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Development and Validation of Spectrophotometric method for Simultaneous estimation of Lafutidine and Domperidone in combined dosage form by area under curve method

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Abstract

A simple, accurate, rapid and precise spectrophotometric method has been developed for simultaneous estimation of Lafutidine and Domperidone in pharmaceutical dosage form. This method was based on UV spectrophotometric determination of two drugs, using Area under Curve method. It involves measurement of area under curve in the range of 268-278 nm (For Lafutidine) and 282.2-292.2 nm (For Domperidone) for the analysis in methanol. The linearity was observed in the concentration range of 2-12 µg/ml for Lafutidine and 3-18 µg/ml for Domperidone. The method showed good reproducibility and recovery with % RSD less than 2. Method was found to be rapid, specific, precise and accurate, can be successfully applied for the routine analysis of Lafutidine and Domperidone in bulk, and combined dosage form without any interference by the excipients. The method was validated according to ICH guidelines.

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Introduction

Lafutidine (LAF) is 2-(furan-2-ylmethylsulfinyl)-N-[4-[4-(piperidin-1-ylmethyl) pyridin-2-yl] oxybut-2-enyl]acetamide[1] .It belongs to the class of H2-receptor antagonists. Used in the treatment of peptic ulcer and gastro-oesophageal reflux disease (GERD). The literature reports some of the analytical methods like LC–ESI–MS method for the quantitation of

lafutidine in human plasma Application to pharmacokinetic studies [2], A single LC–tandem mass spectrometry method for the simultaneous determination of four H2 antagonists in human plasma[3], Determination of lafutidine in human plasma by high-performance liquid chromatography-electrospray ionization mass spectrometry: application to a bioequivalence study[4]. Determination of lafutidine in human plasma by HPLC-MS [5], Analytical method for determination of Lafutidine by RP-HPLC [6], and in serum by RP-HPLC method [7].

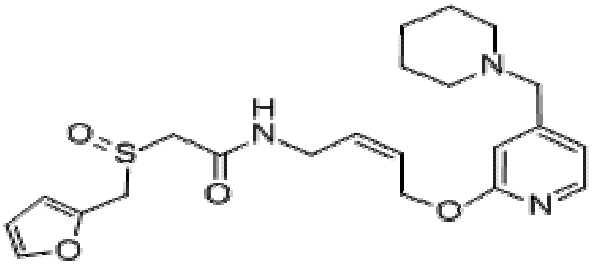

Fig.1: Structure of Lafutidine

Domperidone (DOM) chemically (5-chloro-1-{1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl] -4- piperidinyl} benzimidazolin-2-one) [8-10] is a dopamine antagonist with antiemetic properties. It stimulates gastro-intestinal motility and is used as an antiemetic for the short term treatment of nausea and vomiting. Literature reports many analytical methods like UV spectrophtometric methods, Tandem liquid chromatography, LC- tandem MS and RP –HPLC methods for determination of domperidone alone and in combination with other drugs [11-24].

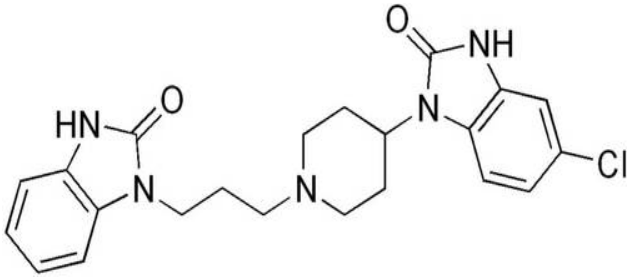

Fig.2: Structure of Domperidone

The validation of method carried out as per ICH guidelines [25]. However, there are no reported methods for simultaneous estimation of both drugs in combination. This paper presents two simple, rapid, reproducible and economical method for the simultaneous estimation of both the drugs.

Experimental Condition

Instrument

A Shimadzu UV-VIS Spectrophotometer 1800 with 1.0 cm matched quartz cells was used.

Materials and Method

Standard gift samples of Lafutidine and Domperidone were procured From Ajanta Pharmaceuticals Ltd, Mumbai and Dwarkesh Pharmaceuticals Pvt. Ltd, Gujarat**.** Combined dosage formulation containing Lafutidine and Domperidone were purchased from local market (LAFUDAC-D).

Preparation of standard stock solution (100 µg/ml)

The stock solution (100 µg/ml) of LAF and DOM were prepared separately by dissolving accurately about 10 mg of drug in Methanol and the volume was made up to 100 ml with Methanol to prepare standard stock solution (100 µg/mL).

Preparation of Calibration curve of LAF and DOM

The standard stock solution (100 µg/ml) of LAF and DOM were further diluted to obtain the final concentration 2, 4, 6, 8, 10, 12 µg/ml and 3, 6, 9, 12, 15, 18 µg/ml respectively.Both the solutions were scanned in the spectrum mode from 200.0nm to 400.0nm. The maximum absorbance of LAF and DOM was observed at 273 nm and 287.2nm, respectively.

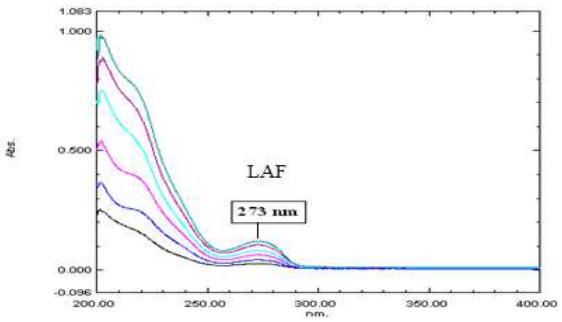

Fig. 3: Overlain Spectra of Lafutidine at 273 nm.

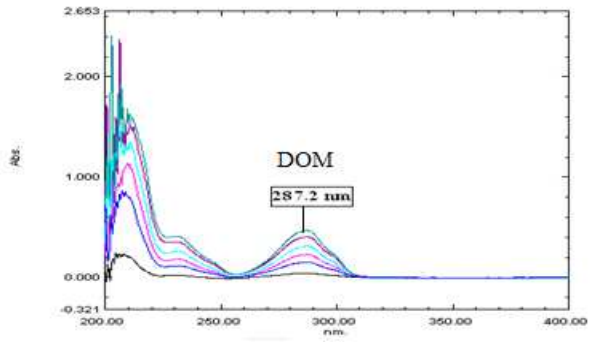

Fig. 4: Overlain Spectra of Domperidone at 287.2 nm.

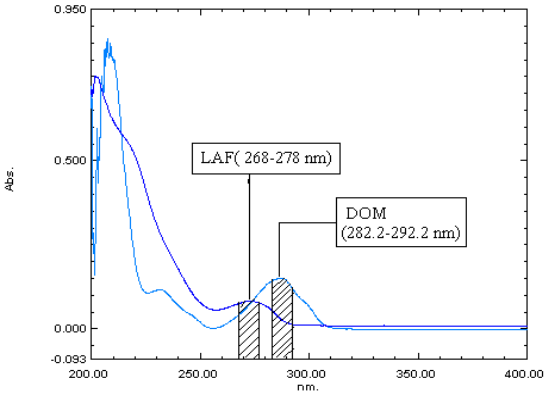

Fig. 5: Overlain spectra of Lafutidine and Domperidone

From the overlain spectra of both drugs obtained after scanning of standard solution of LAF and DOM, area under the curve in the range of 268-278 nm and 282.2-292.2 nm was measured for the analysis respectively. The absorptivity values calculated. The calibration curve was plotted with concentration v/s area under the curve and regression equation was calculated.

Determination of Absorptivity values:

Absorptivity = Absorbance/ Concentration of that component in gm/l.

Concentration of LAF and DOM was calculated using following formula;

$C_{LAF} = A_2ay_1 - A_1ay_2 / ax_2ay_1 - ax_1ay_2$ - (1)

$C_{DOM} = A_1ax_2 - A_2ax_1 / ax_2ay_1 - ax_1ay_2$ - (2)

Where,

C_{LAF} = Concentrations of LAF,

C_{DOM} = Concentrations of DOM,

A_1 = Area at 268-278 nm,

A_2 = Area at 282.2-292.2 nm,

ax_1 = Absorptivity value of LAF at 268-278 nm,

ax_2 = Absorptivity value of LAF at 282.2-292.2 nm,

ay_1 = Absorptivity value of DOM at 268-278 nm,

ay_2 = Absorptivity value of DOM at 282.2-292.2 nm.

Procedure for the assay of LAF and DOM in Capsule

For the estimation of drugs in the commercial formulations, twenty capsules containing 10 mg of LAF and 30 mg of DOM were weighed and average weight was calculated. The capsules were crushed and powdered in glass mortar. For the analysis of drugs, quantity of powder equivalent to 5 mg of LAF and 15 mg of DOM was transferred to 50 ml volumetric flasks and dissolved in sufficient quantity of Methanol. It was sonicated for 30 mins and volume was made up to obtain a stock solution of 10 µg/ml LAF (maintaining 30 µg/ml of DOM). This solution was then filtered through Whatmann filter paper no. 1. The concentration of both LAF and DOM was determined by measuring absorbances of sample solutions in wavelength range of 268-278 nm (for LAF) and 282.2-292.2 nm (for DOM) using equation 1 and 2. Results of capsule analysis are shown in Table 1.

Validation: The method was validated according to ICH guidelines to study linearity, accuracy, precision, LOD and LOQ.

Linearity

The measurement of linearity was evaluated by analyzing different concentrations of the standard solution of LAF and DOM. For both the methods, the Beer law was obeyed in the concentration range 2-12 µg/ml and 3-18 µg/ml for LAF and DOM respectively (Table-3). The absorbance was plotted against the corresponding concentrations to obtain the calibration graphs.

Precision

The reproducibility of the proposed methods was determined by performing tablet assay at different time intervals on same day (Intra-day precision) and on three different days (Inter-day precision) (Table - 3).

Limit of Detection and Limit of Quantitation

The LOD and LOQ were separately determined based on calibration curve. The residual standard deviation of a regression line or the standard deviation of y- intercepts of regression lines were used to calculate the LOD and LOQ (Table- 3). The detection limit (LOD) may be expressed as: LOD = 3.3 σ/S and the quantitation limit (LOQ) may be expressed as: LOQ =10 σ/S Where, σ = the standard deviation of the response S = the slope of the calibration curve.

Accuracy (% Recovery studies)

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (50%, 100% and 150%). Percent recovery was calculated for LAF and DOM, by this method (Table-2). Here three times repetition done with proposed procedure.

Table No: 1 Result of analysis of capsule Formulation:

Drugs	Label claim	Amount Found	% label claim*	S.D.	R.S.D.
LAF	10 mg	9.880	98.80	0.058459	0.591664
DOM	30 mg	30.02	100.06	0.132552	0.441545

* Indicates mean of six determinations.

Table 2: Result of Accuracy

Drug	Level of Recovery	Amt. of drug taken µg/ml	Amt of std.drug taken(spiked amt) µg/ml	% of drug estimated*	R.S.D.
LAF	0%	2	0	98.89	0.106
	50%	2	1	99.56	0.0352
	100%	2	2	99.09	0.177
	150%	2	3	100.90	0.099
DOM	0%	6	0	100.21	0.0905
	50%	6	3	99.77	0.0918
	100%	6	6	100.30	0.0498
	150%	6	9	99.43	0.131

*Average of three determinations. LAF=Lafutidine, DOM=Domperidone

Table 3: Regression analysis and Validation Parameters

Parameters	LAF	DOM
Linearity Range	2-12 µg/ml	3-18 µg/ml
Correlation Coeffecient	0.9977	0.9957
Precision (%RSD) Intraday Interday	0.75-1.71 0.80-1.69 0.75-1.71	0.57-1.89 0.57-1.29 0.98-1.89
LOD (µg/ml)	0.6440	0.8029
LOQ (µg/ml)	1.9515	2.4331
Assay (% Recovery)	98.89-100.90	99.43-100.30

Result and Discussion

The present work provides an accurate, reproducible, sensitive method for the simultaneous analysis of LAF & DOM in bulk and capsule formulation. Linear relationships between drug concentrations were obtained over the range of at 2-12 µg/ml & 3-18 µg/ml for LAF and DOM respectively. Under experimental conditions described assay of capsule, linearity, accuracy studies and precision, LOD and LOQ were estimated. Correlation coefficient was found to be > 0.995. The results of commercial capsule formulation are presented in Table 1. The % assay was found to be 98.89- 100.90% for LAF and 99.43-100.30% for DOM, and S.D. and R.S.D. for six determinations of capsule sample, by this method, was found to be less than 2.0 indicating the precision of this method. No interference was observed from the pharmaceutical adjuvants /excipients.

Conclusion

The UV spectrophotometric method was developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed method are within limits, indicating high degree of precision of the method. The results of the recovery studies performed indicate the method to be accurate. Hence, it can be concluded that the developed spectrophotometric method is accurate, precise and can be employed successfully for the estimation of LAF and DOM in bulk and formulation.

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References

1) The Merck Index - An encyclopedia of chemicals, drugs and biologicals, published by Merck Research Laboratories, 14th edition, Lafutidine, (5347), 926.
2) Wei-Dong C ,Yan L, Hao Li, Ye Xiong, Xiao-Dong L, Guang-Ji W, Lin Xie, Simple,sensitive and rapid LC–ESI–MS method for the quantitation of lafutidine in human plasma: Application to pharmacokinetic studies, J Pharmaceut Biomed, 2006; 41(1):256-260.
3) Xiuhong S, He Xian-chen, "A single LC–tandem mass spectrometry method for the simultaneous determination of four H2 antagonists in human plasma", Key Laboratory of Drug Quality Control and Pharmacovigilance, Ministry of Education, 2009.
4) Lili Wu , Zunjian Z, Yuan T, Wei Li, Fengguo Xu, Yun Chen, Huilin Wei, Determination of lafutidine in human plasma by high-performance liquid chromatography electrospray ionization mass spectrometry: application to a bioequivalence study,J Mass Spectrom, 2009; 877(31):3953-3959.
5) Zheng H, Chen Ya-li, Wang Li, Fang Shu-xian., Determination of lafutidine in human plasma by HPLC-MS, Chin. J.Clin. Pharm., 2008; 01:023.
6) Sumithra M., Shanmuga P. , Srinivasulu K., Analytical Method Development and Validation of Lafutidine in Tablet dosage form by RP-HPLC, Int. J. ChemTech, 2011; 3: 1403-1407.
7) Zheng Yong, Chen Mei, Zhoa Chun-jingo, Determination of lafutidine in serum with reverse high performance liquid chromatography, Journal of Pediatric Pharmacy, 2006; 03.

8) Indian Pharmacopoiea, 6th Edition, Ministry of Health and Family welfare, published by The Indian Pharmacopoiea Commission, Ghaziabad, vol-II, (2010), 1245-46.

9) British Pharmacopoiea, 6th Edition (6.1-6.5), vol-I, (2010), 739-741.

10) The Merck Index - An encyclopedia of chemicals, drugs and biologicals, published by Merck Research Laboratories, 14th edition, Domperidone, (3418), 578.

11) Rajendraprasad Y, Rajasekhar K., Shankarananth V., Yaminikrishna V,Saikumar S, Venkata P, Spectrophotometric method for the estimation of domperidone in bulk and pharmaceutical formulations, Journal of Pharmacy Research., 2009; 2 : 1593-94.

12) Varalakshmi M., Vijaya Ratna J, Krishnachaitanya K., RP-HPLC method development and validation of Domperidone Maleate, International Journal of Pharmaceutical Research & Development, 2011; 3(4) :61-64.

13) Smit M J, Sutherland F C, Hundt H K, Swart K J, Hundt A F, Rapid and sensitive liquid chromatography–tandem mass spectrometry method for the quantitation of domperidone in human plasma, J. Chromat. A, 2002; 949(1): 65-70.

14) Maria K S, Kamila K S, High-performance liquid chromatographic analysis for the determination of domperidone in human plasma, J. Chromatography B, 2000; 744:207.

15) Maurizio C, Marina C R, Leandro R , UV spectroscopic study and conformational analysis of Domperidone, J. Molecular Structure, 1995; 350: 43.

16) Mohammed S A , Mohsin G, Khatri A R , Stability indicating simultaneous determination of domperidone (DP),methylparaben (MP) and propylparaben by high performance liquid chromatography (HPLC), J. Pharma. Biomed. Anal., 2006; 41: 358.

17) Charde M; Walode S; Tajne M; Kasture A, UVspectrophotometric estimation of ranitidine and domperidone in tablet formulations, Indian J Pharm Sci, 2006; 68: 658-659.

18) Sohan S C, Amir I M, Ganesh R. PawbakeB W , Sagar B W, Simultaneous Spectrophotometric Estimation Of Dexrabeprazole And Domperidone In Capsule Dosage Form, International Journal of Pharmaceutical Quality Assurance ,2010;2(2):31-34.

19) Patel A H, Patel J K, Patel K N, Rajput G, Rajgor NB, Development and Validation of Derivative Spectrophotometric Method for Simultaneous Estimation of Domperidone and Rabeprazole Sodium in Bulk and Dosage Forms, International Journal on Pharmaceutical and Biological Research, 2010; 1(1):1-5.

20) Lakshmana P S, Shirwaikar A, Shirwaikar A, DineshKumar C., Joseph A, Kumar R, Simultaneous Estimation of Esomeprazole and Domperidone by UV Spectrophotometric Method, Indian J Pharm Sci., 2008; 70(1): 128–131.

21) Sahu R, Preeti N, Deepti J, Simultaneous Spectrophotometric Estimation of Famotidine and Domperidone in combined tablet dosage form, Indian J. Pharm. Sci., 2006; 68 (4): 503-506.

22) Karthik A, Subramanian G, Kumar A R, Udupa N, Simultaneous estimation of paracetamol and domperidone in tablets by reverse phase HPLC method , Indian J Pharm Sci, 2007 ;69: 142-144.

23) Rakeshkumar S, Ramakrishna S ,Pragya G, RP-HPLC method development and validation for simultaneous estimation of ranitidine HCL and Domperidone in combined tablet dosage form, Indian J Pharm Sci, 2010; 1(8): 77-87.

24) Bhavna P, Zarna D, Ronak D, Chetan R, Vidya Sagar G, Mehta RS, Simultaneous Estimation of Lansoprazole and Domperidone in Combined Dosage Form by RP-HPLC , Asian J. Research Chem, 2009;2(2):210-212.

25) The International Conference on Harmonization, Q2 (R1), Validation of Analytical Procedure: Text and Methodology, 2005.