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Research

Analytical method development and validation for simultaneous estimation of rabeprazole and domperidone by using rp-hplc

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Abstract

A rapid, precise, accurate, specific and simple RP-HPLC method was developed for the simultaneous estimation of Rabeprazole and Domperidone in bulk and its combined pharmaceutical dosage form. A High-performance liquid chromatograph WATERS, software: Empower 2, 2695 separation module, 996 PDA detector, using Phenomenex Luna C18 (4.6mm×250mm) 5 µm or equivalent column, with mobile phase composition of Methanol: Phosphate Buffer pH-3.0 (70:30v/v) was used. The flow rate of 1.0 ml min-1 and effluent was detected at 230 nm. The retention time of Rabeprazole and Domperidone was found to be 1.870min and 2.499minutes respectively. Linearity was observed over concentration range of 10-50µg ml-1 for Rabeprazole and 16-80µg ml-1 for Domperidone respectively. The accuracy of the proposed method was determined by recovery studies and the Rabeprazole was found to be 99.1% and Domperidone was found to be 98.8% respectively. The proposed method is applicable to routine analysis of Rabeprazole and Domperidone in bulk and pharmaceutical formulations. The proposed method was validated for various ICH parameters like linearity, limit of detection, limits of quantification, accuracy, precision, range and specificity.

Keywords: Rabeprazole, Domperidone, RP-HPLC, Robustness and ICH Guidelines.

INTRODUCTION

Strategy Of Method Development

Method development ought to be supported many issues. It's desirable to possess most sample data to form development quick and desired for meant analytical technique application, physical and chemical properties area unit most desirable as primary data. Moreover, separation goal has to outline at starting so; acceptable technique is developed for the aim. AN LC technique development is extremely vast space for even prescribed drugs with restrictive demand of international standards. So, before technique validation and usage at internal

control several aspects have to be compelled to focus as per ICH tips. Method development is supported a sample and goals moreover as offered resources for action however few basic steps for technique development area unit is mentioned as given below.

Steps in technique development

1. Sample data, define separation goals
2. Sample pre-treatment, want of special HPLC procedure
3. choice of detector and detector settings
4. choice of LC method; preliminary run; estimate best separation conditions
5. Optimize separation conditions
6. Check for issues or demand for special procedure
7. technique validation

Sample information

1. variety of compounds gift
2. Chemical structure of compounds
3. Chemical nature
4. relative molecular mass of compounds
5. pKa Value(s) of compounds
6. Sample solubility
7. Sample stability and storage
8. Concentration vary of compounds in sample
9. Ultraviolet illumination spectra of compounds or properties for detection of compounds

RP-HPLC continues to be comparatively new technique, and literature isn't invariably offered on operative conditions for a selected application. The primary step in developing AN RP-HPLC analysis, or the other variety of natural process analysis, is to outline the matter and state the aim of study. So as to outline the matter, the subsequent question ought to be asked:

1. Is that the analysis aiming to be used habitually for an oversized variety of samples? Is case of operation and ease of nice importance?
2. May be a qualitative and / or qualitative analysis required?
3. Is it necessary to separate all the constituents within the sample or solely a tiny low cluster of constituents?
4. Area unit the constituents similar in structure or wide diverse?
5. Area unit the constituents gift in similar concentrations, or is one constituent presenting an oversized quantity and alternative solely in trace amounts?
6. Will sample be simply ready for RP-HPLC analysis?
7. Area unit there compounds gift that will interfere with the analysis of constituents of interest?
8. Will peaks within the recording be promptly identified?

Different methods of analysis

The following techniques are available for separation and analysis of components of interest.

Spectral methods

The spectral techniques are used to measure electromagnetic radiation which is either absorbed or emitted by the sample. E.g. UV-Visible spectroscopy, IR spectroscopy, NMR, ESR spectroscopy, Flame photometry, Fluorimetry.2

Electro analytical methods

Electro analytical methods involved in the measurement of current voltage or resistanceas a property of concentration of the component in solution mixture. E.g. Potentiometry, Conductometry, Amperometry.[2]

Chromatographic methods

Chromatography is a technique in which chemicals in solutions travel down columns or over surface by means of liquids or gases and are separated from each other due to their molecular characteristics. E.g. Paper chromatography, thin layer chromatography (TLC), High performance thin layer chromatography (HPTLC), High performance liquid chromatography (HPLC), Gas chromatography (GC).[2]

Miscellaneous Techniques

Mass Spectrometry, Thermal Analysis.

Hyphenated Techniques

GC-MS (Gas Chromatography – Mass Spectrometry), LC-MS (Liquid Chromatography – Mass Spectrometry), ICP-MS (Inductivity Coupled Plasma- Mass Spectrometry), GC-IR (Gas Chromatography –

Infrared Spectroscopy), MS-MS (Mass Spectrometry – Mass Spectrometry). Analytical techniques that are generally used for drug analysis also include biological and microbiological methods, radioactive methods and physical methods etc.

MATERIALS AND METHODS

Rabeprazole, Domperidone from Sura Pharma Labs, HPLC from WATERS, software: Empower 2, 2695 separation module. 996 PDA detector. Water and Methanol for HPLC from LICHROSOLV (MERCK). Anhydrous di hydrogen phosphate from Finar chemicals.

HPLC method development
TRAILS
Preparation of Standard Solution
Accurately weigh and transfer 10 mg of Rabeprazole and 10mg of Domperidone working standard into a 10 ml and 10 ml of clean dry volumetric flasks add about 10ml and 10 ml of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 0.48ml of Rabeprazole from stock solution and 0.3ml of Domperidone into a 10ml volumetric flask and dilute up to the mark with diluents.
Procedure
Inject the samples by changing the chromatographic conditions and record the chromatograms, note the conditions of proper peak elution for performing validation parameters as per ICH guidelines.

Validation
Preparation of mobile phase
Preparation of Phosphate buffer (pH-3.0)
Dissolve 0.9g of anhydrous dihydrogen phosphate and 1.298 g of Citric acid mono hydrate in sufficient water to produce 1000mL. Adjust the pH-3 by using ortho phosphoric acid.

Preparation of mobile phase
Accurately measured 700 ml (70%) of Methanol and 300 ml of Phosphate buffer pH-3 (30%) were mixed and degassed in digital ultra sonicater for 15 minutes and then filtered through 0.45µ filter under vacuum filtration.

Diluent Preparation
The Mobile phase was used as the diluent.

RESULTS AND DISCUSSION

(Optimized Condition)

Mobile phase	: Methanol: Phosphate Buffer pH-3 (70:30v/v)
Column	: Phenomenex Luna C18 (4.6mm×250mm) 5 µm
Flow rate	: 1 ml/min
Wavelength	: 230 nm
Column temp	: Ambient
Sample Temp	: Ambient
Injection Volume	: 10 µl
Run time	: 4 minutes

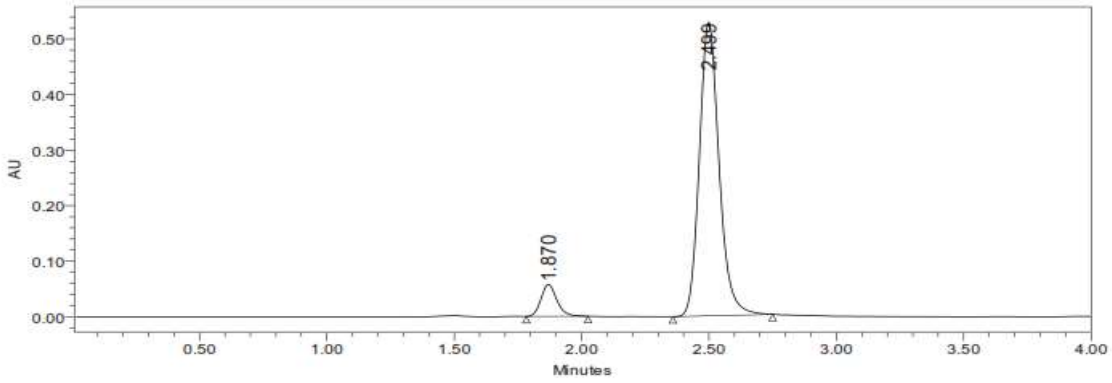

Fig 1: Optimised Chromatogram

Table 1: Peak Results for Optimised Chromatogram

S. No.	Peak name	R_t	Area	Height	USP Resolution	USP Tailing	USP plate count
1	Rabeprazole	1.870	5664027	299752			2314
2	Domperidone	2.499	5033532	210321	4.6	1.3	2921

□ *Theoretical plates must be not less than 2000;* □ *Tailing factor must be not less than 0.9 and not more than 2.*
□ *It was found from above data that all the system suitability parameters for developed method were within the limit.*

Assay (Standard)

Showing assay standard results

S.No.	Name	Rt	Area	Height	USP Resolution	USP Tailing	USP plate count	Injection
1	Rabeprazole	1.866	2762937	399854		1.3	2300.1	1
2	Domperidone	2.496	2534375	210326	4.6	1.3	2937.7	1
3	Rabeprazole	1.866	2774613	386542		1.3	2344.7	2
4	Domperidone	2.497	2526189	226741	4.7	1.3	3008.8	2
5	Rabeprazole	1.868	2776429	364121		1.3	2344.2	3
6	Domperidone	2.498	2546248	231494	4.7	1.3	2990.7	3

Assay (Sample)

Showing assay sample results

S.No.	Name	Rt	Area	Height	USP Resolution	USP Tailing	USP plate count	Injection
1	Rabeprazole	1.870	2732203	294531		1.3	2314	1
2	Domperidone	2.495	2507543	216321	4.6	1.3	2954	1
3	Rabeprazole	1.873	2751843	286473		1.3	2369	2
4	Domperidone	2.499	2509101	216354	4.6	1.3	2944	2
5	Rabeprazole	1.874	2744776	312684		1.3	2329	3
6	Domperidone	2.501	2515628	206571	4.6	1.3	2990	3

Showing assay results

S.No.	Name of compound	Label claim	Amount taken (from combination tablet)	%purity
1	Rabeprazole	150mg	149.867	99.852%
2	Domperidone	300mg	299.786	99.764%

$$\%ASSAY = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Weight of standard}}{\text{Dilution of standard}} \times \frac{\text{Dilution of sample}}{\text{Weight of sample}} \times \frac{\text{Purity}}{100} \times \frac{\text{Weight of tablet}}{\text{Label claim}} \times 100$$

The retention time of Rabeprazole and Domperidone was found to be 1.8mins and 2.4mins respectively. The % purity of Rabeprazole and Domperidone in pharmaceutical dosage form was found to be 99.8% and 99.7% respectively.

Precision

Table 2: Results of method precession for Rabeprazole

S.No.	Name	Rt	Area	Height	USP plate count	USP Tailing
1	Rabeprazole	1.861	2766870	294578	2684	1.3
2	Rabeprazole	1.862	2771971	286541	2347	1.3
3	Rabeprazole	1.862	2771958	302657	2674	1.3
4	Rabeprazole	1.866	2780299	293412	2451	1.3
5	Rabeprazole	1.868	2789695	283154	2678	1.3
6	Rabeprazole	1.866	2766870	296759	2861	1.3
Mean			2774611			
Std. Dev			8873.946			
% RSD			0.3			

Table 3: Results of method precession for Domperidone

S.No.	Name	Rt	Area	Height	USP plate count	USP Tailing	USP Resolution
1	Domperidone	2.490	2534539	193240	2761	1.3	4.7
2	Domperidone	2.491	2539247	201647	2489	1.3	4.6
3	Domperidone	2.492	2544661	193472	2367	1.3	4.6
4	Domperidone	2.497	2548839	196475	2845	1.3	4.6
5	Domperidone	2.498	2558822	201394	2347	1.3	4.7
6	Domperidone	2.498	2534539	182641	2647	1.3	4.6
Mean			2543441				
Std. Dev			9415.761				
% RSD			0.3				

- *%RSD for sample should be NMT 2.*
- *The %RSD for the standard solution is below 1, which is within the limits hence method is precise.*

Intermediate precision/Ruggedness

Table 4: Results of Intermediate precision for Rabeprazole

S.No.	Name	Rt	Area	Height	USP plate count	USP Tailing
1	Rabeprazole	1.869	2781856	294651	2647	1.3
2	Rabeprazole	1.872	2761510	284123	2781	1.3
3	Rabeprazole	1.872	2748811	274561	2984	1.3
4	Rabeprazole	1.873	2790831	281241	2475	1.3
5	Rabeprazole	1.874	2785112	286471	2647	1.3
6	Rabeprazole	1.872	2781932	294512	2489	1.3
Mean			2775009			
Std. Dev			16222.05			
% RSD			0.5			

Table 5: Results of Intermediate precision for Domperidone

S.No.	Name	Rt	Area	Height	USP plate count	USP Tailing	USP Resolution
1	Domperidone	2.497	2536301	211541	2495	1.4	4.6
2	Domperidone	2.499	2541972	206141	2694	1.4	4.6
3	Domperidone	2.500	2521259	198641	2785	1.4	4.7
4	Domperidone	2.500	2537081	206741	2947	1.4	4.6
5	Domperidone	2.500	2549869	209487	2742	1.4	4.6
6	Domperidone	2.500	2536301	193481	2914	1.4	4.6
Mean			2537131				
Std. Dev			9370.087				
% RSD			0.3				

- *%RSD of five different sample solutions should not more than 2*
- *The %RSD obtained is within the limit, hence the method is rugged.*

ACCURACY

Table 6: Accuracy (recovery) data for Rabeprazole

%Concentration (at specification Level)	Area	Amount Added (ppm)	Amount Found (ppm)	% Recovery	Mean Recovery
50%	2771991	15	14.9	98%	
100%	5664027	30	29.99	99.9%	99.1%
150%	8337191	45	44.95	99.6%	

- *The % Recovery for each level should be between 98.0 to 102.0%.*

Linearity

Linearity Results: (for Rabeprazole)

Concentration(ppm)	Area
10	892464
20	1866364
30	2777423
40	3709213
50	4601317

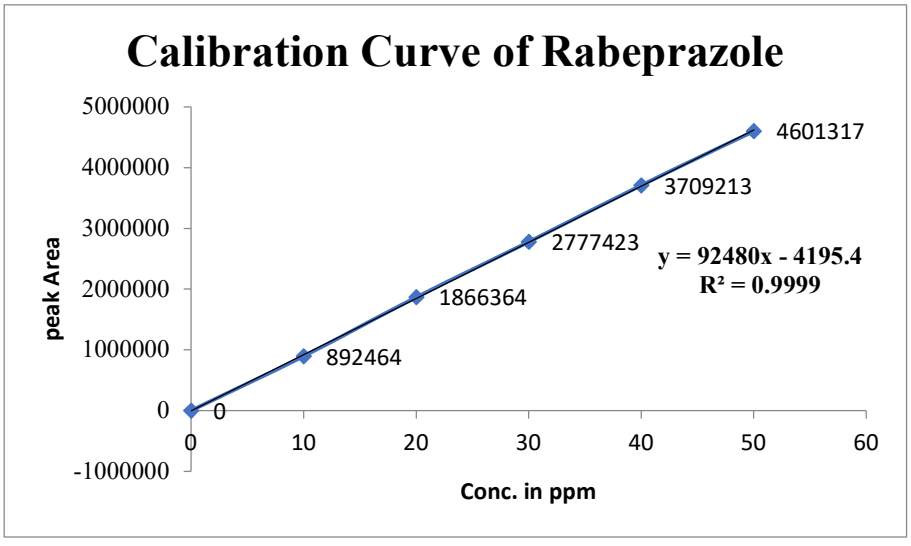

Fig 2: Calibration Graph for Rabeprazole

Correlation coefficient should be not less than 0.999.

Linearity Results: (for Domperidone)

Concentration (ppm)	Area
16	920032
32	1752782
48	2521426
64	3326009
80	4217393

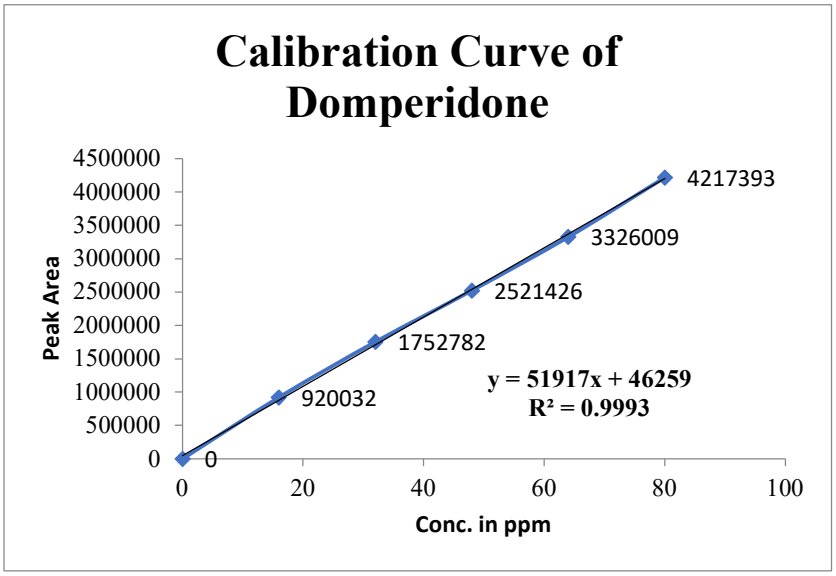

Fig 3: Calibration Graph for Domperidone

Correlation coefficient should be not less than 0.99.

Table 7: Analytical performance parameters of Rabeprazole and Domperidone

Parameters	Rabeprazole	Domperidone
Slope (m)	92480	51917
Intercept (c)	4195	46259
Correlation coefficient (R^2)	0.999	0.999

Correlation coefficient (R^2) should not be less than 0.999

Table 8: System suitability results for Rabeprazole

S.No.	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	0.9	2231.8	1.3
2	1.0	2344.7	1.3
3	1.1	2071.6	1.3

** Results for actual flow (1.0 ml/min) have been considered from Assay standard.*

Table 9: System suitability results for Domperidone

S.No.	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	0.9	2953.6	1.3
2	1.0	3008.8	1.3
3	1.1	2704.0	1.3

** Results for actual flow (1.0ml/min) have been considered from Assay standard.*

Table 10: System suitability results for Rabeprazole

S.No.	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1	10% less	2867.2	1.2
2	*Actual	2344.7	1.2
3	10% more	2347.8	1.2

Table 11: System suitability results for Domperidone

S.No.	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1	10% less	3336.1	1.2
2	*Actual	3008.8	1.2
3	10% more	3010.3	1.2

** Results for actual mobile phase have been considered from Assay standard.*

SUMMARY AND CONCLUSION

High performance liquid chromatography is at present one of the most sophisticated tool of the analysis. The estimation of Rabeprazole and Domperidone was done by RP-HPLC. The Phosphate buffer was pH-3 and the mobile phase was optimized with consists of Methanol: Phosphate buffer (pH-3) mixed in the ratio of 70:30 % v/v. A Phenomenex Luna column C18 (4.6 x 150mm, 5µm) or equivalent chemically bonded to porous silica particles was used as stationary phase. The solutions were chromatographed at a constant flow rate of 1 ml/min. The linearity range of Rabeprazole and Domperidone were found to be from 10-50µg/ml, 16-80µg/ml respectively. Linear regression coefficient was not more than 0.999, 0.999. The values of % RSD are less than 2% indicating accuracy and precision of the method. The percentage recovery varies from 99.9-99.9% of Rabeprazole and Domperidone. LOD and LOQ were found to be within limits. The results obtained on the validation parameters met ICH and USP requirements. It inferred the method was found to be simple, accurate, precise and linear. The method was found to be having suitable application in routine laboratory analysis with high degree of accuracy and precision.

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