WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 3, 1465-1482. Research Article ISSN 2277– 7105

# APPLICATION OF CENTRAL COMPOSITE DESIGN IN DEVELOPMENT OF VALIDATED STABILITY INDICATING HPTLC METHOD FOR DETERMINATION OF LANSOPRAZOLE AND DOMPERIDONE IN COMBINED DOSAGE FORM

**A.G. Barsagade*, R.B. Kakde and S. R. Karmankar**

Department of Pharmaceutical Sciences, R. T. M. Nagpur University, Amravati Road, Nagpur – 440033, Maharashtra, INDIA.

Article Received on
10 Jan. 2022,

Revised on 31 Jan. 2022,
Accepted on 21 Feb. 2022

DOI: 10.20959/wjpr20223-23219

***Corresponding Author**
**A.G. Barsagade**
Department of Pharmaceutical Sciences, R. T. M. Nagpur University, Amravati Road, Nagpur - 440033, Maharashtra, INDIA.

## ABSTRACT

The objective of current study was to develop a validated, specific stability indicating normal-phase high performance thin layer chromatographic method for simultaneous estimation of lansoprazole and domperidone in their combined dosage form. The forced degradation studies were performed on pure lansoprazole and domperidone and also on their combined dosage form using acid, base, neutral, oxidation, thermal and photo stress to show the stability indicating capability of the developed method. Significant degradation products were observed in acidic, basic, neutral and oxidation stress. No degradation products were obtained after photo and thermal stress condition. The chromatographic method was optimized using samples generated in forced degradation studies. Good separation between the peaks corresponding to the active pharmaceutical ingredients, lansoprazole and domperidone, and degradation product from the analyte were achieved on silica gel $60F_{254}$ TLC plate using toluene: methanol 8:2 (v/v) as mobile phase. Densitometric quantification was performed at 295 nm by reflectance scanning. The $R_F$ value of domperidone and lansoprazole were 0.34 ± 0.03 and 0.50 ± 0.03 respectively. As a pre validation part, robustness test was performed by applying a central composite design (CCD) to study the effect of critical factors on the method performance. Validation of the developed method was conducted as per ICH requirements. Response were a linear function of concentration of lansoprazole over the range 375–3000 ng/band by peak area with correlation coefficient 0.99693 and domperidone over the range 250–2000 ng/band by peak area with correlation coefficient 0.99372. The limit

of detection of lansoprazole was 1.70 ng/band for peak area and the limit of detection of domperidone was 4.06 ng/band for peak area. Results from analysis of a commercial tablet formulation were 100.62 ± 0.0357 % and 100.00 ± 0.0388 % by peak area for lansoprazole and domperidone respectively. Recoveries were 100.06 ± 0.4690 % and 99.66 ± 0.2482 % by peak area for lansoprazole and domperidone respectively. The developed HPTLC method was found to suitable to check the quality of lansoprazole and domperidone combined dosage form.

**KEYWORDS:** HPTLC, lansoprazole, domperidone, degradation products, validation, central composite design.

## INTRODUCTION

Lansoprazole (LAN) is chemically 2-({[3-methyl-4-(2, 2, 2-trifluoroethoxy) pyridin-2-yl] methane} sulfinyl)-1H-1,3-benzodiazole (Fig. 1) is a proton pump inhibitor which inhibits stomach acid production. Domperidone (DOM) is chemically 5-chloro-1-{1-[3-(2-oxo-2, 3-dihydro-1H-1, 3-benzodiazol-1-yl) propyl] piperidin-4-yl}-2, 3-dihydro-1H-1, 3-benzodiazol-2-one **(**[Fig. 2) is a specific blocker of dopamine receptors. Domperidone is given in order to relieve nausea and vomiting.[1-3]

Literature survey revealed estimation of LAN and DOM by UV Spectroscopy in tablet and capsules single[4-7] and in combination with other drugs[8-14], HPLC in single[15-24] and in combination with other drugs[25-33] and HPTLC in combination with other drugs[34-36] has been reported. No stability indicating HPTLC method have been published for simultaneous estimation of LAN and DOM in combined dosage form in presence of their degradation products. The present research work was to develop suitable stability indicating HPTLC method for simultaneous estimation of LAN and DOM in combined dosage form in presence of their degradation products and validated as per ICH guideline.[37] Forced degradation studies were performed on drug substance to show the stability indicting nature of the method and to ensure its compliance in accordance with International Conference of Harmonization (ICH) guideline. Robustness test was performed using central composite design with k factor having $2^{k}$ factorial runs, 2k axial experiments and two center points to study the effect of critical factors on the method performance.

In this manuscript we describe a simple, specific stability-indicating HPTLC method which is useful for analysis of LAN and DOM and its degradation products in pharmaceutical preparations on the basis of peak area.

## MATERIAL AND METHODS

### Chemicals and reagents

Pharmaceutical grade Lansoprazole were procured as a gift samples from Zydus Cadila Healthcare Ltd., Ahmadabad, Guj, (India) and Domperidone were procured as a gift samples from VAMA Pharma, Nagpur, MS, (India), LEEDOM-15 (contains Lansoprazole 15 mg, Domperidone 10 mg) a capsule formulation were obtained commercially.

Toluene, methanol, hydrochloric acid, sodium hydroxide and hydrogen peroxide 30% of analytical grade were used throughout the work.

### Preparation of standard solution

For LAN, an accurately weighed 15.0 mg of LAN was transferred to 10.0 ml volumetric flask and dissolved in 5.0 ml of methanol. The volume was completed to 10.0 ml with methanol. One milliliter of resulting solution was pipetted in 10.0 ml volumetric flask and the volume was made up to 10.0 ml with methanol to furnish a solution of concentration 150 µg/ml of LAN.

For DOM, an accurately weighed 10.0 mg of DOM was transferred to 10.0 ml volumetric flask and dissolved in 5.0 ml of methanol. The volume was completed to 10.0 ml with methanol. One milliliter of resulting solution was pipetted in 10.0 ml volumetric flask and the volume was made up to 10.0 ml with methanol to furnish a solution of concentration 100 µg/ml of DOM.

For mixed standard stock solution, an accurately weighed 15.0 mg of LAN and 10.0 mg of DOM were transferred to 10.0 ml volumetric flask and dissolved in 5 ml of methanol. The volume was completed to 10 ml with methanol.

For the working mixed standard solution, form mixed standard stock solution, 1 ml was further diluted to 10.0 ml with methanol to furnish a solution of concentration 150 µg/ml and 100 µg/ ml of LAN and DOM respectively.

**Preparation of sample solution**

Twenty capsule's pellets were weighed and finely powdered. An accurately weighed amount of pellets powder equivalent to 15.0 mg of LAN and 10.0 mg of DOM was transferred into a 10.0 ml volumetric flask. Then 5.0 ml of methanol was added in it. The flask contents were sonicated for 10 min to make the contents homogeneous. This solution was then diluted up to the mark with methanol. The resultant solution was filtered through Whatman Grade I filter paper. One milliliter of filtrate was transferred to a 10 ml volumetric flask and then volume was made up to the mark with methanol to furnish a sample solution containing 150 µg/ml of LAN and 100 µg/ml of DOM.

Six replicate of pellets powder equivalent to 15.0 mg of LAN and 10.0 mg of DOM was transferred into six 10.0 ml volumetric flask and homogenous sample solutions were prepared in a similar manner.

**Chromatography**

Chromatography was performed on 10 cm × 20 cm HPTLC plates coated with silica gel 60 $F_{254}$. Before use plates were washed with AR-grade methanol and activated at 115°C for 30 min. Samples (5 µl) were applied to the plates as bands 5 mm wide and 3 mm apart by use of a CAMAG Linomat IV automatic sample applicator equipped with a Hamilton syringe. The application rate was 5 s/µl.

Linear ascending development to a distance of 180 mm was performed in a 20 cm × 20 cm CAMAG twin-trough chamber using toluene: methanol 8:2 (v/v) as mobile phase. Before the insertion of the plate, the chamber was saturated with mobile phase vapour for 10 min at room temperature and after the insertion of plate again saturated for 10 min. After development the plate was removed and dried with hot air drier. Densitometric scanning was performed at 295 nm with a CAMAG TLC Scanner III in reflectance–absorbance mode controlled by CATS 4 software (version 1.4.1; CAMAG) resident in the system. The slit dimensions were 4.00 mm × 0.45 mm and the scanning speed 20 mm/s. The radiation source was a deuterium lamp emitting continuous UV radiation between 190 and 360 nm. The amounts of the compounds chromatographed were determined from the intensity of diffusely reflected light.

**Experimental design approach (Robustness study using central composite design)**

The experimental design approach using central composite design (CCD) combines a fractional factorial with incomplete block design methodology to avoid extreme vertices and to present an approximately rotatable design with three levels per factor. Central composite design, as a three level factorial design with k factors, requires $2^k$ factorial runs, 2k axial runs symmetrically spaced at along each variable axis and at least one center point. The factors and ranges selected for consideration were based on previous univariate studies of method development and chromatographic intuition. Ten experiments with two center points were conducted by selection of two factors, methanol content in mobile phase (A) and saturation time (B) and considered retention factor as a response of both drugs using the level, described in Table1. The nominal value for these two factors, A and B were 2 ml, 20 min respectively. In context to this, minimum and maximum content of methanol (A) were fixed as 1.8 and 2.2 ml respectively. Similarly, minimum and maximum values for saturation (B) were selected as 15 and 25 min respectively. The data generated were analyzed using Design Expert (Version 8.7.0.1, Stat-Ease Inc., Minneapolis, MN, USA) statistical software. The significance of the relevant factors were calculated using test for Analysis of Variance (ANOVA). ANOVA for linear regression partitions the total variation of a sample into components. These components were then used to compute an F- ratio that evaluates the effectiveness of the model. If the probability associated with the F-ratio is low, the model is considered a better statistical fit for the data. All experiments were performed in randomized order to minimize the bias effects of uncontrolled factors.

**Method Validation**

**Stress studies and specificity**

Stress testing of drug substances can help to identify the likely degradation products, which can, in turn, help to establish the degradation pathways and the intrinsic stability of the drug substances. Specificity is the ability of the method to measure the responses of the analyte in the presence of its related substances. All stress degradation studies were performed at initial drug concentrations of 1.5 and 1.0 mg/ml for LAN and DOM, respectively. Acid hydrolysis was performed in 0.01M HCl at room temperature for 10 min. The study in basic solution was conducted in 0.1M NaOH at 80°C for 1 h. Neutral hydrolysis was performed at 60°C for 30 min. Oxidation studies were conducted at room temperature in 3% hydrogen peroxide for 1 h. For photo degradation studies, the drug sample was exposed to sun light for 7 days. The drug sample was exposed to dry heat at 60°C for 7 days. Samples were withdrawn at

appropriate times and subjected to HPTLC analysis after suitable dilution to evaluate the ability of the proposed method to separate LAN and DOM from their degradation products. Assessment of the mass balance in the degraded samples was conducted to confirm that the amount of degraded product detected in stressed samples matched with the amount present before the stress was applied. Quantitative determination of LAN and DOM was conducted in all stressed samples against qualified working standards, which is tabulated in Table 2.

**LOD and LOQ**

The LOD is the lowest analyte concentration that can be detected. LOQ is the lowest analyte concentration that can be quantified with acceptable accuracy and precision. The limits of detection (LOD) and quantification (LOQ) were calculated from the standard deviation of the response and the slope of calibration plot. LOD and LOQ were established, in accordance with ICH definitions, by use of the equations LOD = 3.3σ/S and LOQ = 10σ/S, where σ is the standard deviation of the regression line and S is the slope of the calibration plot.

**Linearity**

Linearity test solutions of LAN and DOM were prepared at concentration levels of 187.5 to 600.0 µg/ml and 25.0 to 400.0µg/ml respectively. Linearity test solutions were prepared by diluting the stock solution to the required concentrations. Linearity was established by least-squares linear regression analysis of the calibration data. Peak areas were plotted against the respective concentrations and linear regression analysis performed on the resulting curves.

**Precision**

The system precision was evaluated by measuring area of six bands of qualified working standard for LAN and DOM and calculating the percentage of relative standard deviation (RSD). The assay method precision was evaluated by conducting six independent assays of test samples of LAN and DOM against qualified working standards and calculating the percentage of relative standard deviation (RSD). The intermediate precision of the method was also verified using different analysts and different days.

**Accuracy**

The accuracy of an analytical procedure expresses the closeness of agreement between the value, which is accepted either as a conventional true value or an accepted reference value, and the value found (17). The accuracy of the assay method was evaluated in triplicate at three concentration levels, i.e., 80, 100 and 120% of the label claim. Standard addition and

recovery experiments were conducted to determine the accuracy of LAN and DOM for the quantification of drug in the samples.

## RESULTS AND DISCUSSION

### HPTLC method development and optimization

Initially, pure drugs solution was chromatographed using single solvents to ascertain the movement of the drug. Use of toluene: methanol 8:2 (v/v) as mobile phase gives well separated peaks of drugs and separation of degradation products from drugs as well. The $R_F$ value of DOM and LAN were found to be 0.34 ± 0.03 and 0.50 ± 0.03 respectively. Typical HPTLC densitogram (295 nm) was obtained from standard solution is shown in Fig. 3.

Then samples obtained from forced degradation were then chromatographed with the same mobile phase and it was found that densitogram obtained after acidic hydrolysis gave four degradation products of LAN at $R_F$ value0.13 ± 0.03 (LDP-I), 0.27 ± 0.03 (LDP-II), 0.40 ± 0.03 (LDP-III) and 0.60 ± 0.03 (LDP-IV), alkaline hydrolysis gave degradation product of LAN at $R_F$ values 0.44 ± 0.03 (LDP-V), Neutral Hydrolysis gave three degradation products of LAN at $R_F$ values 0.15 ± 0.03 (LDP-VI), 0.22 ± 0.03 (LDP-VII) and 0.43 ± 0.03 (LDP-VIII), Oxidation gave degradation product of LAN at $R_F$ values 0.19 ± 0.03 (LDP-IX) (Fig. 4). No degradation products were obtained after photo and heat stress condition. No degradation product of DOM was found when same stress conditions applied alone or in combination with LAN. Toluene: methanol 8:2 (v/v) was therefore used as mobile phase and resulted in sharp, well defined, symmetrical peaks with no fronting when scanning was performed at 295 nm. The ass of LAN and DOM was unaffected by the presence of degradation products, which confirms that the LC method is stability-indicating. There was no interference from common excipients present in the capsule's pellets. Linear ascending development to a distance of 180 mm was performed in a 20 cm × 20 cm CAMAG twin-trough chamber. Before the insertion of the plate, the chamber was saturated with mobile phase vapour for 10 min at room temperature and after the insertion of plate again saturated for 10 min. After development the plate was removed and dried with hot air drier. Densitometric scanning was performed at 295 nm with a CAMAG TLC Scanner III in reflectance–absorbance mode controlled by CATS 4 software (version 1.4.1; CAMAG) resident in the system. The slit dimensions were 4.00 mm × 0.45 mm and the scanning speed 20 mm/s. The radiation source was a deuterium lamp emitting continuous UV radiation

between 190 and 360 nm. The amounts of the compounds chromatographed were determined from the intensity of diffusely reflected light

**Robustness**

All experiments in robustness test were performed in a random order to minimize the effects of uncontrolled factors that may introduce bias to the response. Response surfaces and perturbation plots were constructed to evaluate the effect of the factors on the retention factor of both drugs. Perturbation plots reveal the change in response from its nominal value for both drugs with all other factors held constant at a reference point, and steepest slope or curvature indicates sensitiveness to specific factor. Fig. 5 shows that the both factors i.e. methanol content in the mobile phase and saturation time had significant effect on retention factor of LAN and DOM. As increasing levels of methanol content resulted in an increase in the retention factor of both drugs as well as saturation time also affect the retention factor of both drugs.

The 3D response surface plots based on the equation were generated as a function of the significant variables (fig. 6) which shows graphical representation of the variation of response i.e. retention factor as a function of methanol content of mobile phase and saturation time. Therefore, the control of these parameters were important because from the results it was concluded that both factors had significant factors affecting robustness study. The model was also validated by analysis of variance (ANOVA) using Design Expert software and the results are as presented in Table 3. Significant effects had p-value less than 0.05. Adequate Precision defined as a signal-to-noise ratio greater than 4 is desirable, and the obtained ratio for both drugs indicated an adequate signal (Table 3). The low standard deviation and high adjusted R-square values indicated a good relationship between the experimental data and those of the fitted models. The predicted R-square value was in acceptable concordance with the adjusted R-square value for both drugs. The final equation, in terms of actual components and factors, is as shown in the Table 3.

**Validation of the method**

**LOD and LOQ**

The LOD of LAN and DOM were 1.70 and 4.06 ng per band for peak area respectively. The LOQ of LAN and DOM were 5.18 and 12.32 ng per band for peak area respectively.

**Linearity**

Linearity was established by least-squares linear regression analysis of the calibration data. Calibration plots were linear over the concentration range 375-3000 ng/band by area for LAN and 250-2000 ng/band by area for DOM. Peak areas were plotted against the respective concentrations and linear regression analysis performed on the resulting curves. Equation for the calibration plots of LAN was Y= 5670 + 8.339 X, for peak area. Correlation coefficient was 0.99693 for peak area. Equation for the calibration plots of DOM was Y= 1047+ 6.198 X, for peak area. Correlation coefficient was 0.99372 for peak area.

**Precision**

The percentage RSD of system, method and intermediate precision study was well within ± 2.0%.

Results of system, method and intermediate precision are summarized in Table 4.

**Accuracy**

The percentage recoveries were 100.06 ± 0.4690 % and 99.66 ± 0.2482 % by peak area for LAN and DOM respectively. The RSD value was found to be less than 2% (Table 5).

The method enables simple, specific and accurate analysis of lansoprazole and domperidone and its degradation products in combined dosage form. The CCD was applied for robustness study to determine the significant effect of some critical factors. From this statistical data it was concluded that both methanol content in mobile phase and saturation time had significant effect on the retention factor of both drug substances. This method was validated as per ICH guidelines. The method can therefore be used for routine quality-control analysis of lansoprazole and domperidone in combined dosage forms.

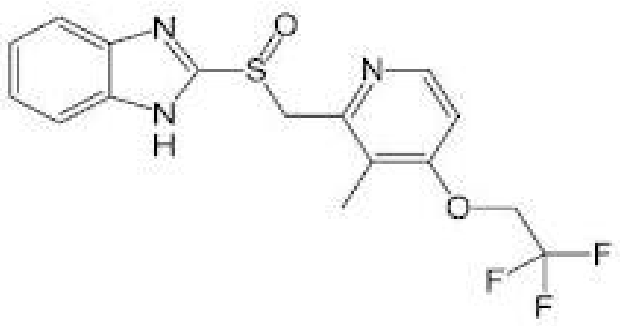



**Fig. 1: Chemical structure of lansoprazole.**

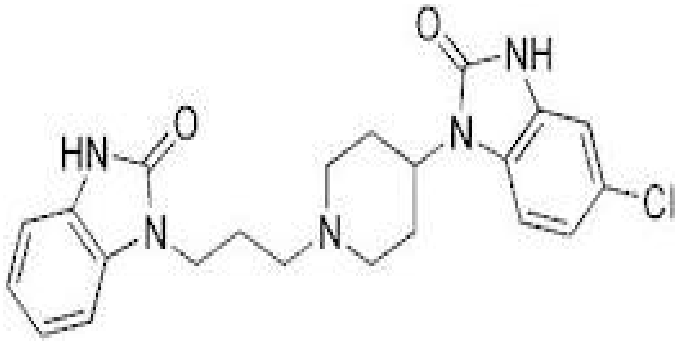



**Fig. 2: Chemical structure of domperidone.**

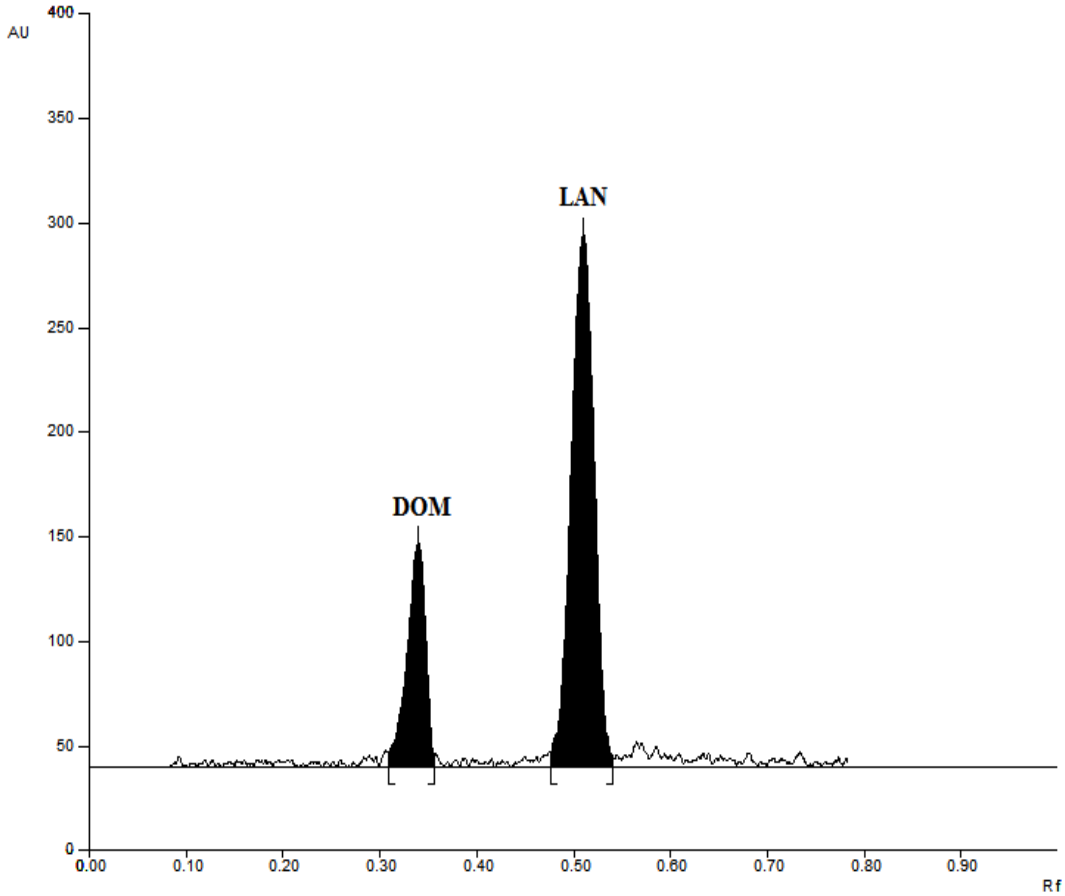
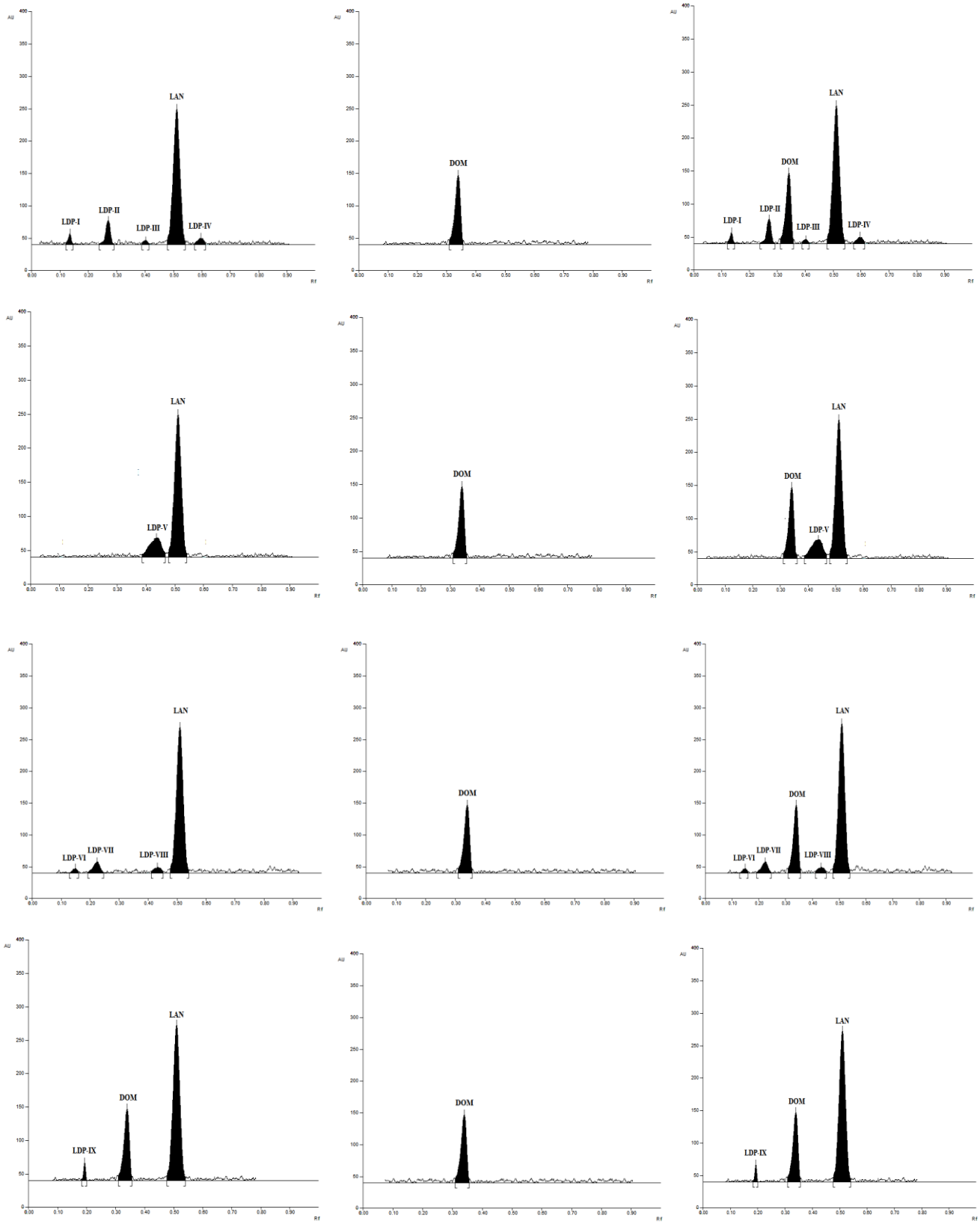



**Fig. 3: Densitogram of lansoprazole (LAN) and domperidone (DOM) combination.**




**powder in A) 0.01 N HCL, 10 min. at room temperature, B) 0.1 N NaOH, 1hr. at 80°C, C) Neutral hydrolysis, 30 min. at 60°C, D) 3% $H_2O_2$, 1 hr. at room temperature.**

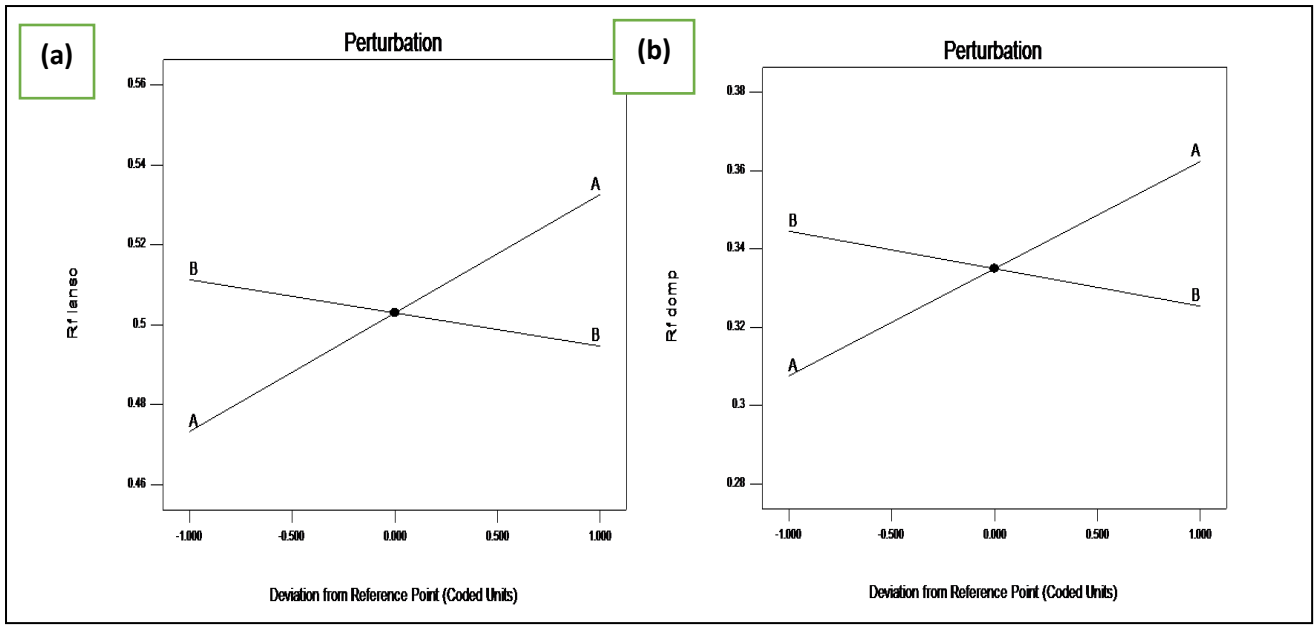



**Fig. 5: Perturbation of each factor A and B on (a) Rf value of LAN and (b) Rf value of DOM.**

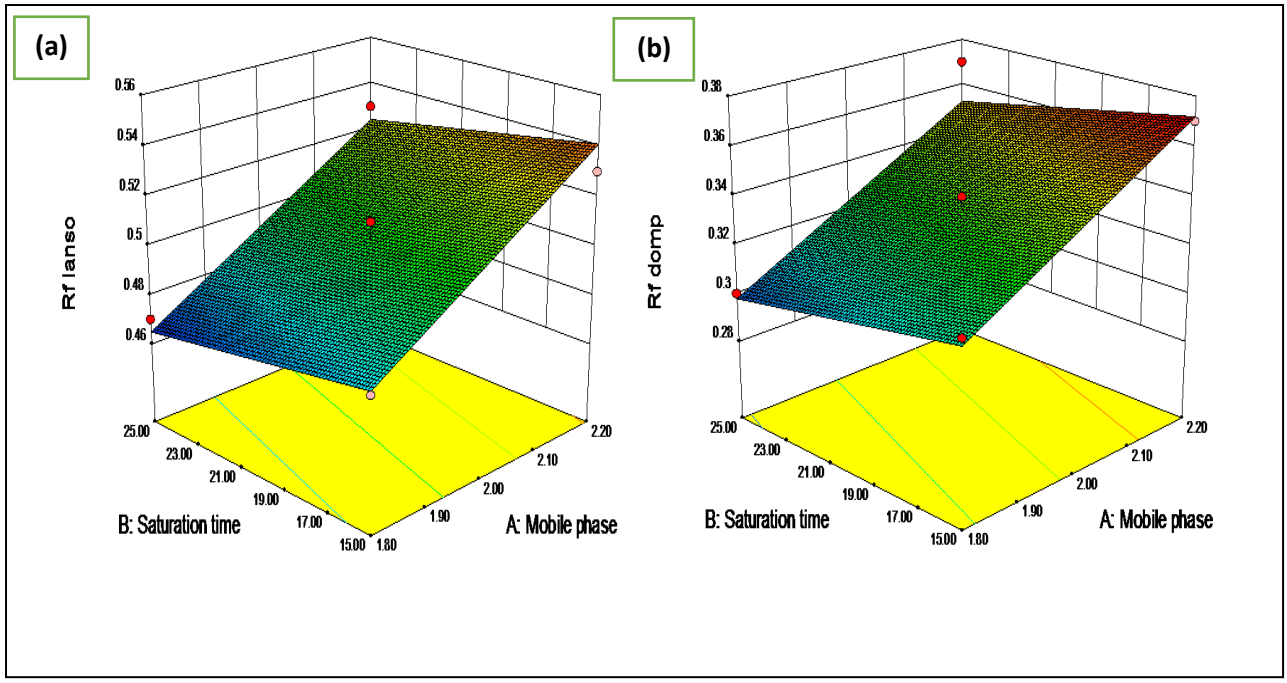



**Fig. 6: Three dimensional plot of response surface methodology (RSM) for Rf value: (a) LAN and (b) DOM.**

**Table 1: Central Composite Design Model For Robustness Study with Obtained Response.**

| STD | Run | Point Type | Factor 1 A: Methanol content in mobile phase | Factor 2 B: Saturation time | Response 1 Rf of LAN | Response 2 Rf of DOM |
|---|---|---|---|---|---|---|
| 9 | 1 | Center | 2.00 | 20.00 | 0.50 | 0.34 |
| 4 | 2 | Factorial | 2.20 | 25.00 | 0.53 | 0.37 |
| 3 | 3 | Factorial | 1.80 | 25.00 | 0.47 | 0.30 |
| 10 | 4 | Center | 2.00 | 20.00 | 0.51 | 0.34 |
| 5 | 5 | Axial | 1.72 | 20.00 | 0.46 | 0.29 |
| 8 | 6 | Axial | 2.00 | 27.07 | 0.48 | 0.31 |
| 6 | 7 | Axial | 2.28 | 20.00 | 0.55 | 0.36 |
| 7 | 8 | Axial | 2.00 | 12.93 | 0.52 | 0.35 |
| 2 | 9 | Factorial | 2.20 | 15.00 | 0.53 | 0.37 |
| 1 | 10 | Factorial | 1.80 | 15.00 | 0.48 | 0.32 |

**Table 2: Result of Degradation Study.**

| Formulation | | Normal | Acid | Alkali | Oxide | Neutral | Heat | Photo |
|---|---|---|---|---|---|---|---|---|
| LEEDOM-15 | LAN | 99.94 | 81.99 | 95.15 | 95.33 | xx | 99.91 | 99.97 |
| | DOM | 100.69 | 100.83 | 100.87 | 100.78 | xx | 100.74 | 100.85 |

**Table 3: Pridicted Response Model And Statistical Parameters Obtained From Anova For Ccd.**

| Response (Rf value) | LAN | DOM |
|---|---|---|
| Type of model | Linear | Linear |
| Model F value | 63.51 | 32.60 |
| Model p-value | <0.0001 | <0.0003 |
| Std. Dev. | 7.731E-003 | 0.010 |
| % Coefficient of variance | 1.54 | 3.03 |
| PRESS | 9.246E-004 | 1.653E-003 |
| R-Squared | 0.9478 | 0.9030 |
| Adj R-Squared | 0.9328 | 0.8753 |
| Pred R-Squared | 0.8846 | 0.7781 |
| Adeq Precision | 19.811 | 13.916 |
| Polynomial equation model for Y | Rf lanso = + 0.23969 + 0.14830 * Mobile phase - 1.66421E-003 * Saturation time | Rf domp = + 0.099541+ 0.13687 * Mobile phase -1.91421E-003* Saturation time |

**Table 4: System, Method, and Intermediate Precision Data.**

| LEEDOM-15 (Average weight: 258.4 mg) | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Validation Parameters** | | **LAN** | | | **DOM** | | |
| | | **Mean** | **SD[±]** | **RSD [%]** | **Mean** | **SD[±]** | **RSD [%]** |
| System Precision [a)] | | 11920.76 | 15.4795 | 0.1298 | 4032.34 | 31.8198 | 0.7891 |
| Method Precision [a)] | | 100.62% | 0.0357 | 0.0355 | 100.00% | 0.0388 | 0.0388 |
| Intermediate precision | Interday [b)] | 99.90% | 0.0457 | 0.0458 | 100.90% | 0.0882 | 0.0874 |
| | Intraday [b)] | 99.97% | 0.0893 | 0.0893 | 100.42% | 0.1521 | 0.1515 |
| | Different Analyst [b)] | 100.76% | 0.0450 | 0.0447 | 99.88% | 0.0744 | 0.0745 |

a) Mean from six analyses (n =6)

b) Mean from 3 analyses (n =3)

n = Number of samples, SD = standard deviation; RSD = relative standard deviation

**TABLE 5: ACCURACY DATA.**

| | **Level [%]** | **Wt. of sample (mg)** | **Wt. of drug(mg)** | **Amount of standard added (mg)** | **Calculated Wt. Of drug (mg)** | **[%] Recovery** |
|---|---|---|---|---|---|---|
| LAN | 80 | 258.1 | 14.98 | 12.2 | 12.29 | 100.73 |
| | | 258.2 | 14.98 | 12.0 | 12.08 | 100.66 |
| | | 258.0 | 14.97 | 12.1 | 12.16 | 100.49 |
| | 100 | 258.4 | 15.00 | 15.0 | 15.01 | 100.06 |
| | | 258.3 | 14.99 | 15.1 | 15.09 | 99.93 |
| | | 258.0 | 14.97 | 15.1 | 15.08 | 99.86 |
| | 120 | 258.2 | 14.98 | 18.1 | 18.00 | 99.44 |
| | | 258.2 | 14.98 | 18.0 | 17.99 | 99.94 |
| | | 258.4 | 15.0 | 18.1 | 18.01 | 99.50 |
| | Mean ±SD | | | | | 100.06±0.4693 |
| | RSD [%] | | | | | 0.4690 |
| | Level [%] | Wt. Of sample (mg) | Wt. of drug(mg) | Amount of standard added(mg) | Calculated Wt. Of drug (mg) | [%]Recovery |
| DOM | 80 | 258.1 | 9.98 | 8.1 | 8.05 | 99.38 |
| | | 258.2 | 9.99 | 8.1 | 8.06 | 99.50 |
| | | 258.0 | 9.98 | 8.0 | 7.96 | 99.50 |
| | 100 | 258.4 | 10.0 | 10.1 | 10.08 | 99.80 |
| | | 258.3 | 9.99 | 10.1 | 10.09 | 99.90 |
| | | 258.0 | 9.98 | 10.1 | 10.07 | 99.70 |
| | 120 | 258.2 | 9.99 | 12.0 | 12.02 | 100.16 |
| | | 258.2 | 9.99 | 12.1 | 12.04 | 99.50 |
| | | 258.4 | 10.0 | 12.1 | 12.05 | 99.58 |
| | Mean ±SD | | | | | 99.66±0.2474 |
| | RSD [%] | | | | | 0.2482 |

**ACKNOWLEDGMENTS**

The authors extend their sincere thanks Zydus Cadila Healthcare Ltd., Ahemadabad and VAMA Pharma, Nagpur (India), for providing gift sample of pure lansoprazole and domperidone respectively. We are very thankful to University Grant Commission for providing Rajiv Gandhi National Fellowship to carry out our research work. We also extend our thanks to Head of Department, Department of Pharmaceutical Sciences; RTM Nagpur University for providing the necessary facilities.

**REFERENCES**

1. en.wikipedia.org (retrieved on 25-05-2015).
2. British Pharmacopoeia. Monograph for Lansoprazole. London: The Stationary Office Medicinal and Pharmaceutical Substances, 2011; 867.
3. British Pharmacopoeia. Monograph for Domperidone London: The Stationary Office Medicinal and Pharmaceutical Substances, 2011; 533.
4. Ozaltín N. Determination of lansoprazole in pharmaceutical dosage forms by two different spectroscopic methods. J Pharm Biomed Anal, 1999; 20: 599-606.
5. Kumar AA, Venkata Ramana K, Narasimha Raju Ch, Sudhakara Rao G. A Simple uv spectrophotometric method for determination of lansoprazole in bulk and pharmaceutical dosage forms. Int J Pharm Chem Bio Sci., 2012; 2: 524-8.
6. Okram ZD, Kanakapura B, Jagannathamurthy RP, Basavaiah VK. Development of a simple UV-spectrophotometric method for the determination of lansoprazole and study of its degradation profile. Quim. Nova, 2012; 35: 386-91.
7. Yeniceli D, Dogrukol-Ak D, Tuncel M. Determination of lansoprazole in pharmaceutical capsules by flow injection analysis using UV-detection. J Pharm Biomed Anal, 2004; 36: 145-48.
8. Sherje AP, Kasture AV, Gujar KN, Yeole PG. Simultaneous spectrophotometric determination of lansoprazole and domperidone in capsule dosage form. Indian J Pharm Sci., 2008; 70: 102–5.
9. Moustafa AAM. Spectrophotometric methods for the determination of lansoprazole and pantoprazole sodium sesquihydrate. J Pharm Biomed Analysis, 2000; 22: 45-58.
10. Choudhary N, Siddiqui I, Rai I, Singh S, Sharma S, Gautam H. Simultaneous estimation of lansoprazole and naproxen by using UV spectrophotometer in tablet dosage form. Der Pharma Chemica, 2013; 5: 67-74.

11. Prabu SL, Shirwaikar A, Kumar CD, Joseph A, Kumar R. Simultaneous estimation of esomeprazole and domperidone by uv spectrophotometric method . Indian J Pharm Sci., 2008; 70: 128–31.
12. Kumar PR, Prakash PB, Krishna MM, Yadav MS, Deepthi CA. Simultaneous estimation of domperidone and pantoprazole in solid dosage form by UV spectrophotometry. E-J of Chem., 2006; 3: 142-5.
13. Kalra K, Naik S, Jarmal G, Mishra N. Spectrophotometric method for simultaneous estimation of paracetamol and domperidone in tablet formulation. Asian J Res. Chem., 2009; 2: 112-4.
14. Kakde RB, Gedam SN, Chaudhary NK, Barsagade AG, Kale DL, Kasture AV. Three-wavelength Spectrophotometric Method for Simultaneous Estimation of Pantoprazole and Domperidone in Pharmaceutical Preparations. Int J Pharm Tech Res., 2009; 1: 386-9.
15. Luo Y, Xu L, Xu M, Feng J, Tang X. A validated, specific, stability-indicating HPLC method for determination of lansoprazole enteric capsules and related impurities. Asian J Pharm Sci., 2012; 7: 149-54.
16. Kumar SM, Kumar DS, Rajkumar T, Kumar EU, Geetha AS, Diwedi D. Development and validation of RP-HPLC method for the estimation of lansoprazole in tablet dosage form. J Chem Pharm Res., 2010; 2: 291-5.
17. Rao PV, Kumar MN, Kumar MR. A Novel, Validated Stability-Indicating UPLC Method for the Estimation of Lansoprazole and its Impurities in Bulk Drug and Pharmaceutical Dosage Forms. Sci Pharm., 2013; 81: 183–93.
18. El-Sherif ZA, Mohamed AO, El-Bardeicy MG, El-Tarras MF. Stability-Indicating Methods for the Determination of Lansoprazole. Spectrsc Lett., 2005; 38: 77-93.
19. Karol MD, Granneman GR, Alexander K. Determination of lansoprazole and five metabolites in plasma by high-performance liquid chromatography. J Chromatogr B: Biomed Sci Appl, 1995; 668: 182-6.
20. Katsuki H, Yagi H, Arimori K, Nakamura C, Nakano M, Katafuchi S, Fujioka Y, Fujiyama S. Determination of R(+)- and S(–)-Lansoprazole using chiral stationary-phase liquid chromatography and their enantioselective pharmacokinetics in humans. Pharm Res., 1996; 13: 611-15.
21. Aoki I, Okumura M, Yashiki T. High-performance liquid chromatographic determination of lansoprazole and its metabolites in human serum and urine. J Chromatogr B: Biomed Sci Appl, 1991; 571: 283-290. Pharm Sci., 2010; 13(1): 1-10.

22. Borner K, Borner E, Lode H. Quantitative determination of lansoprazole in human serum by HPLC. Chromatographia, 1997; 45: 450-2.
23. Sharma S, Sharma AK, Singh O, Chaturvedi AK, Verma V, Arya RK, Singh UK. RP-HPLC method development and validation of domperidone in solid dosage form. The Pharma Innovation, 2012; 1: 32-6.
24. Min-Shu W, Ling G, Xiao-Hui C, Guang-Ji W. Determination of Domperidone in Human Plasma by LC-MS and its pharmacokinetics in healthy Chinese Volunteers. ACTA Pharmacol, 2002; 23: 285-8.
25. Patel B, Dedania Z, Dedania R, Ramolia C, Sagar GV and Mehta RS. Simultaneous estimation of lansoprazole and domperidone in combined dosage form by RP –HPLC. Asian J Res Chem., 2009; 2: 210-2.
26. Ahmed S, Vani R. Stability indicating method development and validation for simultaneous estimation of lansoprazole and domperidone in bulk and its pharmacutical dosage form by RP-HPLC. World J Pharm Pharm Sci., 2015; 4: 656-65.
27. Janardhanan VS, Manavalan R, Valliappan K. Stability Indicating HPLC Method for the simultaneous determination of pantoprazole, rabeprazole, lansoprazole and Domperidone from their combination dosage forms. Int J Drug Dev Res., 2011; 3: 323-35.
28. Reddy P, Jayaprakash M, Sivaji K, Jyothesh Kuamr GT, Reddy ECS, Reddy BR. Determination of pantoprazole sodium and lansoprazole in individual dosage form tablets by RP-HPLC using single mobile phase. Int J Appl Bio Pharm Technol, 2010; 1: 683-8.
29. Ekpe A, Jacobsen T. Effect of various salts on the stability of lansoprazole, omeprazole, and pantoprazole as determined by high-performance liquid chromatography. Drug Dev Industrial Pharm., 1999; 25: 1057-65.
30. Sivakumar T, Manavalan R, Valliappan K. Development and validation of a reversed-phase HPLC method for simultaneous determination of domperidone and pantoprazole in pharmaceutical dosage forms. ACTA Chromatogr, 2007; 18: 130-42.
31. Krishnaiah V, Rami Reddy YV. Development and validation of HPLC method for simultaneous determination of omeprazole and domperidone. Der Pharma Chemica, 2012; 4: 455-9.
32. Noubarani M, Keyhanfar F, Motevalian M, Mahmoudian M. Improved HPLC method for determination of four PPIS, omeprazole, pantoprazole, lansoprazole and rabeprazole in human plasma. J Pharm Pharm Sci., 2010; 13: 1-10.
33. Bharathi DV, Hotha KK, Jagadeesh B, Chatki PK, Thriveni K, Mullangi R, Naidu A. Simultaneous estimation of four proton pump inhibitors—lansoprazole, omeprazole,

pantoprazole and rabeprazole: development of a novel generic HPLC-UV method and its application to clinical pharmacokinetic study. Biomed Chromatogr, 2009; 23: 732-9.

34. Vijey Aanandhi M, Thiyagarajan N, Koilraj M, Shanmugasundaram P, Sujatha R. Simultaneous estimation of domperidone and lansoprazole in capsule formulation by HPTLC method. RASAYAN J Chem., 2009; 2: 15-7.
35. Patel BH, Suhagia BN, Patel MM, Patel JR. HPTLC determination of rabeprazole and domperidone in capsules and its validation. J Chromatogr Sci., 2008; 46: 304-7.
36. Pawar SM, Patil BS, Patil RY. Validated HPTLC method for simultaneous quantitation of famotidine and domperidone in bulk drug and formulation. Int J Adv Pharm Sci., 2010; 1: 54-9.
37. ICH. Q2(R1) Validation of Analytical Procedures: Text and Methodology. International Conference on Harmonization, Geneva; 2005 November.