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Research Article

DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF DOMPERIDONE AND LAFUTIDINE IN PHARMACEUTICAL TABLET DOSAGE FORM

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ABSTRACT

A simple, rapid, selective, sensitive, linear, precise and accurate RP-HPLC method was developed and validated for simultaneous estimation of Domperidone and Lafutidine in pharmaceutical tablet dosage form. Separation of the drugs was achieved on a reverse phase by C_{18}: 250 x 4.6 mm, 5µ, Hypersil column at ambient temperature using a mobile phase consisting of Acetonitrile and Phosphate buffer adjusted p^H 6.5 with ortho-phosphoric acid in the ratio of (70:30), at a flow rate of 1 ml/min was employed. The UV detection wavelength was 270 nm and 20 µl of sample was injected. The linearity was found for Domperidone 15-90 µg/ml and for Lafutidine 5-30 µg/ml with a correlation coefficient of 0.999. Retention times were 2.3 min and 3.1 min for Domperidone and Lafutidine respectively. The recoveries for the two compounds were above 99%. The method was validated as per the ICH guidelines for its sensitivity, linearity, accuracy and precision. The percentage RSD for precision and accuracy of the method was found to be less than 2%. The method was successfully employed for routine quality control analysis of Domperidone and Lafutidine in Pharmaceutical Dosage forms.

Keywords: Domperidone, Lafutidine, RP-HPLC, UV detection, Validation.

INTRODUCTION

Domperidone 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[1]. It is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalisis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms.

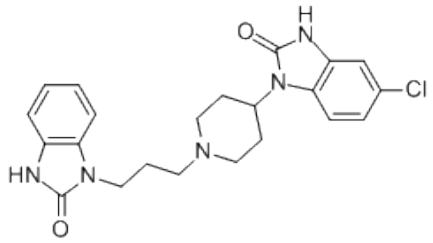

Fig. 1: Structure of Domperidone

Lafutidine is Chemically 2-(furanylmethylsulphinyl)-N-[(Z)-4-[4-(piperidinyl-methyl)-pyridin-2-yl)oxybut-2-enyl]acetamide.It is a second generation histamine receptor antagonist (H_2-RA) possessing an antisecretory effect as well as gastro protective activity against several necrotizing agents independent of its antisecretory action.[2-4]

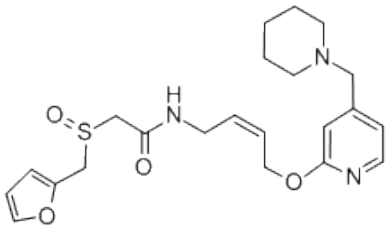

Fig. 2: Structure of Lafutidine

Literature survey reveals that, there are several spectroscopic, FT-IR[5], HPLC[6-9], HPTLC[10]and LC-MS[11]. methods for the estimation of both Domperidone and Lafutidine individually as well as in combination with other drugs.

There are few UV[12-17]and HPLC methods are reported for the simultaneous analysis of Domperidone and Lafutidine in their combined dosage form. So that need was felt, to develop new methods to analyze the drugs simultaneously. A successful attempt has been made to estimate two drugs simultaneously by RP-HPLC method. The present work demonstrates simple, rapid, accurate, reproducible and economical method for the simultaneous determination of Domperidone and Lafutidine in tablet formulation by RP-HPLC method.

MATERIALS AND METHODS

Chemicals and Reagents

Domperidone and Lafutidine was obtained from Swiss garnier healthsciences Puducherry, India, as gift samples. Acetonitrile (HPLC Grade) and Methanol (HPLC Grade) were purchased from E. Merck (India) Ltd. Worli, Mumbai, India. While sodium dihydrogen phosphate (AR Grade), Disodiumhydrogenphosphate, ortho-phosphoricacid (AR Gade) Mumbai, India. The 0.45 µm filters were purchased from Advanced Micro devices, Chandigarh, India. MilliQ water was used throughout the experiment. Tablets were purchased from Zuventus health care Ltd, containing Domperidone 30 mg and Lafutidine 10 mg per tablet.

Instrumentation and chromatographic conditions

The liquid chromatographic system consisted of Waters HPLC model (E-2695) containing variable wave length programmable UV detector. Chromatographic analysis was performed using C_{18}:250 X 4.6mm, 5µ, Hypersil column. Shimadzu Analytical balance, Model (Unibloc) was used for weighing purpose. The Mobile phase in the ratio of 70:30 v/v, which was filtered through a membrane filter and degassed before use. P^H was adjusted to 6.5 using Ortho-phosphoric acid. The chromatography performed at a flow rate of 1.0 ml/min using the above mentioned mobile phase. The column temperature was ambient and the UV Detection wave length was 270 nm. The Injection volume was 20µl. Runtime was 20 min. and the Retention time was 2.3 min. for Domperidone and 3.1 min. for Lafutidine.

Preparation of Standard solutions

About 30 mg of Domperidone and 10 mg of Lafutidine was weighed and transferred in to a 50 ml volumetric flask and made up to the volume with Mobile phase. (Acetonitrile, Phosphate buffer.) From this 10 ml was pipette out in to a 100 ml volumetric flask and made up to the volume with Mobile phase. The final concentration was found to be 60 µg/ml and 20 µg/ml for Domperidone and Lafutidine respectively.

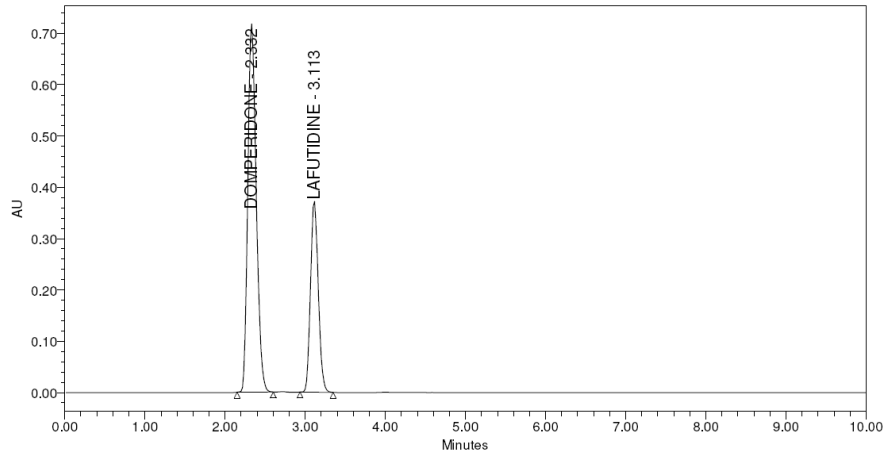

Fig. 3: Chromatogram of Standard Domperidone and Lafutidine

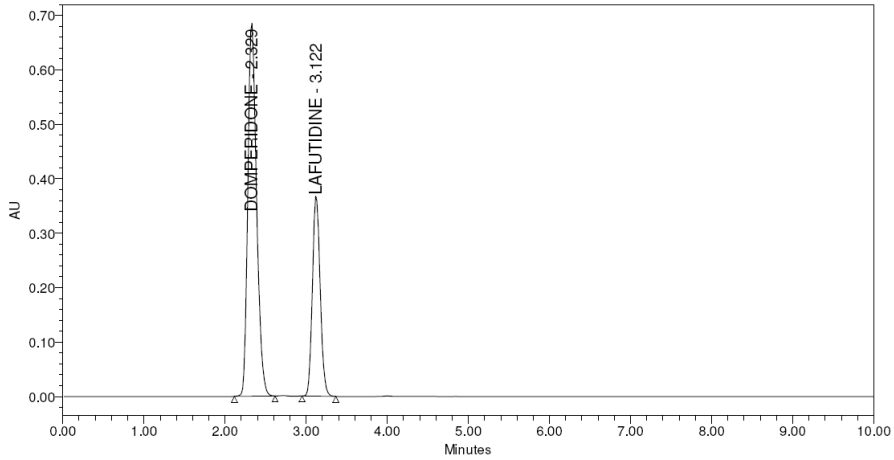

Fig. 4: Chromatogram of Sample Domperidone and Lafutidine

Preparation of Sample Solution

Twenty tablets were weighed and ground to a fine powder. The average weight of the tablet was 245 mg which was taken in a 50 ml volumetric flask and made up to the volume with Mobile phase. From this 10 ml was pipette out in to a 100 ml volumetric flask and made up to the volume with mobile phase. The final concentration was to be 60 µg/ml and 20 µg/ml for Domperidone and Lafutidine respectively.

Preparation of Buffer

1.56 gm of Sodium di hydrogen phosphate was dissolved in 1000 ml of water and adjust the pH- 6.5 using diluted O-phosphoric acid.

Method Development

After several trails with various solvents, mobile phase system composed of Acetonitrile and sodium phosphate buffer of P^H 6.5 in the proportion of 70:30 respectively was chosen for the simultaneous estimation of Domperidone and Lafutidine in combined dosage form by RP-HPLC. This mobile phase composition offered maximum resolution for the drug at the detection wavelength of 270 nm.

Mobile phase with the flow rate of 1 ml/min gave optimum separation with good resolution between the peaks. A reverse phase C18 column was used as stationary phase. The retention time of Domperidone and Lafutidine were found to be 2.3 and 3.1 minutes, respectively. The total time of analysis was less than 5 minutes.

The percentage label claim (%Recovery) for Domperidone and Lafutidine were found to be 99.94% and 99.76% respectively.

Method Validation

From the calibration curve constructed by plotting concentration vs. peak area, it was found that there exists a linear relationship in the concentration range of 15 to 90 µg/ml for Domperidone with 0.999 as the value of correlation coefficient and for Lafutidine the linearity in the range of 5 to 30 µg/ml with 0.999 as the value of correlation coefficient.

System suitability studies were carried out in which the Resolution between the peaks was found to be 4.27. The symmetric factors for Domperidone and Lafutidine were 1.24 and 1.12, respectively. Domperidone was found to have a value of 2168 as its number of Theoretical plates and for Lafutidine it was 4944.

For Precision, the sample solution at working concentration was analyzed in replicate as per the assay method. The percentage relative standard deviations for the assay values were found to be 0.27 and 0.31 for Domperidone and Lafutidine, respectively.

The accuracy of the method was studied by performing assay studies at 50%, 100% and 150% level. The values were found to be 99.12 and 99.30 at 50% level, 99.36 and 99.19 at 100% level and 99.53 and 99.78 at 150% for Domperidone and Lafutidine, respectively.

Robustness of the method was studied changing the parameters like column temperature, buffer P^H and mobile phase composition. There was no change in system suitability parameters.

RESULTS AND DISCUSSION

System suitability

System suitability was studied under each validation parameters by injecting six replicates of the standard solution. The results obtained were within acceptable limits (Tailing factor =2 and Theoretical plate's =2000)

Table 1: System Suitability Parameters for DOM and LAF

Parameter	DOM	LAF
% RSD of Retention time	0.04	0.03
% RSD of Peak area	0.08	0.06
No. of Theoretical plates	2168	4944
Tailing factor	1.24	1.12
LOD ug/ml	0.16810	0.37890
LOQ ug/ml	0.50920	1.14810

Specificity

By comparing the chromatograms of blank, standard and sample (Prepared from Formulation), it was found that there is no interference due to excipients in the tablet formulation and also found good correlation between the retention times of standard and sample.

Precision

The precision of the method was demonstrated by inter-day and intra-day variation studies. In the intra-day studies, six repeated injections of standard and sample solutions were made and the response factor of drug peak and % RSD were calculated.

Table 2: Precision study of DOM and LAF (System Precision)

S. No.	RT		AUC	
	DOM	LAF	DOM	LAF
1	2.333	3.117	5169435	2457128
2	2.331	3.119	5137993	2438250
3	2.331	3.115	5163407	2453608
4	2.331	3.116	5138037	2439744
5	2.333	3.118	5161903	2448675
6	2.333	3.119	2442732	367187
Mean	2.332	3.117333	5152969	2446690
SD	0.001095	0.001633	13728.39	7692.816
RSD %	0.05	0.05	0.27	0.31

Method Precision

S. No.	RT		AUC	
	DOM	LAF	DOM	LAF
1	2.329	3.124	5096016	2424709
2	2.329	3.123	5106106	2427754
3	2.331	3.125	5102402	2428367
4	2.330	3.124	5105268	2427551
5	2.329	3.123	5103974	2426331
6	2.329	3.123	5108382	2428073
Mean	2.3295	3.123667	5103691	2427131
SD	0.000837	0.000816	4265.486	1377.365
RSD %	**0.04**	**0.03**	**0.08**	**0.06**

Linearity

Six points calibration graphs was constructed covering a concentration range 15-90 µg/ml and 5-15 µg/ml respectively for Domperidone and Lafutidine. Linear relationships between the peak area signal of drugs the corresponding drugs concentration was observed. The standard deviation of the slope and intercept were low.

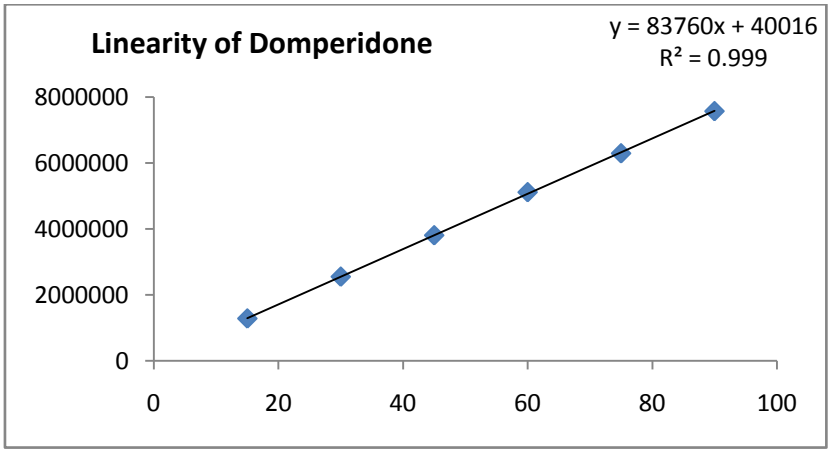

Fig. 5: Linearity curve of Domperidone

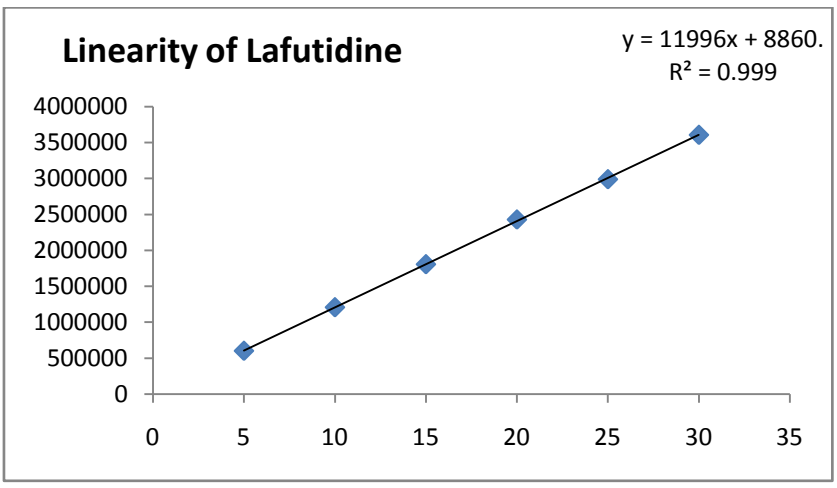

Fig. 6: Linearity curve of Lafutidine

Table 3: **Linearity Data for Domperidone**

Concentration(mcg/ml)	Peak Area
15	1283786
30	2552288
45	3807818
60	5114494
75	6293686
90	7572405
Linear Dynamic range	15-90 µg/ml
Correlation coefficient (r)	0.999
Slope(m)	83760
Intercept(c)	40016

Table 4: Linearity Data for Lafutidine

Concentration(mcg/ml)	Peak Area
5	602884
10	1209174
15	1808001
20	2430132
25	2990618
30	3608210
Linear Dynamic range	5-30 µg/ml
Correlation coefficient (r)	0.999
Slope (m)	11996
Intercept (c)	8860

Accuracy

Accuracy of the method was determined by recovery experiments. The solutions were analyzed in triplicate at each level as per the proposed method.The % recovery and % RSD was calculated and results are obtained. Satisfactory recoveries were obtained by the proposed method. This indicates that the proposed method was accurate.

Robustness

The robustness study was performed by slight modification in Temparature, flow rate, p^H of the buffer and composition of the mobile phase. The drug concentration was analyzed under these changed experimental conditions. It was observed that when Mobile phase ratio and flow rate was changed there is no significant changes in Rt.

Table 5: Acuracy data for Domperidone and lafutidine

Level	Amount of the drug added (µg/ml)	Total amount (µg/ml)	Amount recovered %	% Recovery
Domperidone				
50%	30	90	49.56	99.12
100%	60	120	99.36	99.36
150%	90	150	149.30	99.53
Lafutidine				
50%	10	30	49.56	99.12
100%	20	40	99.19	99.36
150%	30	50	149.67	99.53

Table 6: Robustness Mobile phase ratio change

S. No.	ACN: Buffer (65:35)		ACN: Buffer (75:25)	
	AUC			
	DOM	LAF	DOM	LAF
1.	5148739	2472308	5210875	2450292
2.	5265440	2508636	5201795	2500391
3.	5171523	2455319	5191235	2600198
S.D	61858.22	27236.78	9829.29	76314.21
Mean	5195234	2478754	5201302	2516960
RSD	0.011	0.010	0.001	0.030

Table 7: Robustness flow rate change

S. No.	0.9ml/min		1.1ml/min	
	AUC			
	DOM	LAF	DOM	LAF
1.	5515519	2619732	4890344	2325687
2.	5275440	2599871	5200134	2498197
3.	5399198	2610998	5399198	2519078
S.D	120058.7	9954.498	256457	106141.3
Mean	5396719	2610200	5163225	24477654
RSD	0.022	0.003	0.049	0.043

CONCLUSION

The proposed method for the assay of Domperidone and Lafutidine in tablets is very simple and rapid. It should be emphasized that it is isocratic and the mobile phase do not contain high costly solvents. The method was validated for specificity, linearity, precision, accuracy and robustness. It could be used for the rapid and reliable determination of Domperidone and Lafutidine in tablet formulation. The validated method was applied for the assay of commercial tablets containing Domperidone and Lafutidine.

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