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Method Development and Validation for the Simultaneous Estimation of Domperidone and Lafutidine in Bulk and Pharmaceutical Dosage Form by RP-HPLC Method

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Abstract: *Present work is to develop a new method for the simultaneous estimation of Domperidone and Lafutidine in pharmaceutical tablet dosage form by RP-HPLC Method. Literature survey reveals that, there are several spectroscopic, FT-IR, HPTLC and LC-MS. Methods for the estimation of both Domperidone and Lafutidine individually as well as in combination with other drugs. There are Few UV and HPLC methods are reported for the simultaneous analysis of DOM and LAF in their combined dosage form. so that need was felt, to develop new methods to analyse 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 DOM and LAF in tablet formulation by RP-HPLC method.*

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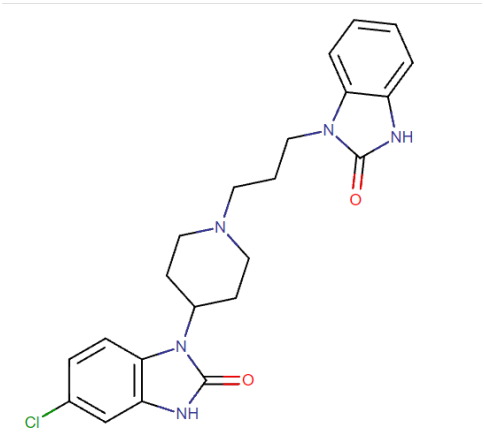
I. Literature Review:

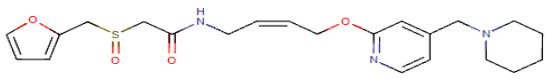
A reverse phase HPLC method for the determination of Omeprazole and Domperidone form tablet formulation was acrried out on a Hypersil, ODS, C-18 column using a mobile phase of methanol:0. 1M ammonium acetate. The flow rate and runtime were 1 ml/min and 1o min respectively. The eluent was monitored at 280nm. The linearity was found to be in the range of 10-60 µg /ml for Omeprazole and 5-30 µg /ml for Domperidone

II. Drug Profile:

Domperidone:
Chemical formula : $C_{22}H_{24}CIN5O_2$
IUPAC Name: 5-Chloro-1-(1-[3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1yl)propyl]piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one



LAFUTIDINE:
Chemical formula : $C_{22}H_{29}N_3O_4S$
IUPAC Name: 2-(furan-2-yl methyl sulphinyl)-N-[(Z)-4-[4-(piperidinyl- methyl)-pyridin-2yl)oxybut-2-enyl] acetamide



III. Results &Discussion:

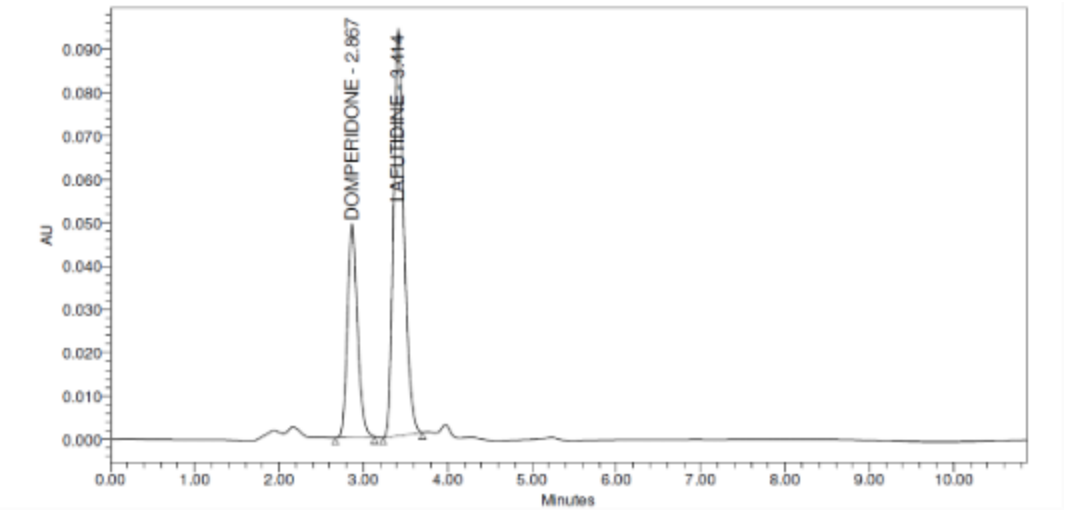
Standard Preparation of Domperidone & Lafutidine:
Solution -A: About 1 mg of Domperidone was weighed and transferred into a 100 ml volumetric flask and made upto to the volume with methanol. From this 1 ml^{o}was pipette out into 100 ml volumetric flask and made upto the volume with same diluent.
Solution-B: About 1 mg of Lafutidine was weighed and transferred into a 100 ml volumetric flask and made upto to the volume with methanol. From this 1 ml was pipette out into 100 ml volumetric flask and made upto the volume with same diluent.

Solution -C:Mix the 1 ml solution and 1 ml of solution B in 10 ml volumetric flask.
Chromatographic conditions for optimized method

Column	C_{18}.250×4.6mm,5µ
Mobile phase	Acetonitrile: Sodium phosphate buffer(70:30)
Diluent	Methanol
Flow Rate	1.0ml/min
Temperature	25°c
Injection Mode	Auto injector(vial)
Run Time	20 minutes

VALIDATION PARAMETERS:
SYSTEM SUITABILITY : System suitability is studied under each validation parameters by injecting six replicates of the standard solution.

S.No	Parameters	Domperidone	Lafutidine
1	Theoretical plates	2168	4944
2	Resolution	-	4.27
3	Tailing factor	1.24	1.12

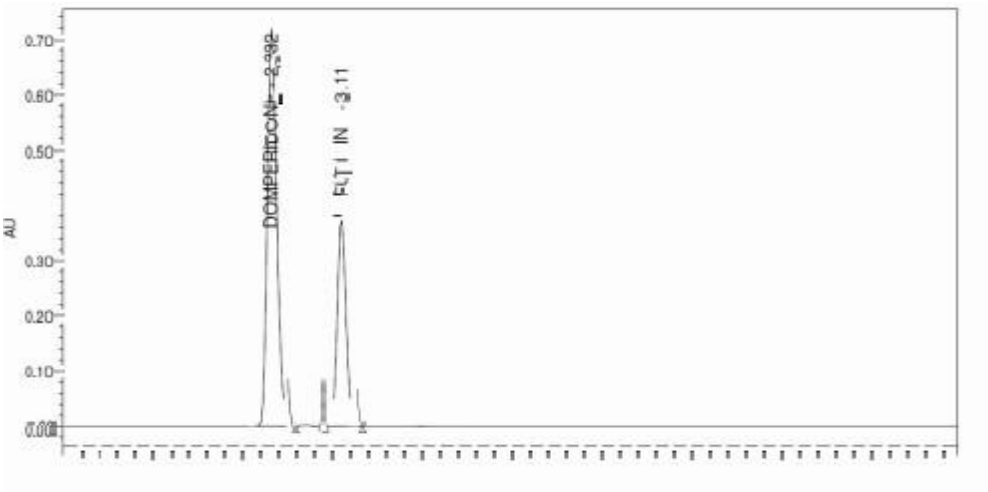


: system suitability Chromatogram

Specificity:

Name of the Solution	Retention time in minutes	
	DOM	LAF
Blank	No peak	No peak
Placebo	No peak	No peak
Standard	2.3	3.1
Sample	2.3	3.1

Result: No peak observed due to blank, placebo at the retention time of Domperidone and Lafutidine



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

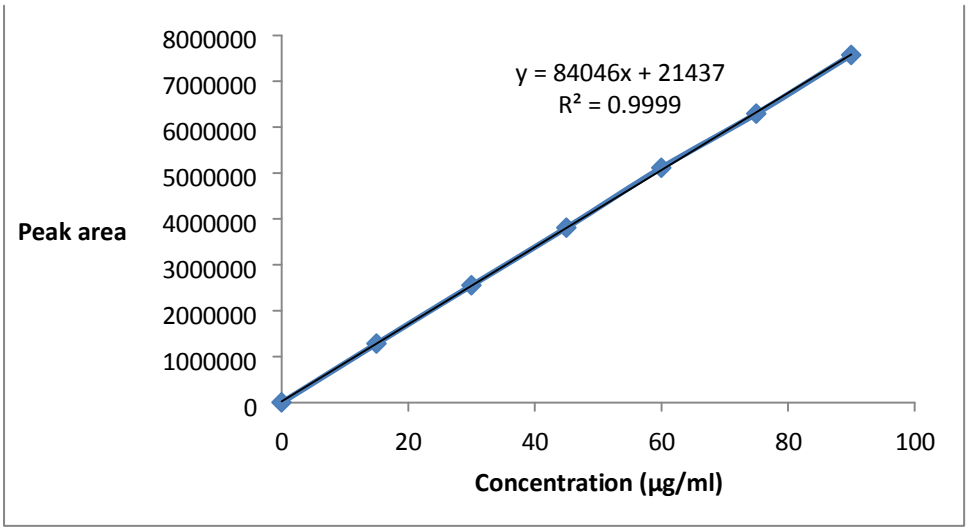
Mean	2.3295	3.123667	5103691	2427131
SD	0.000837	0.000816	4265.486	1377.365
RSD%	0.04	0.03	0.08	0.06

Intermediate Precision:

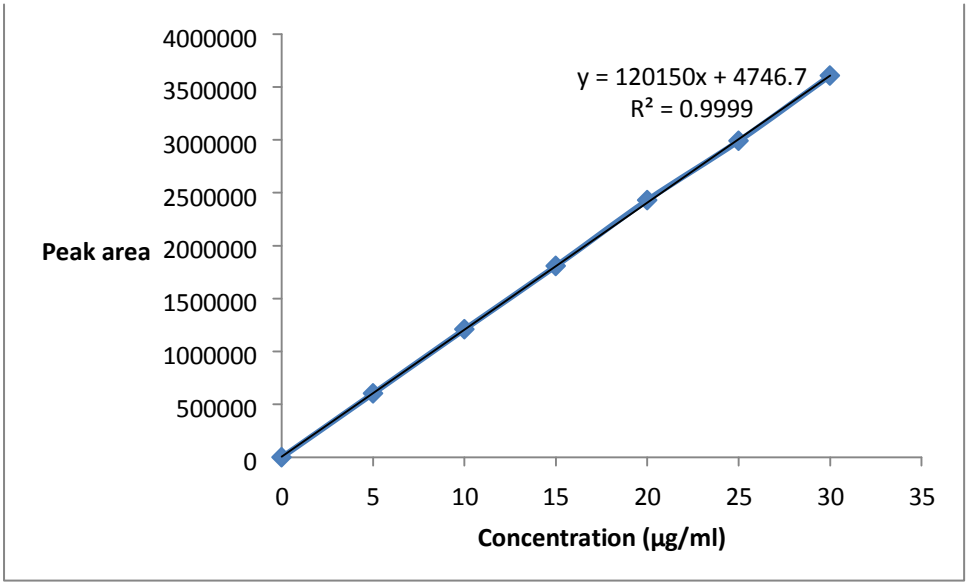
S.No	RT		AUC	
	DOM	LAF	DOM	LAF
Analyst 1	2.636	4.270	763057	11322148
Analyst 2	2.635	4.269	767941	11287864
Analyst 3	2.636	4.278	792341	11453986
Analyst 4	2.636	4.277	792006	11470402
Mean	2.63575	4.2735	778836.25	11383600
SD	0	0.00465475	15529.66828	92069.7312
RSD%	0	0.1	1.9	0.8

Linearity:

DO	M	LAF	
Concentration(µg)	Area	Concentration(µg)	Area
15	1283786	5	602884
30	2552288	10	1209174
45	3807818	15	1808001
60	5114494	20	2430132
75	6293686	25	2990618
90	7572405	30	3608210



Calibration curve of Domperidone



Calibration curve of Lafutidine

The linearity range of Domperidone and Lafutidine was 15 to 90µg/ml and 5 to 30µg/ml respectively. The regression equation for Domperidone was y= 84046x + 21437 and Lafutidine was y = 120510x + 4746.7. The correlation coefficient for both the drugs was 0.9999

Accuracy:

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	99.30
100%	20	40	99.19	99.19
150%	30	50	149.67	99.78

Robustness:

Robustness data of mobile phase ratio ACN: Phosphate Buffer (65:35)

S.No	AUC	
	DOM	LAF
1	5148739	2472308
2	5265440	2508636
3	5171523	2455319
S.D	61858.22	27236.78
Mean	5195234	2478754
%RSD	0.011907	0.010988

Robustness data of mobile phase ratio ACN: Phosphate Buffer (75:25)

S.No	AUC	
	DOM	LAF
1	5210875	2450292
2	5201795	2500391

3	5191235	2600198
S.D	9829029	76314.21
Mean	5201302	2516960
%RSD	0.00189	0.03032

Robustness data of Flow rate of 0.8ml/min

S. No	AUC	
	DOM	LAF
1	5515519	2619732
2	215440	2599871
3	5399198	2610998
S.D	120058.7	9954.498
Mean	5396719	2610200
%RSD	0.022247	0.003814

Robustness data of flow rate of 1.2ml/min

S. No	AUC	
	DOM	LAF
1	4890344	2325687
2	5200134	2498197
3	5399198	2519078
S.D	25627	16141.3
Mean	5163225	24477654
%RSD	0.049664	0.043364

LOD and LOQ: LOD: 30 mg of Domperidone and 10 mg of Lafutidine were taken into a 50 ml volumetric flask, make up with mobile phase and sonicated for 15 min.
10 ml of the above solution was pipette out into 100 ml volumetric flask and made up with mobile phase.
From the above solution 1 ml was taken into 100 ml volumetric flask and made up with the mobile phase.
LOD for Domperidone and Lafutidine was 7µg/ml and 4µg/ml respectively.
LOQ: 30 mg of Domperidone and 10 mg of Lafutidine were taken into a 50 ml volumetric flask, make up with mobile phase and sonicated for 15 min.
10 ml of the above solution was pipette out into 100 ml volumetric flask and made up with mobile phase.
From the above solution 2.5 ml was taken into 100 ml volumetric flask and made up with the mobile phase.
LOD for Domperidone and Lafutidine was 18 µg/ml and 12 µg/ml respectively.

IV. Summary

A very few analytical methods appeared in the literature for the determination of Domperidone and Lafutidine are generally based HPLC, UV, Spectro-fluorimetry that have been reported for the quantification of Domperidone and Lafutidine

In the present work, an attempt was made to provide a new, simple, accurate method effective quantitative simultaneous determination of Domperidone and Lafutidine as an active pharmaceutical ingredient as well as in pharmaceutical preparations without the interferences of other constituent in the formulations.

For routine analytical purposes it is always of interest to establish methods capable of analyzing a large number of samples in a short time period with good accuracy and precision. The main purpose of this study was to develop accurate, precise and economic methods for the determination of Domperidone and Lafutidine

A RP-HPLC method is developed and validated for various parameters as per ICH guidelines:

The system suitability parameters prove that the proposed method is equally suitable for estimation of Domperidone and Lafutidine, the chromatogram for Domperidone and Lafutidine are found to be satisfactory on Waters India, 250X4.6 mm, 5µm Hypersil column, using mobile phase composition of Acetonitrile: Sodium phosphate buffer [70:30(v/v)] with flow rate of 1.0 ml/min. Both the peaks are found to be symmetrical as found from symmetry factor of 1.01 for Domperidone and Lafutidine.

The resolution of the proposed method is found to be satisfactory, with peak showing complete base line separation. The retention time for Domperidone is about 2.3 min. and Lafutidine is about 3.1 min. The proposed system of stationary phase and mobile phase is ideally suitable for the estimation as indicated by good number of theoretical plates 2168 per meter for Domperidone and 4944 per meter for Lafutidine. The sensitivity of the method is good and also linearity which is observed

The accuracy of method is determined by recovery with spiked concentration of pure drug at three levels for Domperidone and Lafutidine. The recovery of drug is well within the acceptance limits of 98-102%.

The method is rugged and robust as observed from insignificant variation in the results of analysis on changes in mobile phase composition ratio, flow rate, analysis being performed by different analysts and on different days respectively. In all the above cases the recovery is found to be within the limit.

V. Conclusion

Based on the above observations and reports it is concluded that the present study (Development and validation of RP-HPLC method for simultaneous estimation of Domperidone and Lafutidine in pharmaceutical tablet dosage form.) which is developed and validated as per the ICH guidelines is very obvious, affordable, dynamic, low-cost, rapid and easy to perform with small sample volume and good repeatability. It can be adopted for the routine quality control analysis of simultaneous determination of Domperidone and Lafutidine because of good resolution of the chromatographic peaks.

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