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METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATON OF DOMPERIDONE AND LANSOPRAZOLE BY RP-HPLC

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Abstract

A simple, rapid, sensitive, accurate RP-HPLC Method has been develop for simultaneous estimation of Domperidone and Lansoprazole. The best chromatographic separation was performing on a Zorbax Eclipse XDB–C18 (4.6×250mm×5µ) column by using methanol: water (70:30) as mobile phase at a flow rate of 1mL/min. A retention time for Domperidone and Lansoprazole was found to be 3.19 and 4.79 minutes respectively. Developed method was validated according to ICH Q2 (R1) guidelines. The method was found to be linear between the range of 2-30µg/ml for Domperidone and Lansoprazole. The precision (intra-day, inter-day, repeatability) data of this method was found to be within limits (% RSD ≤ 2%).

Keywords: Domperidone, Lansoprazole, Method development, Validation, RP-HPLC Method.

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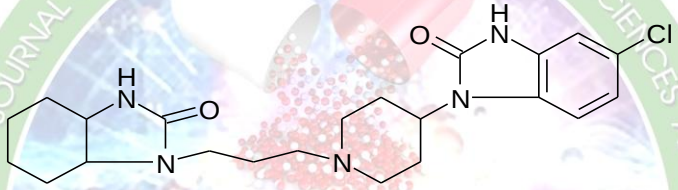
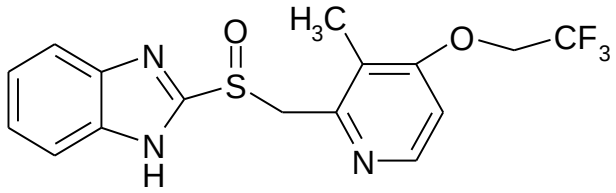
INTRODUCTION

Domperidone is chemically named as 5-chloro-1-{1-[3-(2-oxo-2, 3-dihydro-1H-1, 3 benzodiazole-1-yl)propyl]piperidin-4-yl}-2,3-dihydro-1H-1,3-benzodiazole-2-one [1]. It is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release and is used as antiemetic and tool in the study of dopaminergic mechanisms. Domperidone act as a gastrointestinal emptying (delayed) adjuvants and peristaltic stimulant. The gastroprokinetic properties of Domperidone are related to its peripheral dopamine receptor blocking properties [2]. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal sphincter pressure. Antiemetic: The antiemetic properties of Domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level [3].



Domperidone

Lansoprazole is a chemically named as 2-({[3-methyl-4-(2, 2, 2- trifluroethoxy) pyridine-2-yl] methane} sulfinyl)-1H-1, 3-benzodiazole [4]. Lansoprazole is a proton pump inhibitor which prevents the stomach from producing acid. Lansoprazole belongs to a class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anti-cholinergic or histamine H2-receptor antagonist properties, but rather suppress gastric acid secretion by specific inhibition of the (H+, K+)-AT Pase enzyme system at the secretary surface of the gastric parietal cell [5,6] because this enzyme system regarded as the acid (proton) pump within the parietal cell. Lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final steps of acid production [7].



Lansoprazole

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Literature survey revealed that few analytical methods have been developed for the determination of Domperidone and Lansoprazole individually and in combination with other drugs [8-15]. Hence an attempt has been made to develop a simple, accurate, precise and reproducible RP-HPLC method for simultaneous estimation of Domperidone and Lansoprazole in bulk with validation as per recommendation of ICH guidelines.

MATERIAL & METHODS

Instrumentation:

HPLC system of Agilent (1220 LC) with Zorbax Eclipse XDB-C18 (4.6×250mm×5µ) column was used for chromatographic separation. A Shimadzu UV/Visible spectrophotometer, Model 1800 with spectral bandwidth of 2 nm. Digital Ultrasonic sonicator (Leelasonic and Dakshin) was used for sonication. A Shimadzu electronic analytical balance (AX-200) was used for weighing the sample.

Materials:

Domperidone and Lansoprazole sample was received as gift samples by Cipla Ltd. pharmaceutical company Mumbai and Zydus Cadila Ahmadabad.

Preparation of Mobile phase:

Mobile phase was prepared by mixing 70 volumes of Methanol, 30 volumes of Water in ratio 70:30 v/v .The mobile phases was sonicated and filtered through 0.45 membrane filter.

Stock solution of Domperidone and Lansoprazole:

Accurately weigh 10mg of Domperidone and 10mg of Lansoprazole transferred to 100 ml volumetric flask and dissolves in Methanol: Water (70:30) with shaking and then volume made up to the mark with same solvent to obtain standard stock solutions of each drug of concentration 100 µg/ml. The stock solutions were filtered through a 0.2 µ membrane filter paper.

Chromatographic conditions:

Mobile phase A: Methanol, Mobile Phase B: Water (70:30) v/v Wavelength for Domperidone is 285.4 nm and for Lansoprazole is 284.4 nm. Column used Was Zorbax Eclipse XDB-C18 (4.6×250mm×5µ) with a flow rate of 1.0 ml/min.

Analysis of Laboratory Mixture

Accurately weighed quantity of 10 mg of DOM and 10 mg of LANSO were transferred to 100 ml volumetric flask, dissolved in methanol: Water (70:30) and volume was made up to mark with same solvent. From stock solution suitable aliquot was transferred to 10 ml volumetric flask and diluted to mark with the mobile phase, to obtain the concentration of 10µg/ml of Dom and

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10µg/ml of LANSO. Five different laboratory mixtures of DOM and LANSO were prepared by appropriately weighing the quantities of drug sample so as to get the concentration 10µg/ml of DOM and 10µg/ml of LANSO. A volume of 20 µL of solution was injected with the help of Hamilton Syringe. All measurements were repeated three times for each concentration and from The Peak area, the amounts of both the drugs were calculated.

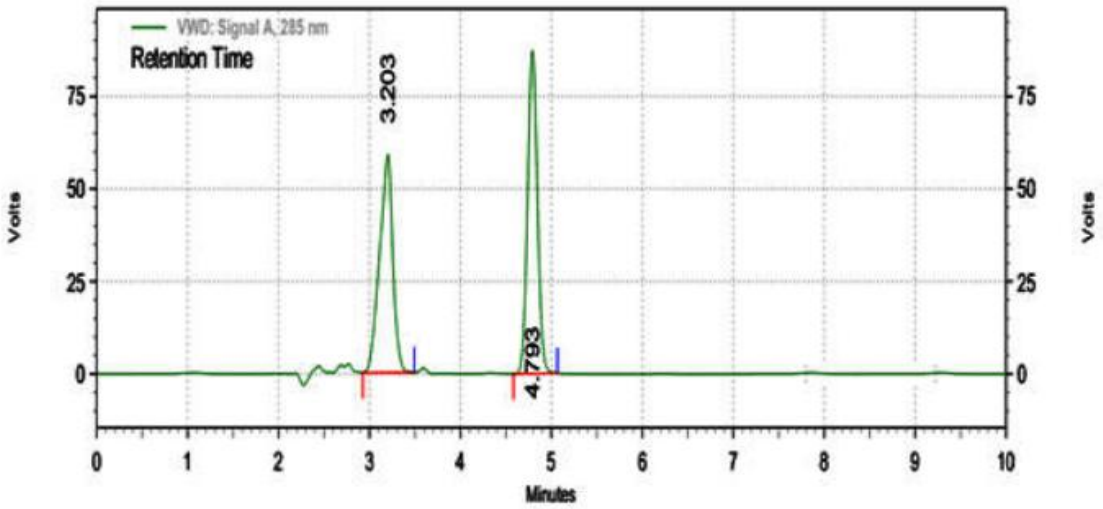

Fig. 1: Chromatogram obtained by using Laboratory mixture

Table 1: Results of Lab. Mixture

Sr. No.	Wt. of std (mg)		Wt. of sample (mg)		Result (%RSD)	
	DOM	LANSO	DOM	LANSO	DOM	LANSO
1	10	10	10	10	0.4502	0.125
2	10	10	10	10	0.4486	0.234

Method Validation

Solution of Domperidone and Lansoprazole (0.2, 0.6, 1.0, 1.4, 1.8, 2.2, 2.6, 3.0 ml) were pipette out from 100 µg/ml stock solution in eight different volumetric flask and diluted with same solvent to attain concentration of 2,6,10,14,18,22,26,30 µg/ml respectively.

Linearity:

The linearity of analytical procedure is its ability to produce a response, which are directly proportional to the concentration of analyte in sample. Concentration solutions ranging from 2-30 µg/ml were run to obtain a plot of area v/s conc. for linearity.

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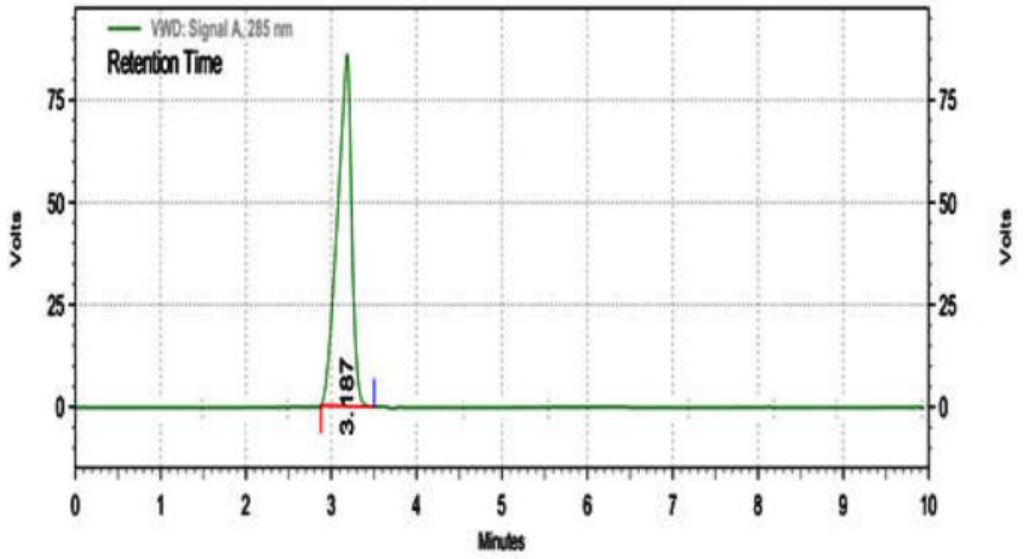

Fig. 2: HPLC chromatogram of DOM

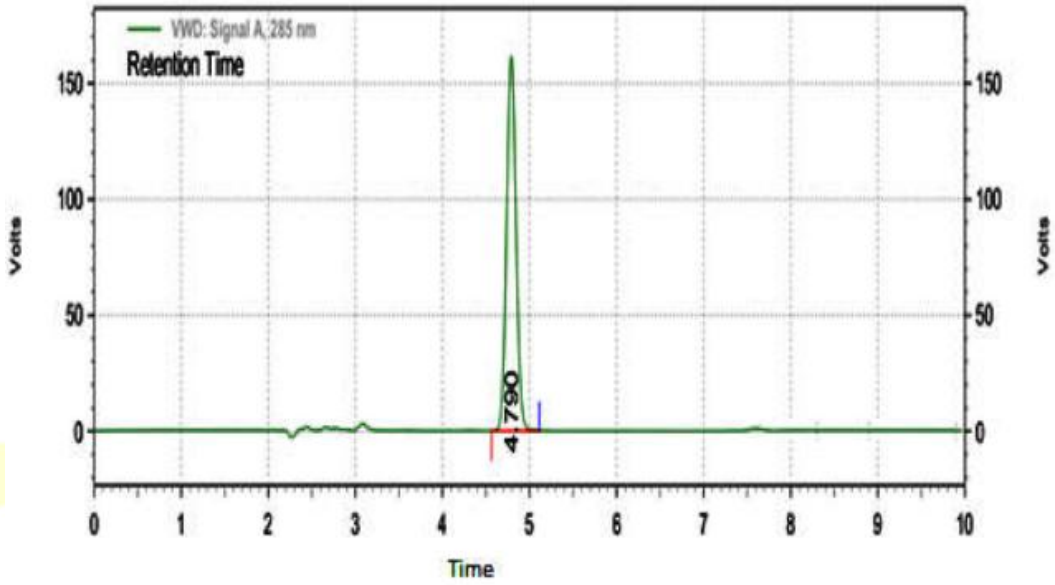

Fig. 3: HPLC chromatogram of LANSO

Table 2: Linearity Data

Conc. (µg/ml)	Area	
	DOM	**LANSO**
2	1113650	1426583
6	3240949	4293756
10	5169248	6798985
14	7595548	9669243
18	9922846	12198462
22	12250147	14998857
26	14476447	17783418
30	16704746	20483869

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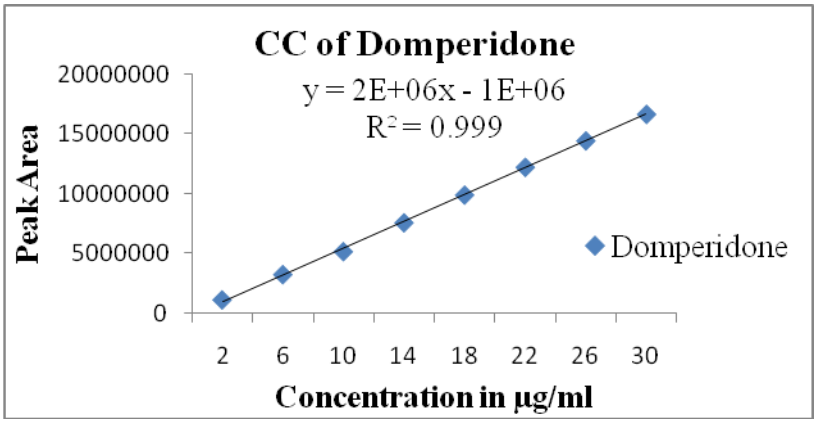

Fig. 4: Calibration curve of Domperidone

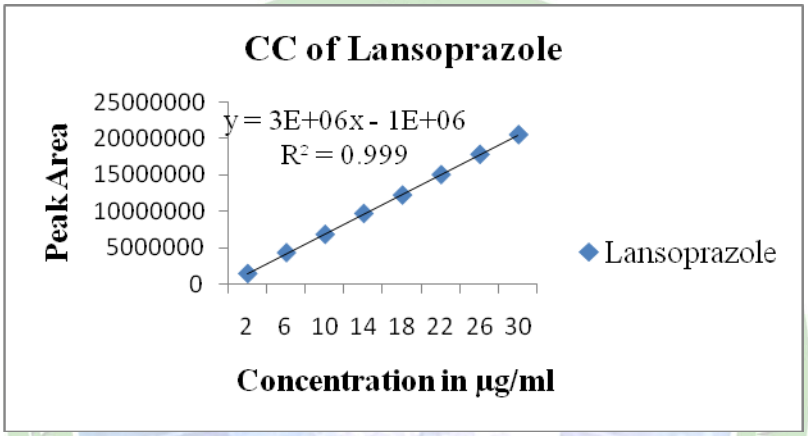

Fig. 5: Calibration curve of Lansoprazole

Accuracy

Accuracy of an analytical method is the closeness of the test results obtained by that of the true value. Accuracy of proposed method has been carried out by recovery studies. It was performed by recovery study using standard addition method at 80,100, and 120 % level.

Table 3: Accuracy Data

Sr. No.	Accuracy Test Conc.	Result (% RSD)	
		DOM	LANSO
1	80%	0.02647	0.03612
2	100%	0.01991	0.02653
3	120%	0.06089	0.18797

Precision

It demonstrates that the analytical method is capable to yield closeness of data values between a series of measurements obtained from multiple sampling of the same homogenous sample. Standard concentration sample was analyzed three times on day to day interval (interday precision), three times on different time intervals (morning and evening) in same day (intraday

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precision), repeatability was evaluated by performing six replicate injections of standard test solution.

Table 4: Precision Data

Sr.No.	Precision	Result (% RSD)	
		DOM	LANSO
1	Interday Day 1 Day 2 Day 3	 0.0623 0.1241 0.1946	 0.1207 0.2643 0.4120
2	Intraday Morning Afternoon Evening	 0.0826 0.0924 0.0723	 0.6289 0.1946 0.0652

Ruggedness

Ruggedness was determined by assaying sufficient number of aliquots of homogenous sample to be able calculate statistically valid estimates of standard deviation or relative standard deviation. Ruggedness was determined by studying the variation in sample analyzed by two different analysts.

Table 5: Ruggedness Data

Sr.No.	Ruggedness	Result (% RSD)	
	Analyst to analyst variation	DOM	LANSO
1	Analyst 1	0.4694	0.5256
2	Analyst 2	0.3541	0.9568

Sensitivity

Sensitivity of the proposed method was estimated in terms of Limit of Detection (LOD) and Limit of Quantitation (LOQ). LOD = 3.3 SD/S and LOQ = 10 SD/S, where SD is the residual standard deviation and S is the slope of the line. LOD was found to be 3.34, 2.95 for DOM and LANSO. LOQ was found to be 10.14, 8.96 for DOM and LANSO.

RESULT & DISCUSSION

Retention time were found to be 3.187 min. for DOM and 4.790 min. for LANSO, so run time is within 5 min. hence the method is rapid and economical. Hence mobile phase Methanol: Water (70:30 v/v), flow rate 1mL/ min was selected. Precision of the method was assessed as intra-day and interday variations and repeatability and found to be precised as the % R.S.D values are less than 2. The accuracy of the method was checked at three different levels i.e. 80, 100 and 120 % with affordable % recovery in the range of 99.49 - 99.94 %. LOD was found to be 3.34 and 2.95 for DOM and LANSO respectively. LOQ was found to be 10.14 and 8.96 for DOM and LANSO

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respectively. This indicates that adequate sensitivity of the method. This shows that the method and system both are suitable for the simultaneous estimation of Domperidone and Lansoprazole. Validation results show satisfactory precision, specificity, accuracy, linearity, robustness which were found to be passing all the acceptance criteria.

CONCLUSION

A new RP-HPLC method has been developed for the simultaneous estimation of Domperidone and Lansoprazole. In this study, different chromatographic conditions were used to develop the method. The best chromatographic separation was found to on a Zorbax Eclipse XDB-C18 (4.6×250mm×5µ) column. Elution was carried out with a mobile phase consisting of Methanol: water (70:30). The UV detection wavelength was 285 nm and 284 nm for Domperidone and Lansoprazole respectively. The method is validated as outlined in USP and ICH guidelines. Therefore, method may be useful for analysis of Domperidone and Lansoprazole in pharmaceutical preparations.

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