SIMULTANEOUS SPECTROPHOTOMETRIC DETERMINATION OF RABEPRAZOLE SODIUM AND DOMPERIDONE MALEATE IN CAPSULES BY CHEMOMETRIC METHODS

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ABSTRACT

Simultaneous spectrophotometric determination of Rabeprazole sodium and Domperidone maleate was performed by partial least-squares (PLS) and principal component regression (PCR) methods do not require any priori graphical treatment of the overlapping spectra of two drugs in the mixture. The absorbance values in the UV-Vis spectra were measured for the 89 wavelength points (from 221-309) in the spectral region 200-400nm considering the intervals of 1nm. The calibration range was found to be 4-20µg/ml for Rabeprazole sodium, 6-30µg/ml for Domperidone maleate with a correlation coefficient of 0.9999 (PLS), 0.9999 (PCR) for Rabeprazole sodium and 0.9999 (PLS), 0.9999 (PCR) for Domperidone maleate. The validation of the multivariate methods was realized by analyzing the synthetic mixtures of Rabeprazole sodium and Domperidone maleate. The numerical calculations were performed with the 'Unscrambler 10.1X' software. The chemometrics analysis methods were satisfactorily applied to the simultaneous determination of Rabeprazole sodium and Domperidone maleate in the pharmaceutical formulation.

Keywords: Domperidone maleate, chemometrics, Rabeprazole sodium, spectrophotometry, partial least square, principal component regression.

INTRODUCTION

Rabeprazole sodium (RABE) is proton pump inhibitor and is not official in any of the Pharmacopoeias and is chemically 2-([4-(-3-methoxypropoxy)-3-methyl-2-pyridyl] methyl) sulfinyl-1H-benzimidazole sodium.¹ Domperidone maleate (DOM) is peripheral dopamine antagonist. It is official in British Pharmacopoeia and European Pharmacopoeia. Chemically it is 5-chloro-1-[1-[3-(2-oxo-2, 3-dihydro-1H-benzimidazol-1-yl) propyl]-piperidin-4-yl]-1, 3-dihydro-2H-benzimidazol-2-one²⁻⁴. Literature survey reveals Rabeprazole sodium and Domperidone maleate were simultaneously estimated by UV spectrophotometric methods⁵⁻⁹, HPLC¹⁰⁻¹² and HPTLC¹³⁻¹⁵. No chemometric method is reported for the simultaneous determination of Rabeprazole sodium and Domperidone maleate in bulk and capsule dosage forms. The present article discusses the attempts made to develop simple, sensitive, reproducible and economical chemometric methods for simultaneous determination of these drugs in dosage forms. In recent years, multivariate calibrations such as classical least-squares (CLS), inverse least-squares (ILS), principal component regression (PCR) and partial least-squares (PLS) are started to apply to the analysis of the analytical data obtained in all the instrumentations¹⁶⁻¹⁷. It is probably the area within chemometrics which has attracted the most interest so far. The approach is useful in the simultaneous spectrophotometric determination of two or more components in a pharmaceutical formulation with overlapping spectra. These are extensively used in quantitative spectral analysis to get selective information from unselective data. These methods have been found to be the method of choice for complex mixtures. The advantage of multi-component analysis using multivariate calibration is the speed of the determination of components in a mixture, avoiding a preliminary separation step. The control analysis on pharmaceutical formulations using the multivariate calibration methods has been proved to be a valid alternative to HPLC. The objective of this paper is to investigate the

ability of PLS and PCR models to quantify the binary mixture of RABE and DOM with overlapped UV spectra and to apply the optimised models in pharmaceutical formulations. The proposed methods are simple and accurate, resulted in a significant reduction in analysis time and proved to be suitable for routine determination of the two components of the standard mixture.

MATERIALS AND METHODS

Instruments and software

Digitized UV/VIS absorbency spectra were collected using a UV-visible spectrometer 2300Techcomp with 1cm quartz cells. The data acquisition was made with UV solutions software at a scan rate of 1000nm min⁻¹ and the slit width of 2nm. The UV spectra of mixtures were recorded over the wavelength 221-309nm with one data point per nm. All spectral measurements were performed using blank solution as a reference. Partial least squares regression, and principal component regression were used for chemometric analysis of data. For all calculations Unscrambler for windows (Version 10.1 X) was used.

Pharmaceutical tablet formulations

A commercial pharmaceutical formulation (RAPEED - D) capsule containing 20mg of RABE and 30mg of DOM was analyzed by the proposed chemometric methods.

Preparation of stock solutions

Stock solutions were prepared by dissolving 40mg of Rabeprazole sodium and 60mg Domperidone maleate in 100ml volumetric flasks and the volume was made up with methanol. The training set containing 4-20µg/ml Rabeprazole sodium and 6-30µg/ml Domperidone maleate working standard solutions were prepared by diluting the stock solutions for each drug according to its linear calibration range.

Table 1: Composition of Calibration (Training Set) Set For PLS and PCR Methods

Rabepazole sodium			Domperidone maleate		
Reference µg/ml	Predicted µg/ml		Reference µg/ml	Predicted µg/ml	
	PLS	PCR		PLS	PCR
4.00	4.03	4.00	6.00	6.09	6.01
4.00	4.03	4.00	12.00	12.07	12.01
4.00	4.02	4.00	18.00	18.00	17.95
4.00	4.01	4.00	24.00	24.06	24.03
4.00	4.00	4.00	30.00	30.01	30.00
8.00	8.03	8.01	6.00	6.07	6.01
8.00	8.03	8.01	12.00	12.06	12.01
8.00	8.02	8.01	18.00	17.98	17.95
8.00	8.01	8.01	24.00	24.05	24.03
8.00	8.00	8.01	30.00	29.99	30.00
12.00	12.04	12.02	6.00	6.05	6.01
12.00	12.04	12.02	12.00	12.04	12.01
12.00	12.03	12.02	18.00	17.96	17.95
12.00	12.02	12.02	24.00	24.03	24.03
12.00	12.01	12.02	30.00	29.97	30.00
16.00	15.95	15.94	6.00	6.04	6.01
16.00	15.95	15.94	12.00	12.02	12.01
16.00	15.94	15.94	18.00	17.95	17.95
16.00	15.93	15.94	24.00	24.01	24.03
16.00	15.92	15.94	30.00	29.96	30.00
20.00	20.03	20.03	6.00	6.02	6.01
20.00	20.03	20.03	12.00	12.00	12.01
20.00	20.02	20.03	18.00	17.93	17.95
20.00	20.01	20.03	24.00	23.99	24.03
20.00	20.00	20.03	30.00	29.94	30.00

Table 2: Composition of Validation (Prediction Set) For PLS and PCR Methods

Rabepazole sodium			Domperidone maleate		
Reference µg/ml	Predicted µg/ml		Reference µg/ml	Predicted µg/ml	
	PLS	PCR		PLS	PCR
6	6.07	6.05	9.00	8.98	8.92
6	6.07	6.05	15.00	15.19	15.14
6	6.06	6.05	21.00	21.09	21.06
10	9.97	9.95	9.00	8.96	8.92
10	9.96	9.95	15.00	15.17	15.14
10	9.95	9.95	21.00	21.07	21.06
14	14.05	14.03	9.00	8.95	8.92
14	14.04	14.03	15.00	15.15	15.14
14	14.03	14.03	21.00	21.06	21.06

Table 3: Summary of statistics in PLS and PCR methods for Rabepazole sodium and Domperidone maleate in the mixture

Drug	Rmse		Rmse		R ²		Intercept		Slope	
	PLS	PCR	PLS	PCR	PLS	PCR	PLS	PCR	PLS	PCR
Rabe	0.0510	0.0459	0.0349	0.0312	0.9999	0.9999	0.0274	0.0036	0.9981	0.9999
Dom	0.1096	0.1010	0.0450	0.0270	0.9999	0.9999	0.0627	0.0017	0.9971	0.9999

Rabe- rabepazole sodium, Dom- Domperidone maleate, RMSEP-Root mean square error of prediction, RMSEC-Root mean square error of calibration and r^2 - Correlation coefficient

Table 4: Analysis of Tablet Formulation (Assay)

Formulation	Label claim	PLS mg/tab found*	PCR mg/tab found*
RAPEED -D	Rabe 20 mg	20.09	20.08
	Dom 30mg	30.0	29.98

*Each value is a mean of six readings

Table 5: Precision Data

S. No.	System precision				Method precision			
	Rabeprazole sodium		Domperidone maleate		Rabeprazole sodium		Domperidone maleate	
	PLS	PCR	PLS	PCR	PLS % purity	PCR % purity	PLS % purity	PCR % purity
1.	12.03	12.03	17.97	17.96	100.62	100.58	100.17	100.11
2.	12.01	12.00	17.93	17.92	100.33	100.29	99.89	99.82
3.	12.03	12.03	17.96	17.95	100.56	100.52	100.11	100.05
4.	12.05	12.05	18.00	17.99	100.56	100.52	100.11	100.05
5.	12.03	12.03	17.97	17.96	100.30	100.26	99.85	99.79
6.	12.05	12.05	18.00	17.99	100.24	100.20	99.80	99.73
AVG	12.03	12.03	18.02	18.00	100.44	100.40	99.99	99.93
S.D	0.0175	0.0176	0.03	0.03	0.1626	0.1632	0.1619	0.1629
%RSD	0.1462	0.1468	0.15	0.15	0.1619	0.1626	0.1619	0.1630

Table 6: Recovery Studies

% of Target	Rabeprazole sodium					Domperidone maleate				
	PLS			PCR		PLS			PCR	
	Added mg	Found mg	% Recovery	Found mg	% Recovery	Added mg	Found mg	% Recovery	Found mg	% Recovery
80	9.6	9.61	100.14	9.60	100.00	14.40	14.36	99.70	14.32	99.47
	9.6	9.62	100.25	9.61	100.11	14.40	14.37	99.81	14.34	99.59
	9.6	9.57	99.64	9.55	99.49	14.40	14.28	99.20	14.25	98.97
	Mean	9.60	100.01	9.59	99.87	Mean	14.33	99.57	14.30	99.34
	SD	0.03	0.33	0.03	0.33	SD	0.0493	0.33	0.047	0.33
	%RSD	0.33	0.33	0.33	0.33	%RSD	0.3440	0.33	0.33	0.33
100	12	11.98	99.87	11.98	99.83	18.00	17.90	99.43	17.88	99.36
	12	12.02	100.13	12.01	100.09	18.00	17.94	99.69	17.93	99.62
	12	11.95	99.62	11.95	99.58	18.00	17.85	99.18	17.84	99.11
	Mean	11.98	99.87	11.98	99.83	Mean	17.89	99.43	17.88	99.36
	SD	0.03	0.26	0.03	0.26	SD	0.0450	0.25	0.045	0.26
	%RSD	0.26	0.26	0.26	0.26	%RSD	0.251	0.26	0.252	0.26
120	14.4	14.46	100.42	14.46	100.44	21.60	21.59	99.97	21.60	100.01
	14.4	14.41	100.09	14.42	100.12	21.60	21.52	99.65	21.53	99.69
	14.4	14.39	99.92	14.39	99.95	21.60	21.49	99.48	21.50	99.52
	Mean	14.42	100.14	14.42	100.17	Mean	21.53	99.70	21.54	99.74
	SD	0.04	0.25	0.04	0.25	SD	0.0513	0.25	0.015	0.25
	%RSD	0.25	0.25	0.25	0.25	%RSD	0.238	0.25	0.238	0.25

Figure 1: Overlaid Spectra of Rabeprazole sodium and Domperidone maleate

Figure 2: Calibration Spectra of Rabeprazole sodium and Domperidone maleate

Figure 3: Prediction Spectra of Rabeprazole sodium and Domperidone maleate

Figure 4: Recovery Spectra of Rabeprazole sodium and Domperidone maleate

Two sets of standard solutions were prepared, the calibration set contained 25 standard solutions and the prediction set contained 9 standard solutions. To a series of 10ml volumetric flasks, aliquots of Rabeprazole sodium and Domperidone maleate solutions, containing appropriate amount of these drugs in the range of calibrations, were added and then the solutions were diluted to 10ml with methanol. UV spectra of the mixtures were recorded in the wavelength range 221-309nm versus a solvent blank, and digitized absorbance was sampled at 1nm intervals. All the solutions were prepared freshly and were protected from light.

Sample preparations

Twenty capsules were accurately weighed and powdered in a mortar. An amount of the powder equivalent was weighed and dissolved in methanol in 100ml calibrated flasks. 20ml of methanol was added and ultra sonicated for 10minutes and the volume was made up to 100ml with methanol and shake well. Then, the solution was filtered through what man filter paper No. 41 and the residue was washed three times with 10ml of solvent and then the volume was completed to 100ml with methanol. The resulting solution was diluted to 1:1.5 in a 100ml calibrated flasks. Both techniques were applied to the prepared sample solutions.

RESULTS AND DISCUSSIONS

The absorption spectra of RABE and DOM solutions in methanol recorded between 221-309nm were shown in Figure 1. The two drugs show an overlap in their absorption.

Experimental design of sample sets

Calibration and test sets for two component systems were designed according to factorial principle five-level factorial design was used to produce a calibration set (Training step) of 25 samples. Calibration spectra are shown in Figure 2. A three-level set was derived to produce a prediction set (Validation step) of nine samples. Prediction spectra are

shown in Figure 3. The compositions of the used calibration and Validation sets are summarized in Tables 1 and 2 respectively.

Selection of optimum number of factors and the spectral region

The most commonly employed validation criterion is to divide the dataset into two subsets, a calibration set and a validation set. The calibration model is calculated using the calibration set. Then, the root mean square errors of calibration and validation, RMSEC – root mean square error of calibration and RMSEP- root mean square error of prediction, are calculated using the calibration model under investigation to predict the samples in the calibration set and validation set, respectively. The results are presented in Table 3.

Market Sample Analysis (Assay)

The proposed PLS and PCR methods were applied to the simultaneous determination of RABE and DOM in commercial capsules. Determination of six replicates was made. Satisfactory results were obtained for each drug in good agreement with the label claims. The results are presented in Table 4.

Precision

The method was found to be precise with six sample preparations for the quantification of RABE and DOM. The precision and intermediate precision variations were calculated in terms of relative standard deviation and the results were found to be less than 2.0% and the results are presented in Table 5.

Recovery Studies

To check the validity of the proposed methods, recovery studies were carried out by addition of the standard to the pre-analyzed formulation. (Standard addition technique)

Recovery spectra are shown in Figure 4 and the results are presented in Table 6.

CONCLUSIONS

The most striking features of chemometric methods are its simplicity and rapidity without requiring time-consuming sample preparation. Chemometric calibration techniques in spectral analysis are widely used in quality control of drugs in mixtures and multi- component pharmaceutical formulations with overlapping spectra, as separation procedures in the drug determinations are not required. A comparative study of the use of PLS and PCR for the simultaneous spectrophotometric determination of Rabepazole sodium and Domperidone maleate has been accomplished. High percentage of recovery shows that the methods are free from interference of the excipients used in the commercial formulation. Results also showed that the developed methods can be applied to a routine analysis, quality control of mixtures and commercial preparations containing these drugs.

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