Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2017, 9(3):103-108

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Spectrometric Determination of Lansoprazole and Domperidone in Tablets by Multivariate Calibration Approach

A Hakan Aktaş* and Hande Havva Toprak

Süleyman Demirel University, Science and Art Faculty, Department of Chemistry, Isparta, Turkey

---

ABSTRACT

Two multivariate calibration-prediction techniques, principal component analysis (PCR) and partial least squares (PLS) were applied to the spectrometric multicomponent analysis of the drug containing lansoprazole (LAN) and domperidone (DOM) without any separation step. The selection of variables was studied. A series of synthetic solution containing different concentrations of LAN and DOM were used to check the prediction ability of the PCR and PLS. The results obtained in this investigation strongly encourage us to apply these techniques for a routine analysis and quality control of the two drugs.

Keywords: Lansoprazole; Domperidone, spectrometry; Multivariate calibration

---

INTRODUCTION

Lansoprazole (LAN): 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)- 2-pyridinyl]methyl]-sulphinyl]-1H-benzimidazole, is a new proton pump inhibitor with action and uses similar to those of pantoprazole. Lansoprazole has been demonstrated to be effective in the treatment of duodenal and gastric ulcers, where inhibition of gastric acid secretion may be beneficial [1]. Relatively few methods have been described for the quantitative determination of LAN in formulations and biological fluids, UV-VIS spectrophotometry [2,3], capillary electrophoresis [4], HPLC [5–7], and polarography [8] were also described for lansoprazole in dosage forms and biological fluids (Figure 1a). Domperidone (DOM), chemically, known as 5-chloro-1-[1-[3-(2,3-dihydro-2- oxo-1H-benzimidazol-1-yl) propyl]-4-piperidinyl]-1,3-dihydro- 2H-benzimidazol-2-one. DOM is a dopamine antagonist used as an antiemetic for the short term treatment of nausea and vomiting of various etiologies [9]. Both drugs are formulated in a binary mixture for the treatment of motion sickness. Few methods for determination of DOM in their binary mixture have been reported in literature, including derivative [10,11] and derivative ratio [12] spectrophotometry, HPLC [13,14] and TLC densitometry [15], capillary electrophoresis [16] methods (Figure 1b).

During the last decade the powerful chemometric methods principal component analysis (PCR) and partial least-squares (PLS) were used in spectral data analysis for the mixtures containing two or more compounds with overlapping spectra [18-19]. These methods have wide range applications, e.g. spectrometric [20,21], chromatographic [22] and electrochemical [23] quantitative analysis.

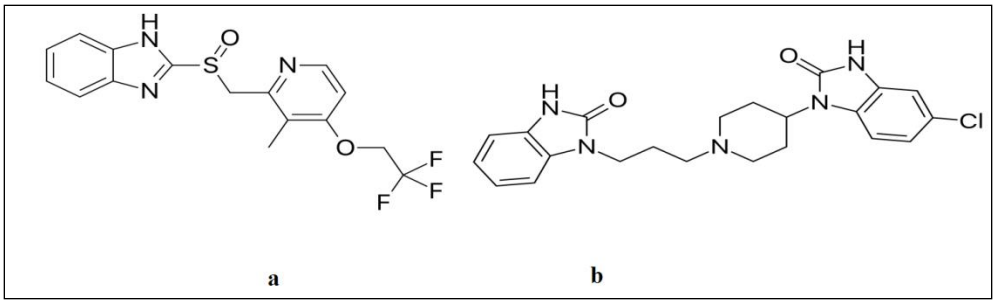

Figure 1: Structure of the drugs a) Lansoprazole b) Domperidone

The multivariate calibration techniques use full spectrum, full automation, multivariate data analysis and the reduction of noise and the advantages of the selection calibration model. In addition these multivariate calibrations do not need any separation procedure, they are very cheap, very easy to apply and very sensitive. For these reasons these multivariate techniques are popular today.

In this study two chemometric methods were applied to analyse the synthetic mixtures and tablets consisting of LAN and DOM in the presence of interferences of the absorption spectra. The application of chemometrics allows the interpretation of multivariate data and is vital to the success of the simultaneous determination of the clinical drugs.

EXPERIMENTAL SECTION

Apparatus

A Shimadzu (Model UV-1700) UV-Visible spectrometer (Shimadzu, Kyoto, Japan), equipped with 1cm matched quartz cells was used for spectrometric measurements.

Standard solutions

All materials used were of analytical grade. Stock solutions of 100 mg/100 mL LAN and DOM were prepared in methanol. The solutions were stable for the least two weeks if they had been stored in a cool (< 25^{o}C) and dark place.

Pharmaceutical preparations

A commercial drug preparations; Lacombi® tablet produced by Celtis Pharm. Ind., Turkey, containing 30 mg lansoprazole and 10 mg domperidone, per tablet were analyzed by the proposed chemometric techniques.

Procedure for dosage forms

An accurately weighed pulverized tablets equivalent to 100 mg of the studied drugs was extracted with 10 mL of M methanol, diluted with water, and sonicated for about 15 min. The extracts were filtered into 100 mL volumetric flasks then washed and diluted to volume with distilled water. Aliquots these solutions were transferred into a series of 10 mL volumetric flasks and the analysis were completed as spectrometric procedure. All the techniques were applied to the final solution.

Chemometrics methods

PLS and PCR are factor analysis method, based on a two stage procedure; a calibration step, in which a mathematical model is built by using component concentrations and spectral data from a set of references, followed by a prediction step in which the model is used to calculate the concentrations unknown sample from its spectrum. These methods are also called .factor methods. because they transform the original variables into a smaller number of orthogonal variables called factors or principal components (PCs), which are linear combinations of the original variables. When multivariate calibration approaches are applied in spectrophotometric multi component analysis, a relationship between spectral and concentration data from reference samples, representing the variables of the system, is established. A new matrix constituted by the new variables PCs and scores is built. The calculation of this new matrix is planned by algorithm specific to the regression method adopted. The major difference in the predictive abilities of these two methods is that PLS seems to predict better than PCR when there are random linear baselines or independently varying major spectral components which overlap with the spectral features of the analysis. The optimal of calibration method depend on the particular experimental conditions. However, PLS seems to a reasonable choice over a wide range of conditions.

RESULTS AND DISCUSSION

Figure 1 shows the absorption spectra for LAN and DOM and their mixture in methanol.

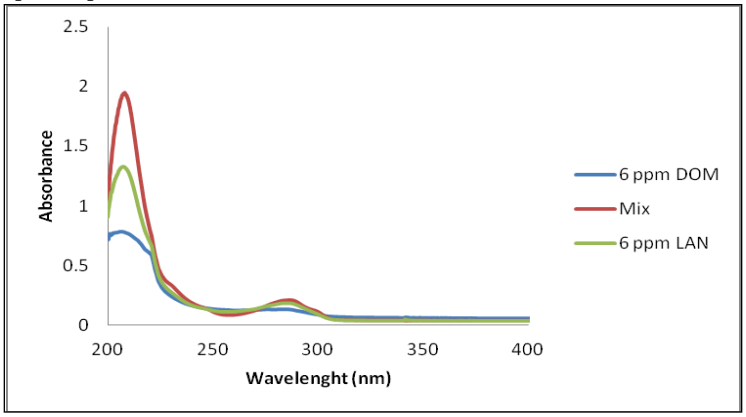

Figure 1: Original absorption spectra of 6,0 µg/mL LAN 6,0 µg/mL DOM and their mixture in methanol

In order to build the two chemometric calibration, a training set was randomly prepared by using the standard mixture solution containing 4.0 - 20.0 µg/mL LAN and 1.5 - 7.5 µg/mL DOM in the variable proportions as shown in Figure 2.

The absorbance data matrix were obtained by measuring at the 21 wavelengths with the intervals $\Delta\lambda$ = 5 nm in the 200 – 300 nm spectral region. The prepared calibrations of three techniques using the absorbance data sets were used to predict concentration of the unknown values of LAN and DOM in their mixture. Linearity range was 2.0 - 10.0 µg/mL for LAN and 1.5 - 7.5 µg/mL for DOM in the multivariate calibration proposed.

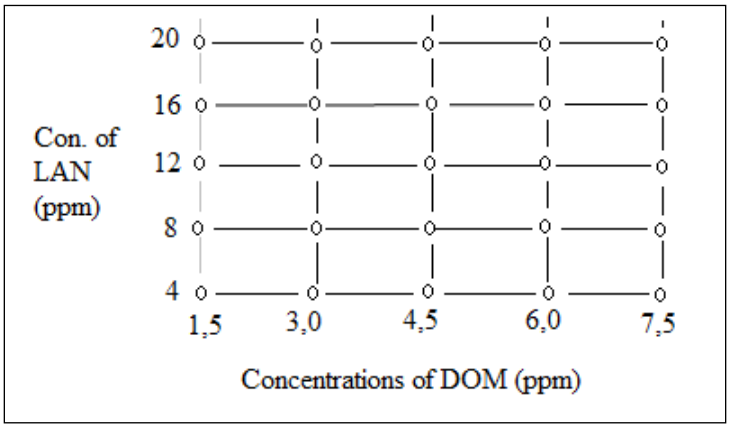

Figure 2: Concentration set design for the preparation of PCR and PLS calibrations

A calibration for each technique was computed in the MINITAB 16.0 and PLS Toolbox 4.0 software by using set consisting of two drugs and their absorbance data. The multivariate calibrations of three techniques were used to predict the unknown concentrations of LAN and DOM in the samples.

Some statistical parameters were given for the validation of the constructed calibrations for the training set and synthetic binary mixtures of both drugs.

The application competence of a calibration model can be explained in several ways. We can also examine these results numerically. One of the best ways to do this by examining the predicted residual error sum-of-squares or PRESS. To calculate PRESS we compute the errors between the expected and predicted values for all the samples, square them, and sum them together.

$$\text{PRESS} = \sum_{i=1}^{n} (C_i^{added} - C_i^{found})^2$$

Strikingly speaking, this is not a correct way to normalize the PRESS values when not all of the data sets contain the same number of samples. If we want correctly compare PRESS values for data sets that contain differing numbers of samples, we should convert to standard error of prediction (SEP), which is given by following formula.

$$\text{SEP} = \sqrt{\frac{\sum_{i=1}^{n}(C_i^{added} - C_i^{found})^2}{n-1}}$$

Where C_i^{added} the added concentration of drug is, C_i^{found} is the found concentration of drug and n is the total number of the synthetic mixtures. The SEP can provide a good measure of how well, on average, the calibration model performs. Often, however, the performance of the calibration model varies depending on the analyte level.

In the application of two chemometric techniques to the synthetic mixtures containing two drugs in variable compositions, the mean recoveries and relative standard deviations for PCR and PLS were found to be 99.99% , 0.01 and 99.97% , 0.01 respectively for LAN and 99.91% and 2.94, 99.71% and 5.25 respectively for DOM (Tables 1 and 2).

Table1: Results obtained for LAN and DOM indifferent synthetic mixtures by using PCR technique

Mixture (µg/mL) Recovery (%)					
LAN	**DOM**	**LAN**	**DOM**	**LAN**	**DOM**
2	1.5	1.99	1.49	99.96	99.96
4	3	3.99	2.99	99.97	99.97
6	4.5	5.99	4.49	99.98	99.97
8	6	7.99	5.99	99.98	99.98
10	7.5	9.99	7.49	99.98	99.98
6	1.5	5.99	1.49	99.98	99.94
6	3	5.99	2.99	99.98	99.96
6	4.5	5.99	4.49	99.98	99.97
6	6	5.99	5.99	99.98	99.98
6	7.5	5.99	7.49	99.98	99.98
2	4.5	1.99	4.49	99.98	99.98
4	4.5	3.99	4.49	99.98	99.97
6	4.5	5.99	4.49	99.98	99.97
8	4.5	7.99	4.49	99.98	99.97
10	4.5	9.99	4.49	99.98	99.96
$\bar{X}$ 99.98 99.97					
RSD* 0.01 0.01					

RSD*: Relative Standard Deviation

Table 2: Results obtained for LAN and DOM indifferent synthetic mixtures by using PLS technique

Mixture (µg/mL) Recovery (%)					
LAN	**DOM**	**LAN**	**DOM**	**LAN**	**DOM**
2	1.5	2.01	1.48	100.37	99.2
4	3	4.1	3.12	102.5	104.19
6	4.5	6.06	4.53	101.02	100.4
8	6	7.96	5.96	99.5	99.42
10	7.5	9.91	7.41	99.1	98.9
6	1.5	5.8	1.29	96.71	86.11
6	3	6.17	3.23	102.91	107.87
6	4.5	5.93	4.44	98.94	98.69
6	6	6.01	5.97	100.2	99.64
6	7.5	5.93	7.45	98.88	99.36
2	4.5	1.87	4.36	93.77	96.91
4	4.5	4.09	4.62	102.42	102.84
6	4.5	6.3	4.75	105.02	105.84
8	4.5	7.65	4.17	95.69	92.85
10	4.5	10.17	4.64	101.72	103.28
$\bar{X}$ 99.91 99.71					
RSD* 2.94 5.25					

RSD*: Relative Standard Deviation

According to the added concentration and the concentration found in samples, the SEP and PRESS values of PCR and PLS techniques were calculated $9.99.10^{-4}$, $1.09.10^{-3}$ and $1.49.10^{-5}$, $1.79.10^{-5}$ respectively for LAN, 0.1561 , 0.1539 and 0.3655, 0.3554 respectively for DOM (Table 3).

Table 3: Statistical parameters in the calibration-prediction

Parameter	Method	LAN	DOM
PRESS	PCR	$1.49.10^{-5}$	$1.79.10^{-5}$
	PLS	0.3655	0.3554
SEP	PCR	$9.99.10^{-4}$	$1.09.10^{-3}$
	PLS	0.1561	0.1539
r	PCR	1	1
	PLS	0.9954	0.9921
Intercept	PCR	-0.0007	-0.0006
	PLS	0.0274	0.0355
Slope	PCR	1	0.9999
	PLS	0.9954	0.9921

The linear regression analysis of the added concentration and the concentration found in the synthetic mixtures were realized for each drug and for each calibration technique. In this regression analysis, the correlation coefficient (r), intercept, slope and relative standard deviation values were found satisfactory for the proposed chemometric techniques in Table3. As can be seen, all the statistic values indicated that all techniques are convenient for the determination of two drugs in synthetic mixtures.

A summary of the assay results for the pharmaceutical formulation is given Table4. The results of all methods were very to each other as well as to the label value of commercial drug formulation.

Table 4: Assay results for the pharmaceutical formulation (mg/tablet)

Drug	PCR	PLS
LAN		
Mean ± SD*	30.02± 0.12	30.12± 1.18
DOM		
Mean ± SD*	9.98±0.84	10.05± 2.60

Results obtained are average of six experiments for each technique; *SD: Standard deviation

CONCLUSION

Two chemometric technique in spectrometric analysis, PCR and PLS, were proposed for the simultaneous determination of LAN and DOM in their binary mixtures. These techniques were applied with great success to two commercial pharmaceutical tablets. The resolution of highly overlapping drug mixtures was achieved by the use of PCR and PLS techniques. A selection of working wavelength having high correlation values with concentration due to interference coming from matrix sample or additional analytes outside the working range. According to the obtained results, it was observed that the PCR method gave more accurate results than the PLS method in this combination of two drugs.The proposed chemometric techniques can be applied for the routine analysis of two drugs in the tablet formulation without any a priori chemical separation and without time consuming.

ACKNOWLEDGEMENT

This research work has been supported by research grants from Süleyman Demirel University Scientific Research Project 4425-YL1-15.

REFERENCES

[1] K Parfitt. The Complete Drug Reference, 32nd edition, The Pharmaceutical Press, Massachusetts, **1999**, 1196-1204.
[2] N Ozaltın. *J Pharm Biomed Anal*, **1999**, 20, 599-606.
[3] AM Wahbi; O Abdel-Razak; AA Gazy; H Mahgoub; MS Moneeb. *J Pharm Biomed Anal*, **2002**, 30, 1133-1142.
[4] A Tivesten; S Folestad; V Schonbacher; K Svensson. *Chromatographia*, **1999**, 49(1), 7-11.

[5] A Ekpe; T Jacobsen. *Drug Dev Ind Pharm*, **1999**, 25, 1057-1065.
[6] ML Montanari; QB Cass; A Leitao; AD Andricopulo; CA Montanari. *J Chromatogr A*, **2006**, 1121, 64-75.
[7] T Uno; N Yasui-Furukori; T Takahata; K Sugawara; T Tateishi. *J Chromatogr B Analyt Technol Biomed Life Sci*, **2005**, 816, 309-314.
[8] N El-Enany; F Belal; M Rizk. *J Biochem Biophys Method*, **2008**, 70, 889-896.
[9] K Parfitt. The Extra Pharmacopoeia: The Complete Drug, 35nd edition, Royal Pharmaceutical Society, London, **2006**.
[10] MY Salem; ES El-Zanfaly; MF El-Tarras; MG El-Bardicy. *Anal Bioanal Chem*, **2003**, 375, 211-216.
[11] C Vinodhini; V Vaidhyalingam; A Ajithadas; A Niramathi; A Shanta. *Indian Drug*, **2002**, 39, 491-493.
[12] MY Salem; MG El-Bardicy; MF El-Tarras; ES El-Zanfaly. *J Pharm Biomed Anal*, **2002**, 30, 21-33.
[13] SS Zarapkar; NP Bhandari; UP Halker. *Indian Drug*, **2000**, 37, 295-298.
[14] AP Argekar; SJ Shah. *J Pharm Biomed Anal*, **1999**, 19, 813-817.
[15] AP Argekar; SG Powar. *J Planar Chromatogr Mod TLC*, **1999**, 12, 272-274.
[16] AA Abdelal; S Kitawaga; H Ohtani; N El-Enany; F Belal; MI Walash. *J Pharm Biomed Anal*, **2008**, 46, 491-497.
[17] R Kramer. Chemometric Techniques in Quantitative Analysis, Marcel Dekker Inc., New York. **1998**.
[18] KR Beebe; BR Kowalski. *Anal Chem*, **1987**, 59(17), A1007-1015.
[19] IA Cowe; JW McNicol; DC Cuthbertson. *Analyst*, **1985**, 110(10), 1227-1232.
[20] RD Bautista; FJ Aberasturi; AI Jimenez; F Jimenez. *Talanta*, **1996**, 43, 2107-2115.
[21] E Dinç; D Balenau; F Onur. *J Pharm Biomed Anal*, **2001**, 26, 949-957.
[22] JLM Vidal; MDG Garcia; MM Galeo; AG Frenich. *Anal Lett*, **1997**, 30(3), 2409-2432.
[23] JJ Berzas; JR Rodriquez; G Castanedo. *Anal Chim Acta*, **1997**, 349, 303-311.