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CHEMOMETRICASSISTEDSPECTROPHOTOMETRIC ESTIMATION OF LANSOPRAZOLE AND DOMEPERIDONE IN BULK AND COMMERCIAL DOSAGE FORM

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Abstract. Chemometric calibrations namely, Partial least square (PLS), principal component regression (PCR) and classical least square (CLS), were developed for the simultaneous determination of domeperidone and lansoprazole from combined pharmaceutical dosage forms. In these methods with chemometric techniques, the calibrations were constructed by using the absorption data matrix, with measurements in the range of 260-310 nm ($\Delta\lambda$ = 1 nm) in their zero order spectra. The chemometric calibrations were realized by using R – software (version 2.1.1). The linearity range was found to be 4-36 μg ml^{-1} and 2-18 μgml^{-1} for DOMP and LANS respectively. The lower correlation coefficient values 0.9998, 0.9999 and 0.9992 for DOMP and 0.996, 0.998 and 0.999 for LANS respectively estimated for CLS, PCR and PLS respectively. The validity of the proposed methods was successfully assessed for analysis of both drugs in laboratory prepared mixtures and in commercial formulations.

Keywords: domperidone; lansoprazole; chemometric; R–software; validation; statistical parameters; standard addition

Introduction

Lansoprazole (LZP) is used in the treatment of acid reflux. It impedes the gastric glands from supplementing gastric acid. LZP has also witnessed its role in suppressing the action of Helicobacter pylori. Study suggest that LZP is metabolized to an active sulfonamide metabolite which constrains the activity of the sulfhydryl group and curtails the hydrogen ion concentration (Alai & Lin, 2015; Baldi, 2005; Matheson & Jarvis, 2001). Domperidone (DMP) is used as a prominent antiemetic drug. DMP curtails esophageal sphincter pressure

thereby intensifying esophageal and gastric peristalsis which ameliorates gastric emptying. Absorption of the drug is characterized by active transport from the upper part of the gastrointestinal tract (GIT) including stomach (Arora et al., 2011; Tripathi, 2013). LZP and DMP estimation has been assisted by many techniques such as ultraviolet visible method (Anil Kumar et al., 2012; Sherje et al., 2008), High Performance Liquid Chromatography (HPLC) (Janardhanan et al., 2011), High Performance Thin Liquid Chromatography (HPTLC) (Aanandhi et al., 2009; Susheel et al., 2007) and ion-pair complex formation reaction (Devi et al., 2013).

However, available methods were of either of high cost or found to be insensitive and invalidated since the result was composed of effective information and ineffective noise. Studies have suggested that instrumental analysis sequined with statistical method such as chemometrics augments the signal-to-noise ratio, optimize exploratory conditions, improve selectivity of determination and raise analytical operation efficiency. The approach is useful in simultaneous determination of two or more components in pharmaceutical dosage form with overlapping spectra (Deming et al.,1988; Kumar et al., 2014; Marwada et al., 2014). Classical Least Squares (CLS), Principal Components Regression (PCR) and Partial Least Square (PLS) are the most fundamental multivariate methods that can calibrate and validate analytical methods (Khajehsharifi et al., 2017; Salem et al., 2002).

Material and mathods

Pure drug samples of Domperidone (DMP) and Lansoprazole (LZP) were procured from sigma-aldrich, Malaysia. The drugs were used without further purification. All the other reagents and solvents were procured as HPLC grade. A Formulated Mixture (FM) of LZP and DMP (30 mg LZP and 10 mg DMP) was used as a commercial dosage form for analysis.

Standard solutions of Domperidone and Lansoprazole

Standard solution of DMP and LZP with of suitable concentrations were formulated in methanolic sodium hydroxide respectively (80:20 v/v). Powder equivalent to 10 FM were weighed and mixed for further analysis. Powder equivalent to one unit of capsule was triturated, dissolved and sonicated for 10 minutes in 100 ml methanolic sodium hydroxide. This solution was suitably diluted with methanolic sodium hydroxide. The concentration of each component in the mixture was accurately resoluted by chemometric assisted spectrophotometric method. Perkin Elmer lambda 35 double beam UV Visible spectrophotometer assisted with UV winlab software was used for spectrophotometric measurements. The resulting data was realized chemometrically using R – software environment.

Calibration sets

Sequential calibration of 9 dilutions each for DMP (5-80 µg ml^{-1}) and LZP (5-25 µg. ml^{-1}) was prepared in methanolic sodium hydroxide solution. The solution was scanned in the wavelength range of 200-400 nm.

Multilevel factorial design of DMP and LZP

Multilevel multi factorial design of five level concentrations for DMP and LZP within the stated range were introduced. The developed method needs proper validation for its application**.** The studies were performed for validation purpose in compliance with ICH guidelines (Beg et al., 2012; Hasnain et al., 2013; 2017).

Statistical parameter

The most general expression for calibration model in chemometric method is the Standard Error of Calibration (SEC) and Standard Error of Prediction (SEP). It can be expressed as the following equation:

$$SEP\ (SEC) = \frac{\sqrt{\sum_{i=1}^{N}(\ Conc_i^{Added} - Conc_i^{Found})^2}}{n}$$

Here, n= number of the calibrated mixtures, = added concentration of DOM and LZP, and predicted concentration of DOM and LZP. The values for SEP are quoted in Table 1.

Calibration spectra were recorded using 25 sets of solution (Table 2). Predicted concentration of LZP and DMP was compared with the actual concentration of each sample of the calibration mixtures. Mean Squares Error of Prediction (MSEP) (Fig 1 A and B, Fig 2 A and B) and Prediction Error Sum of Squares (PRESS) were computed (Table 3).

Linearity

For linearity five replicates of measurement were performed in each concentration. It was established that absorbance and concentration behave linearly at concentration range of 5 – 80 µg/ml for DMP and 5 – 25 µg/ml for LZP.

Table 1. Statistical parameters of chemometric methods in calibration step of Zero-order spectra

Component	CLS	PCR			PLS		
	SEC	SEC	PRESS	RSE[a] (%)	SEC	PRESS	RSE(%)
DMP	0.6652	0.0140	0.0047	0.0654	0.0152	0.0056	0.0713
LMP	0.3861	0.0171	0.0070	0.1599	0.0199	0.0095	0.1857

[a] Relative standard error of calibration of single component

Table 2. Composition of the concentration (calibration) set

Mixture No.	Concentration (μg ml^{-1})	
	DMP	LMP
1	5	5
2	10	5
3	20	5
4	40	5
5	80	5
6	5	10
7	10	10
8	20	10
9	40	10
10	80	10
11	5	15
12	10	15
13	20	15
14	40	15
15	80	15
16	5	20
17	10	20
18	20	20
19	40	20
20	80	20
21	5	25
22	10	25
23	20	25
24	40	25
25	80	25

Table 3. Statistical parameters of chemometric methods in prediction step of Zero-order spectra

Component		DMP	LMP
CLS	SEP	0.9906	0.8009
	A	0.1810	0.3628
	B	1.0335	0.9745
	R	0.9984	0.9968
PCR	SEP	0.3524	0.4562
	A	0.1033	0.2318
	B	0.9938	0.9820
	R	0.9996	0.9996
PLS	SEP	0.3638	0.4657
	a	0.1133	0.2485
	b	0.9887	0.9826
	r	0.9996	0.9996

a, Intercept; *b*, slope; *r*, correlation coefficient

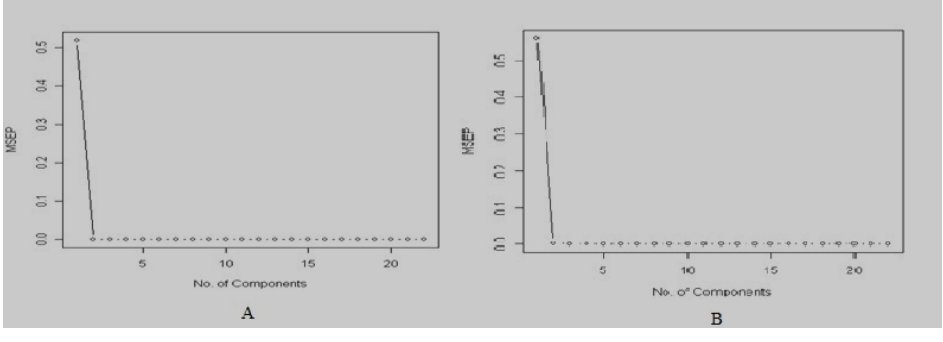

Figure 1. MSEP plots of a calibration set obtained using leave-one- out cross validation of PLS-model for DMP (A) and LZP (B) in UV absorption data

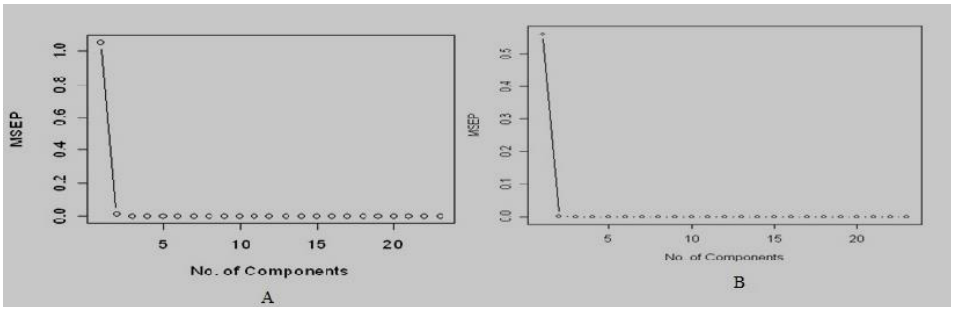

Figure 2. MSEP plots of a calibration set obtained using leave-one- out cross validation of PCR-model for DMP (A) and LZP (B) in UV absorption data

Precision

Precision is well required for any method validation and here it was determined by repeatability measurement and intermediate precision study. The measurement of absorbance was done by performing six replicates of measurement of same using a sample solution. Precision determined in terms of repeatability and intermediate precision studies were expressed as Relative Standard Deviation (RSD) of the absorbance.

Accuracy

For accuracy, standard addition method was used. The measurement of absorbance was done by performing six replicates of measurement of same using a sample solution. Percentage recovery and %RSD values connoted the accuracy of the method.

Limit of detection (LOD) and limit of quantification (LOQ)

The LOD and LOQ were estimated by plotting slope of the calibration curve of drugs and standard deviation of the y-intercept and. LOD and LOQ were analyzed by the following:

LOQ = 10α / S; LOD = 3α / S [α=standard deviation of y-intercept; S= slope of the standard curve].

Robustness

This parameter is essential to detect the effect on absorbance in terms of deliberate variation in the method parameter like wavelength (λ1), pH. The calculation of robustness is based on relative standard deviation of each parameter.

Results and discussion

A highly astute and constructive was designed for concurrent analytical estimation DMP and LZP in commercial dosage form using UV-spectropho-

tometer. Suitable calibrated dilutions each of DMP (5-80 µg ml^{-1}) and LZP (5-25 µg ml^{-1}) in methanolic sodium hydroxide solution (80:20 v/v) was prepared and spectra was analyzed from 200-350 nm. Absorbance was recorded at an interval of 1 nm and λ_{max} were proximated to be 294 nm for the DMP and 287 nm LZP in methanolic sodium hydroxide solution (80:20 v/v). The data was processed using R-software environment. PLS, PCR and CLS algorithms were amalgamated with the recorded matrix of absorption data for all binary calibrated mixtures to actuate and design the equations. DMP exhibits its absorption maxima at 287 nm while LZP shows maxima at 294 nm. The spectra of DMP and LZP were overlapped (Fig. 3). Chemometric calibration was realized to purge problems associated with the overlapped spectra of the selected drug combination.

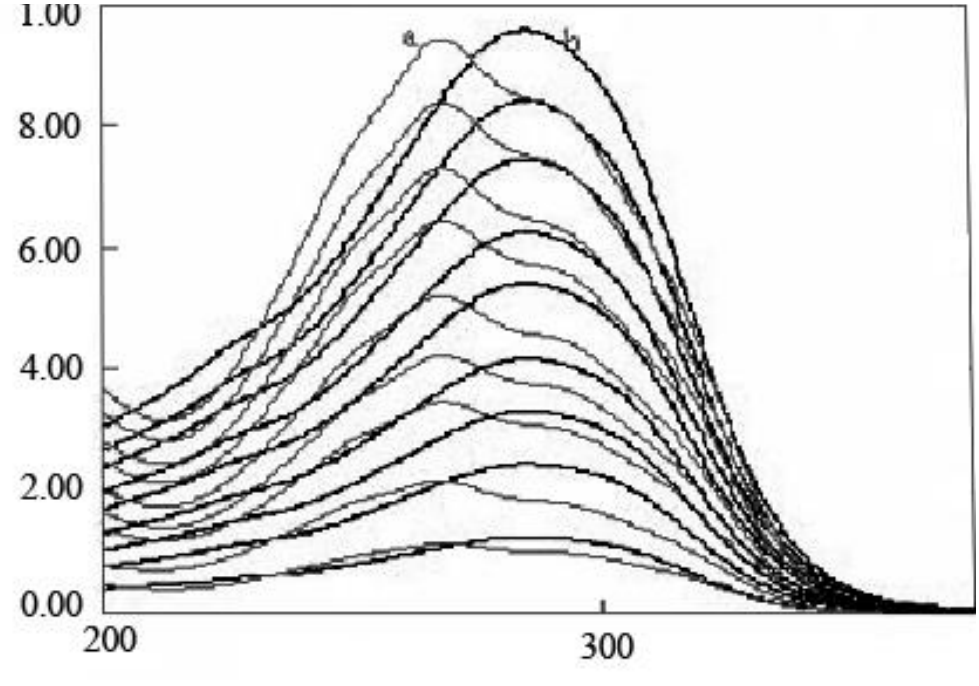

Figure 3. Zero order overlay absorption spectra of standard dilution for DMP (a) and LZP (b)

Optimization and selection of method parameters

Methanolic sodium hydroxide solution (80:20 v/v) was selected as solvent, Zero amplitude was observed for DMP at 280nm and LZP exhibited first derivative spec-

tra at 294 nm Similarly, Zero amplitude was observed for LZP at 290nm and DMP exhibited first derivative spectra at 287 nm.

Linearity and range

The proposed chemometric assisted UV spectrophotometric method for determination of DMP and LZP showed substantial linearity in the concentration range of 5 to 80 μgml^{-1} for DMP and 5 to 25 μgml^{-1} for LZP. The correlation co-efficient following CLS, PCR and PLS method was 0.9998, 0.9999 and 0.9992for DMP and 0.996, 0.998 and 0.999 for LZP respectively.

Precision

Inter and intraday precision for estimation of DMP and LZP were evaluated in terms of % RSD. The binary mixtures of DMP and LZP at five levels within their linearity range were analyzed thrice (repeatability) per day for 3 different days (intermediate precision). The average % RSD of repeatability as CLS, PCR and PLS for DMP was found to be 1.0850, 0.7264, & 1.015 while 1.0025, 0.4156, 0.8274 for LZP respectively. The average % RSD of intermediate precision for determination of DMP and LZP was found to be 1.2162%, 1.0462, 0.5634 and 1.0874, 0.9016, & 0.7371 % respectively. The values confirm the precision of the method.

Accuracy

Proposed method was examined for its selectivity and accuracy by calculating % RSD and mean percentage recovery from five different replicates having concentrations of 10µg/ml for DMP and 20µg/ml for LZP. The recovery as CLS, PCR and PLS of the DMP was found to be 98.7%, 100.8% & 101.4% while 101.2%, 100.2% & 99.6% for LZP respectively and %RSD for DMP & LZP was found to be 0.55 - 0.98% and 0.35 - 0.87% respectively which satisfies the acceptance criteria of the study and envisages that selectivity of the method.

LOQ and LOD

The LOQ and LOD were estimated following ICH recommendations. LOQ and LOD were found to be 0.01735 $\mu g\ ml^{-1}$ and 0.04273 $\mu g\ ml^{-1}$ for DMP and 0.00584 $\mu g\ ml^{-1}$ and 0.01974 $\mu g\ ml^{-1}$ for LZP respectively.

Robustness

Double-beam UV-Vis spectrophotometer perkin elmer (Lambda 35 and 25) were used for robustness. The digital absorbance recorded by Lamda 35 and 25 exhibited negligible difference which signifies the robustness of the calibrated method for the estimation of DMP and LZP. The solutions used solvents in the estimation exhibited negligible absorbance changes for 8 hrs stored at ambient temperature.

Results of analysis of formulated mixture

The values of % recovery of formulated binary mixture as CLS, PCR and PLS of the DMP was found to be 98.7%, 100.8% & 101.4% while 101.2%, 100.2% & 99.6% for LZP respectively. The study ensured that the method is applicable for simultaneous determination DMP and LZP from their binary mixture formulation.

Conclusion

The research work validated a simple and astute analytical method for estimation of DMP and LZP in commercial formulation duly facilitated by chemometric techniques utilizing PLS, CLS and PCR. The lower correlation coefficient following CLS, PCR and PLS methods were calculated as 0.9998, 0.9999 and 0.9992 for DMP and 0.996, 0.998 and 0.999 for LZP respectively. The values was expected due to low concentration differences in these techniques. Withal, further additions of known amount of DMP and LZP revealed negligible changes in the recorded spectra. The results expressed reliable congruency in the examined methods of the formulated binary mixture.

The prudent results justify analytical application for developed method of simultaneous determination of LZP and DMP in the commercial formulation The proposed methods supersede other premium but protracted and costly techniques like HPLC, HPTLC, Mass spectroscopy, NMR etc.

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