mL for DEX and 5-25 µg/mL for PAR. The concentrations of DEX and PAR in each calibration sample are shown in Table 1.

Table 1. Calibration set for constructing PCR and PLS models

µg/mL			µg/mL		
Sample code	DEX	PAR	Sample code	DEX	PAR
C1	3	5	C14	10	20
C2	3	10	C15	10	25
C3	3	15	C16	14	5
C4	3	20	C17	14	10
C5	3	25	C18	14	15
C6	6	5	C19	14	20
C7	6	10	C20	14	25
C8	6	15	C21	18	5
C9	6	20	C22	18	10
C10	6	25	C23	18	15
C11	10	5	C24	18	20
C12	10	10	C25	18	25
C13	10	15			

To evaluate the performance of the chemometric models, a set of 11 independent test samples containing both drugs at various concentration levels was prepared in the same manner. The test set included: (i) five DEX concentrations from the calibration range with a fixed PAR concentration matching that of the commercial formulation; (ii) five PAR concentrations from the calibration range with a fixed DEX concentration matching the commercial level; and (iii) one sample containing both PAR and DEX at concentrations equivalent to those in the commercial product. This design ensured that all validation samples, listed in Table 3, were distinct from those used in calibration. Additionally, as a part of the validation studies, synthetic samples at three different concentration levels (Table 4) were prepared in triplicate to assess intra-day and inter-day precision.

Effervescent tablet sample solutions

Five effervescent tablets were ground into a fine powder using a dry mortar. A portion equivalent to the mass of 0.1 tablet was transferred into a 50 mL volumetric flask. Approximately 20 mL of methanol was added, and the mixture was allowed to stand until foaming stopped, with occasional manual shaking. The flask was then filled to volume with methanol. To ensure complete dissolution of the drugs, the solution was magnetically stirred for 15 minutes and subsequently filtered. A 0.4 mL aliquot of the filtrate was diluted to 10 mL and subjected to spectrophotometric analysis. This procedure was repeated 10 times.

RESULTS AND DISCUSSION

In preliminary experiments, the spectra of individual standard solutions of PAR and DEX at increasing concentrations were recorded between 200-340 nm. The spectra of these solutions are shown in Figure 1, where red represents DEX and blue represents PAR. DEX exhibits a prominent absorption band with a maximum around 255 nm, while PAR shows strong absorbance near 248.4 nm. As can be seen in this figure, significant spectral overlap between DEX and PAR in the UV region makes direct univariate spectrophotometric quantification unsuitable for their mixtures due to signal interference. Figure 1 also displays the UV absorption spectra of their binary mixture (containing 18 µg/mL DEX and 20 µg/mL PAR) in green. The binary mixture spectrum reflects the additive absorbance of both drugs, yet due to the overlapping nature and possible matrix effects in commercial formulations, the resulting profile may not be a straightforward superposition. This overlap underscores the necessity of multivariate calibration methods such as PCR and PLS, which can deconvolute the

mixed spectral information and extract concentration data for each analyte by modeling the latent structure in the dataset. Linear concentration ranges were investigated by plotting the absorbance values at 255 nm for DEX and 248.4 nm for PAR against the corresponding concentrations. The appropriate working ranges were decided as 3–18 µg/mL for DEX and 5–25 µg/mL for PAR.

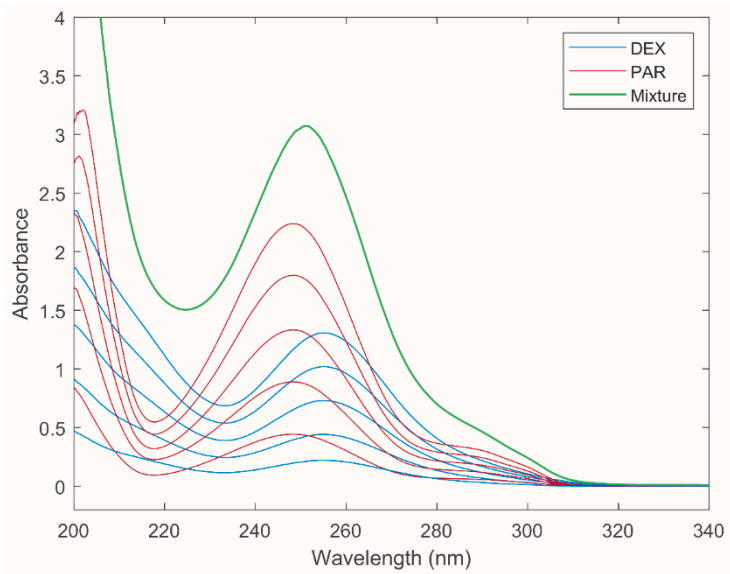

Figure 1. UV absorption spectra of 3.0-18 µg/mL DEX (— blue), 5.0-25.0 µg/mL PAR (— red), and their binary mixture consisting of 18 µg/mL DEX and 20 µg/mL PAR (— green).

Application of chemometric regression methods

Principal component regression (PCR) is a technique that combines principal component analysis (PCA) and multilinear regression. The absorbance data matrix is decomposed by PCA to extract the latent variables (eigenvectors and their corresponding eigenvalues). Then, a multilinear regression is applied in an inverse least-squares manner to construct the PCR calibration using the selected eigenvectors and the mean-centered concentration data (Olivieri, 2018c).

In this study, the PCR model was implemented by calculating the loadings, q , using the equation $q=D\times T^T\times A$, where D is the diagonal matrix containing the inverse of the selected eigenvalues, T is the score matrix, and A is the absorbance matrix of the calibration samples. Then, the regression coefficient, b, was calculated as $b=P\times q$, where P is the matrix of eigenvectors. The predicted concentration matrix, C_{pred}, was obtained using the equation $C_{pred}=b\times A_{sample}$, where A_{sample} is the absorbance matrix of the samples (Dinç et al., 2006; Dinç, 2007). In this work, the absorbance matrix was constructed as absorbance values between 220-320 nm with an increment of 0.1 nm, and was mean-centered.

The optimal number of principal components (i.e., eigenvector–eigenvalue pairs) was determined using the leave-one-out cross-validation technique. In this approach, multiple PCR models are constructed by sequentially excluding one sample from the calibration set, calibrating the model with the remaining samples, and predicting the excluded sample. This process begins with a model containing a single principal component, and the corresponding prediction error is calculated. The excluded sample is then reintegrated into the dataset, and the procedure is repeated for each sample in turn. This entire process is performed iteratively for an increasing number of principal components, up to a maximum of 10 in this study.

For each number of components, cross-validation statistics, including the prediction error sum of squares (PRESS), root mean squared error of cross-validation (RMSECV), and explained variance, were calculated.

Table 2 presents the cross-validation results, while Figure 2 illustrates the RMSECV as a function of the number of principal components. As shown in Figure 2, adding up to three principal components resulted in a significant reduction in prediction error. This finding is further supported by the data in Table 2, which indicates that three principal components account for more than 99.99% of the variance in both compounds. Including additional components yielded minimal improvement, offering little relevant information and posing a risk of overfitting. Therefore, the final PCR model was constructed using three principal components, with the remaining components excluded (Dinç et al., 2005; Olivieri, 2018a).

Table 2. Statistical results of cross-validation

		PRESS		RMSECV		EV	
PCR	PC number	DEX	PAR	DEX	PAR	DEX	PAR
	1	642.549	505.821	5.174	4.591	97.499	97.499
	2	11.022	15.263	0.678	0.797	99.966	99.966
	3	0.889	1.320	0.192	0.234	99.992	99.992
	4	1.004	0.541	0.204	0.150	99.998	99.998
	5	1.030	0.550	0.207	0.151	99.999	99.999
		PRESS		RMSECV		EV	
PLS	LV number	DEX	PAR	DEX	PAR	DEX	PAR
	1	551.068	436.490	4.792	4.265	97.495	54.123
	2	2.766	3.527	0.339	0.383	99.966	99.771
	3	0.193	0.431	0.090	0.134	99.992	99.958
	4	0.616	1.325	0.160	0.235	99.998	99.979
	5	0.421	0.623	0.132	0.161	100.000	99.982

PCR: principal component regression, PLS: partial least squares, PC: principal component, LV: latent variable, PRESS: prediction error sum of squares, RMSECV: root mean squared error of cross-validation, EV: explained variance

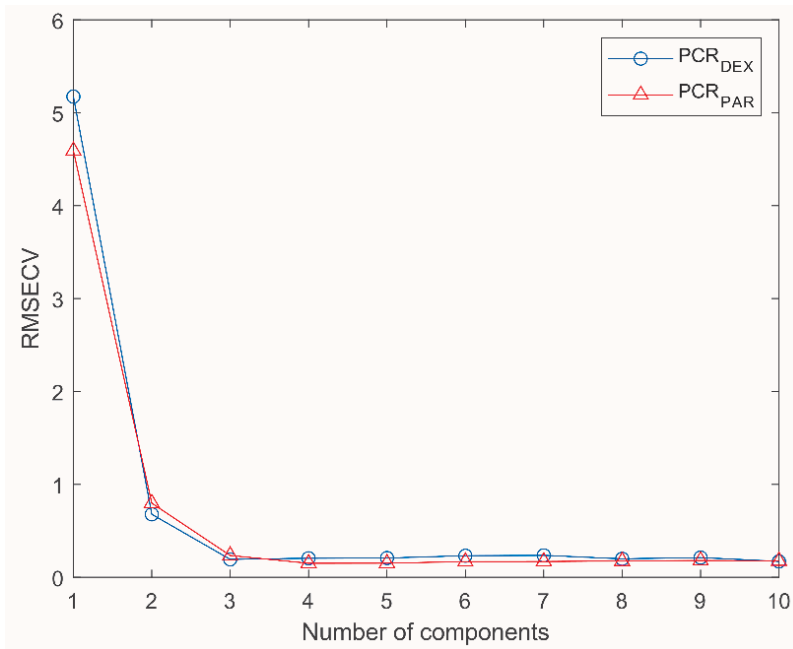

Figure 2. Number of components versus the root mean squared error of cross-validation during cross-validation of the PCR model.

Unlike PCR, PLS uses both absorbance data and concentration data in the decomposition process to estimate the latent variables. It means that the latent variables (principal components) in PCR are analyte-independent, whereas PLS latent variables are analyte-dependent (Olivieri, 2018b; Üstündağ et al., 2015). In the calibration step of PLS, absorbance data A and calibration data C are decomposed into scores and loadings by the following equations, called outer relation (Dinç et al., 2010):

$$A=TP^T+E \quad (1)$$

$$C=UQ^T+F \quad (2)$$

here, and denote score matrices, and represent the loading matrices, and and are the residuals associated with absorbance and concentration data, respectively. PLS minimizes the F while keeping the correlation between A and C using the inner relation U=TD, where D is a diagonal matrix that ensures the relationship between T and U.

In the regression step, the vector of PLS regression coefficients, B, is calculated by the equation $B=W\times(P^T\times W)^{-1}\times Q$, where W is a matrix of weights. Finally, the concentration of the samples, C_{pred}, was computed using the equation $C_{pred}=B\times A_{sample}$ (Dinç, 2007).

As in the PCR method, the absorbance matrix, between 220-320 nm with $\Delta\lambda$=0.1 nm, was used after mean-centering during PLS implementation. Similarly, the optimal number of latent variables in the PLS method was determined by leave-one-out cross-validation. For a maximum of 10 latent variables, PRESS, RMSECV, and explained variance values were calculated. Table 2 presents the cross-validation results, while Figure 3 illustrates RMSECV values as a function of the number of latent variables. As shown in the figure, the inclusion of more than three latent variables results in a slight increase in prediction error. This observation is also supported by Table 2, where the minimum PRESS value was obtained with a PLS model using three latent variables, achieving an explained variance greater than 99.9% for both analytes. Although models with more latent variables accounted for slightly higher variance, they were deemed unsuitable due to the potential risk of overfitting. Consequently, a PLS model with three latent variables was selected as the most appropriate for modeling the calibration data.

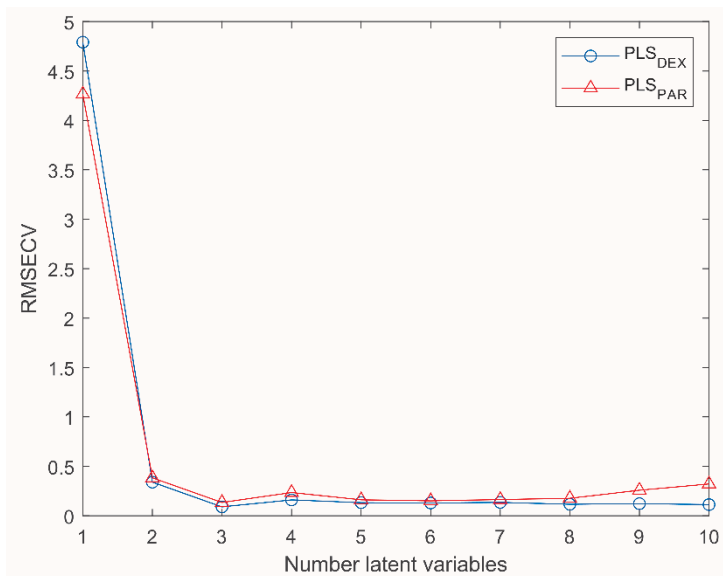

Figure 3. Number of latent variables versus root mean squared error of cross-validation in the PLS method

Analytical validation of the developed methods

The analytical performance of the developed PCR and PLS methods was evaluated by analyzing several validation samples. A set of 11 independent test samples, containing DEX and PAR in several concentration levels different from the levels used in the calibration set, was used for this purpose. The predicted concentrations of DEX and PAR in these samples by PCR and PLS models are listed in Table 3. This table also depicts the percentage recovery of the samples as well as the average and standard deviation of the recovery values. The mean recovery, standard deviation, and relative standard deviation values were found to be appropriate, indicating the suitability of the method for the simultaneous analysis of the mentioned drugs in their mixtures.

Table 3. Recovery results of independent test samples by PCR and PLS methods

Added (μg/mL)			Found (μg/mL)				Recovery (%)			
			PCR		PLS		PCR		PLS	
Code	DEX	PAR	DEX	PAR	DEX	PAR	DEX	PAR	DEX	PAR
M1	3	24	2.92	23.96	2.84	24.08	97.36	99.83	94.76	100.34
M2	6	24	5.69	23.93	5.61	24.06	94.88	99.72	93.55	100.24
M3	10	24	10.09	24.08	10.01	24.21	100.91	100.32	100.06	100.85
M4	14	24	13.84	24.07	13.76	24.20	98.84	100.31	98.26	100.83
M5	18	24	18.05	23.86	17.97	23.99	100.28	99.41	99.81	99.95
M6	4	5	3.98	4.96	3.90	5.09	99.61	99.26	97.49	101.90
M7	4	10	4.07	9.76	3.99	9.89	101.74	97.60	99.67	98.90
M8	4	15	3.94	14.72	3.86	14.85	98.62	98.12	96.56	98.97
M9	4	20	3.94	20.11	3.86	20.23	98.48	100.54	96.48	101.16
M10	4	25	4.02	25.05	3.94	25.18	100.47	100.21	98.39	100.71
M11	4	24	3.99	23.96	3.91	24.09	99.71	99.85	97.65	100.38
						Mean	99.17	99.56	97.52	100.38
						Standard deviation	1.89	0.94	2.07	0.89
						Relative standard deviation	1.90	0.94	2.13	0.88

Additionally, the precision and accuracy of the methods were evaluated by the inter-day (n=3) and intra-day (n = 3) analyses at three concentration levels (5 μg/mL, 10 μg/mL, 15 μg/mL for DEX and 8 μg/mL, 16 μg/mL, 24 μg/mL for PAR). The predicted concentration values were calculated by applying PCR and PLS methods, and the corresponding results (expressed as mean percent recovery, relative standard deviation, and percent relative error values) are summarized in Table 4.

Table 4. Analysis results of intra-day and inter-day samples (n=3)

	Added (µg/mL)		Found (µg/mL)			
			PCR		PLS	
Code	DEX	PAR	DEX	PAR	DEX	PAR
Inter-day	5	8	5.21	7.94	5.12	8.07
	10	16	9.72	16.22	9.63	16.34
	15	24	14.73	24.36	14.64	24.49
Intra-day	5	8	5.09	8.10	5.00	8.23
	10	16	9.97	16.52	9.89	16.65
	15	24	15.27	24.59	15.18	24.73
			Mean recovery (%)			
			PCR		PLS	
			DEX	PAR	DEX	PAR
Inter-day			104.16	99.22	102.32	100.89
			97.18	101.35	96.34	102.15
			98.18	101.50	97.62	102.04
Intra-day			101.85	101.25	100.03	102.92
			99.70	103.26	98.85	104.06
			101.83	102.48	101.21	103.05
			Relative Standard Deviation			
			PCR		PLS	
			DEX	PAR	DEX	PAR
Inter-day			1.00	0.64	1.01	0.63
			0.16	0.40	0.16	0.40
			1.19	0.81	1.19	0.80
Intra-day			3.87	2.03	3.74	2.09
			1.32	0.45	1.31	0.44
			0.40	1.11	0.42	1.09
			Relative Error			
			PCR		PLS	
			DEX	PAR	DEX	PAR
Inter-day			4.16	-0.78	2.32	0.89
			-2.82	1.35	-3.66	2.15
			-1.82	1.50	-2.38	2.04
Intra-day			1.85	1.25	0.03	2.92
			-0.30	3.26	-1.15	4.06
			1.83	2.48	1.21	3.05

The limit of quantification (LOQ) values for both DEX and PAR were calculated using a residual-based approach. Unlike univariate calibration, where LOQ is typically defined using the slope of a calibration curve, multivariate models such as PLS and PCR do not produce a single, well-defined slope. This is because predictions are based on a combination of correlated spectral variables and latent variables, making the direct application of univariate formulas inappropriate. To address this, we applied a residual-based method, consistent with established practices in the chemometric literature (Allegrini & Olivieri, 2014; Felmy et al., 2024; Parastar & Kirsanov, 2020). Specifically, LOQ was calculated using the formula: $LOQ = 10.\sigma/S$, where σ is the standard deviation of the residuals between the measured and predicted concentrations for each analyte in the calibration set, and S represents the model sensitivity, defined as the Euclidean norm of the regression coefficient vector for each analyte. This approach incorporates the prediction error to quantify noise and employs the regression vector norm as a surrogate for sensitivity, thereby providing a performance-based and model-consistent estimate of LOQ. The computed LOQ values of DEX and PAR were 0.51 μg/mL and 0.50 μg/mL for PCR model, and 0.02 μg/mL and 0.02 μg/mL for the PLS model.

Assay results of effervescent tablet solutions

The absorbance matrix of effervescent tablet solutions was subjected to the prediction step of PCR and PLS methods. The predicted concentration of the sample solutions was multiplied by the dilution factor of 12.5, to calculate the DEX and PAR content as milligrams per effervescent tablet. The assay results are summarized in Table 5, indicating a good agreement with the label claim of 50 mg DEX and 300 mg PAR per tablet. F-test and t-test were used to compare the assay results obtained by applying PCR and PLS. As can be seen in Table 5, the computed F- and t-statistics were smaller than the critical values, indicating comparable results in terms of variance and mean. For both drugs, there was no significant difference between the analysis results, provided by PCR and PLS methods.

Table 5. Assay results of commercial effervescent tablets by proposed PCR and PLS methods

	mg/tablet[a]			
	PCR		PLS	
Sample code	DEX	PAR	DEX	PAR
E1	53.47	296.43	52.38	298.05
E2	50.01	295.57	48.97	297.13
E3	48.96	295.83	47.90	297.41
E4	50.81	304.56	49.73	306.16
E5	51.10	305.93	50.01	307.55
E6	51.12	295.49	50.05	297.08
E7	49.96	295.60	48.91	297.19
E8	49.93	298.21	48.88	299.79
E9	51.26	302.98	50.20	304.55
E10	48.87	296.20	47.81	297.78
Mean	50.55	298.68	49.48	300.27
Standard deviation	1.34	4.14	1.33	4.15
Relative standard deviation	2.65	1.39	2.68	1.38
F-stat	1.02	1.00	F-crit =3.18 (p=0.05)	
t-stat	1.79	0.86	t-crit =2.10 (p=0.05)	

[a]Label claim: 50 mg DEX, 300 mg PAR per tablet

CONCLUSION

This study introduces two novel chemometrics-assisted UV/Vis spectrophotometric methods—PCR and PLS—for the simultaneous determination of DEX and PAR in commercial effervescent tablets. Both models used three latent variables and demonstrated strong predictive performance across 11 independent validation samples, with mean recoveries ranging from 97.5% to 100.4% and relative standard deviations below 2.2%, confirming their accuracy and precision. Intra-day and inter-day analyses further supported the methods' robustness, with low relative errors and RSD values. The assay results for commercial tablets closely matched label claims (50 mg DEX and 300 mg PAR), with no significant differences between PCR and PLS outcomes. These methods effectively resolved spectral overlap without requiring separation or complex sample preparation and offer a rapid, cost-efficient alternative to chromatographic techniques. Their strong analytical performance and practical advantages make them promising tools for routine pharmaceutical quality control.

AUTHOR CONTRIBUTION STATEMENT

Conception and design (ZCE, ED), literature search (ZCE), sources (ED), data collection (ZCE), data analysis and interpretation (ZCE, ED), preparing the study text (ZCE), reviewing the text (ZCE, ED)

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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