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Research Article

**THE ANALYTICAL METHOD DEVELOPMENT AND
VALIDATION FOR THE SIMULTANEOUS ESTIMATION OF
DOMPERIDONE AND CINNARIZINE BY USING RP- HPLC****B.Vemalakshmi^{1*}, Dr.N. Neelima², Chaitanya Bangari³, Dr.M.B.Venkatapathi Raju⁴**¹Avanathi Institute Of Pharmaceutical Sciences, Vizianagaram, Ap-531162

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Abstract:

The system suitability the % RSD for the peak area of domperidone and cinnarizine were found to be 0.100016 and 0.040736 respectively. For regression coefficient for both the drugs in linearity was found to be 1, Y- intercept for domperidone and cinnarizine were found to be -73286 and -92028 respectively. The individual % assays of domperidone and cinnarizine for system precession were found to be between 98-102. The % RSD of domperidone and cinnarizine were found to be 0.094872 and 0.014023 respectively. In intermediate precision the individual % assays of domperidone and cinnarizine were found to be between 98 to 102. The % RSD of domperidone and cinnarizine of analyst 1 were found to be 0.065945 and 0.024433 respectively. The % RSD of domperidone and cinnarizine of analyst 2 were found to be 0.082395 and 0.030517 respectively. For accuracy the percentage mean recovery of 80 % domperidone and cinnarizine were found to be 99.98577 and 100.062 respectively, 100% domperidone and cinnarizine were found to be 100.0181 and 99.9292 respectively, 120 % domperidone and cinnarizine were found to be 99.84517 and 99.9976 respectively. For Ruggedness for system-1 the %RSD of domperidone and cinnarizine were found to be 0.079988 and 0.032579 respectively and % assay of domperidone and cinnarizine were found to be 99.99 and 100.07 respectively. For system-2 the %RSD of domperidone and cinnarizine were found to be 0.061879 and 0.026339 respectively and % assay of domperidone and cinnarizine were found to be 99.94 and 99.93 respectively. The LOD of domperidone and cinnarizine were found to be 1.055929 and 0.656951968 respectively. The LOQ of domperidone and cinnarizine were found to be 3.199785 and 1.990763538 respectively.

Keywords: domperidone, cinnarizine, regression coefficient, accuracy and Ruggedness**Corresponding author:****B.Vemalakshmi,**

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INTRODUCTION:

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 acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are related to its peripheral dopamine receptor blocking properties [1]. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing oesophageal and gastric peristalsis and by lowering oesophageal sphincter pressure. The antiemetic properties of domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which - among others - regulates nausea and vomiting [2]

First synthesized by Janssen Pharmaceuticals in 1955, cinnarizine is an anti-histaminic drug mainly used for the control of vestibular disorders and motion sickness. Cinnarizine is a specific calcium channel blocker that primarily works on the central vestibular system to interfere with the signal transmission between vestibular apparatus of the inner ear and the vomiting centre of the hypothalamus. Cinnarizine could be also viewed as a nootropic drug because of its vasorelaxating abilities (due to calcium channel blockage), which happen mostly in brain.

Combination use of cinnarizine with other nootropics, such as piracetam resulted in enhanced effect of boosting brain oxygen supply [3].

According to the literature survey it was found that few analytical methods such as (HPLC, UV-Visible analysis, RP-LC and HPTLC) were reported for the simultaneous estimation of domperidone and cinnarizine. So the aim of present work is to develop and validate RP-HPLC method for the simultaneous estimation of cinnarizine and domperidone in tablet dosage form.

So the present study is planned with following objectives:

- To perform RP-HPLC for the simultaneous estimation of domperidone and cinnarizine in tablet dosage form.⁴
- To optimize the developed method.
- To validate the developed method as per ICH guide lines. [5]

METHOD AND METHODOLOGY:**Materials:**

Standard drugs of domperidone and cinnarizine had been supplied as gift samples from active Pharma labs. Domperidone and cinnarizine tablets containing 20mg cinnarizine and 15mg domperidone (VERTIDOM) have been bought from Apollo pharmacy. HPLC grade methanol and water were acquired from active Pharma labs.

Instrumentation:

The chromatographic system used to carry out development and validation of this assay technique became HPLC – WATERS Model NO.2690/5 series Compact System Consisting of Hypersil-C18 BDS column with PDA detector. Electronic balance (SARTORIOUS) Digital pH meter (POLOMAN) .Sonicator (FAST CLEAN)

Mobile phase preparation:

The mobile phase consisted of Water: Methanol (35:65 v/v). Mobile phase was changed into filtered through a 0.45µm nylon membrane (Millipore Pvt. Ltd. Bangalore, India) and degassed in an ultrasonic bath (FAST CLEAN).

Diluent: 100 %methanol is used as diluent.

Preparation of stock standard solution:

Standard stock solution was prepared by dissolving 15mg of Domperidone and 20mg of Cinnarizine RS drugs in 50ml of diluent taken in two 50ml of volumetric flasks separately and sonicated for 20 minutes, volume is made up to the mark with diluent to get 300µg/ml and 400µg/ml respectively.

Preparation of standard solution:

From the stock standard solution 10ml was taken and diluted to 100 ml with diluent taken in a 100 ml volumetric flask to get 30µg/ml and 40µg/ml of domperidone and cinnarizine respectively.

Preparation of sample drug solution for pharmaceutical formulations:

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 15 mg domperidone and 20 mg cinnarizine was weighed and dissolved in 20 ml methanol with the the useful resource aid of ultrasonication for 10 min. The content was diluted to 50 ml with methanol to furnish a stock test solution. The stock solution was filtered through a 0.45 µm Nylon syringe filter and 10.0 ml of the filtrate became was diluted into a 100.0 ml volumetric flask to give a test solution containing 40µg/ml cinnarizine and 30 µg/ml domperidone.

Optimized chromatographic conditions for Domperidone & Cinnarizine

- Instrument model- Waters 2690/5 with PDA Detector
- Software - Empower -2
- Detection wavelength- 268nm
- Column - Inertsil- ODS, C18, 250*4.6mm, 5 μ
- Mobile Phase - Methanol: Water (65:35)
- Flow Rate - 1ml/min
- Injection Volume- 20 μ l
- Column Temperature- Ambient

Cinnarizine RS drugs in 50ml of diluent taken in two 50ml of volumetric flasks separately and sonicated for 20 minutes, volume is made up to the mark with diluent to get 300 μ g/ml and 400 μ g/ml respectively. From the stock standard solution 10ml was taken and diluted to 100 ml with diluent taken in a 100 ml volumetric flask to get 30 μ g/ml and 40 μ g/ml of dom and cinn respectively.

Preparation of sample drug solution for pharmaceutical formulations:

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 15 mg domperidone and 20 mg cinnarizine was weighed and dissolved in 20 ml methanol with the aid of ultrasonication for 10 min. The content was diluted to 50 ml with methanol to furnish a stock test solution. The stock solution was filtered through a 0.45 μ m Nylon syringe filter and 10.0 ml of the filtrate was diluted into a 100.0 ml volumetric flask to give a test solution containing 40 μ g/ml cinnarizine and 30 μ g/ml domperidone.

Validation data: b[5-14]

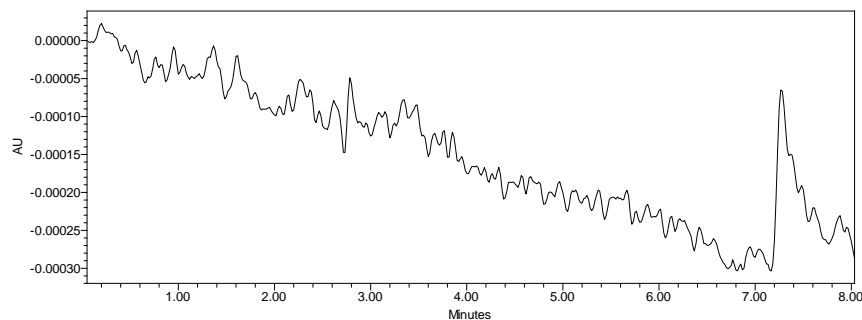
Specificity by direct comparison method:

There is no interference of mobile phase, solvent and placebo with the analyte peak and also the peak purity of analyte peak which indicate that the method is specific for the analysis of analytes in their dosage form.

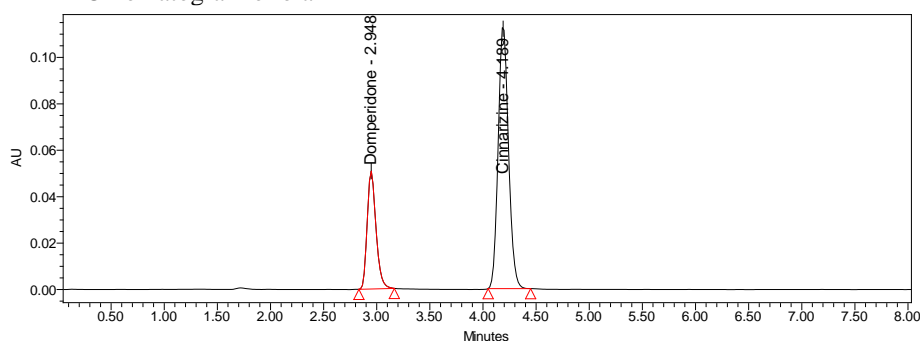
Preparation standard of solution:

Standard stock solution was prepared by dissolving 15mg of Domperidone and 20mg of

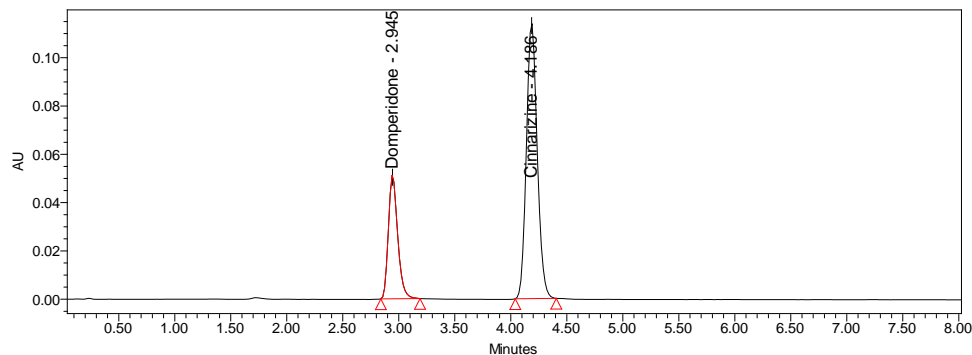
RESULT AND DISCUSSION:



Chromatogram of blank



Chromatogram of standard



Chromatogram of sample

Observation

It is observed from the above data, diluent or excipient peaks are not interfering with the domperidone and cinnarizine peaks.

System suitability:

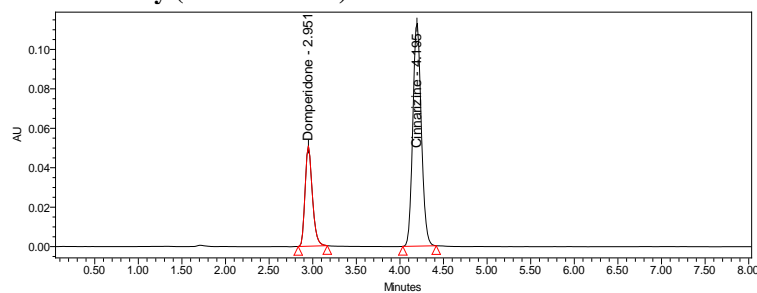
A Standard solution was prepared by using Domperidone and Cinnarizine as per test method and was injected Five times into the HPLC system.

The system suitability parameters were evaluated from standard chromatograms by calculating the % RSD from five replicate injections for Domperidone

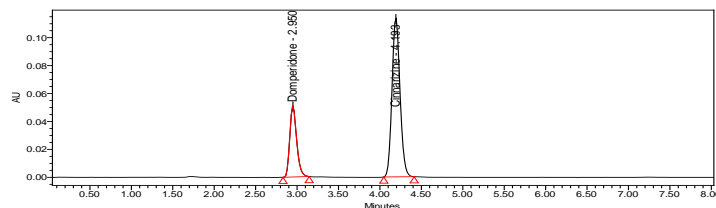
and Cinnarizine combination, retention times and peak areas.

Acceptance criteria:

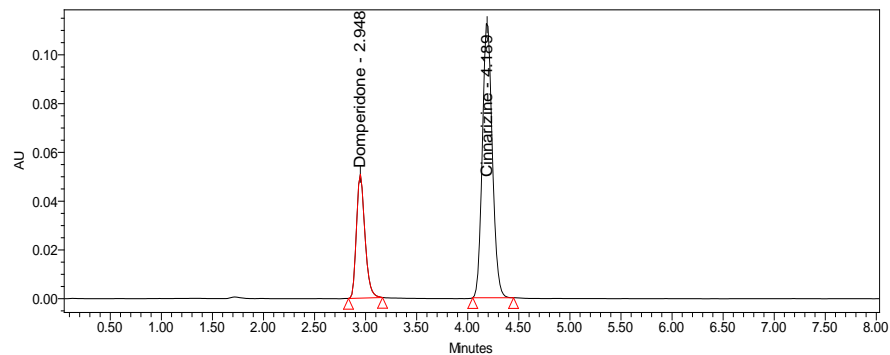
1. The % RSD for the retention times of principal peak from 5 replicate injections of each Standard solution should be not more than 2.0 %
2. The % RSD for the peak area responses of principal peak from 5 replicate injections of each standard Solution should be not more than 2.0%.
3. The number of theoretical plates (N) for the Domperidone and Cinnarizine peaks is NLT 3000.
4. The Tailing factor (T) for the Domperidone and Cinnarizine peaks is NMT 2.0

Chromatograms of system suitability (standards 1-5):

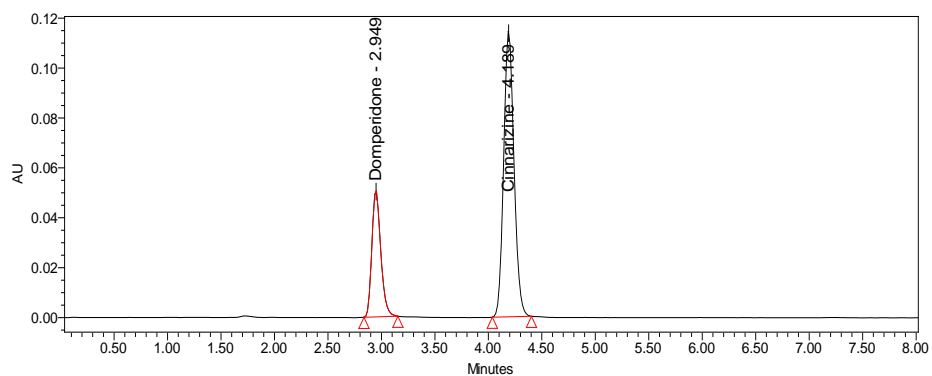
System suitability Chromatogram for standard-- 1



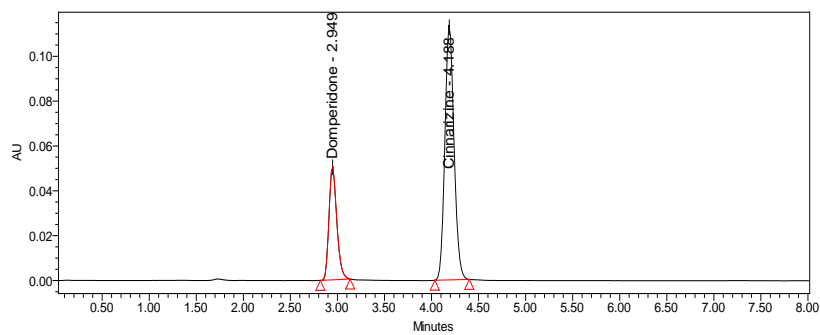
System suitability Chromatogram



System suitability Chromatogram



System suitability Chromatogram



System suitability Chromatogram

Injections	Area	Retention Time	Tailing Factor	Usp Platelet Count
1	292670	2.951	1.226462	5888.298384
2	292770	2.95	1.10346	5901.600147
3	292212	2.948	1.230571	5938.888626
4	292949	2.949	1.235076	5971.415769
5	292892	2.949	1.224755	5968.328903
Mean	292698.6	2.9494	-----	5933.706366
SD	292.7453	0.001140175	-----	37.88228177
% RSD	0.100016	0.038657877	-----	0.638425285

Data of System Suitability for Domperidone

Injections	Area	Retention Time	Tailing Factor	USP Platelet Count
1	766960	4.195	1.097521	8673.795608
2	766634	4.193	1.10346	8798.743035
3	766196	4.189	1.115616	8635.001671
4	766634	4.189	1.11711	8840.161125
5	766951	4.188	1.118248	8753.813298
Mean	766675	4.1908	-----	8740.302947
SD	312.3316	0.00303315	-----	85.26578161
%RSD	0.040738	0.0723764	-----	0.975547211

Data of System Suitability for Cinnarizine

Observation:

The % RSD for the retention times and peak area of domperidone and cinnarizine were found to be less than 2%. The plate count and tailing factor results were found to be satisfactory and are found to be within the limit.

Linearity of test method:

A Series of solutions of Domperidone and Cinnarizine at concentration levels of 18,24,30,36 and 42 $\mu\text{g/ml}$ for dom and 24,32,40,48 and 56 $\mu\text{g/ml}$

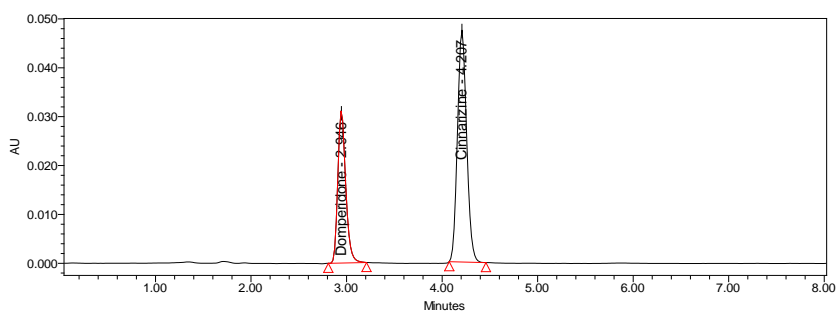
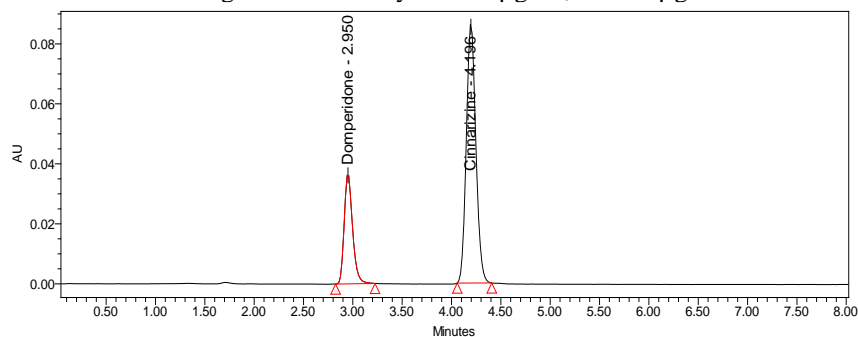
for cinn were prepared by pipetting out 0.6, 0.8, 1.0, 1.2 and 1.4 ml from the stock standard solution in to 10 ml volumetric flasks and diluted with diluent. Measure the peak area response of solution.

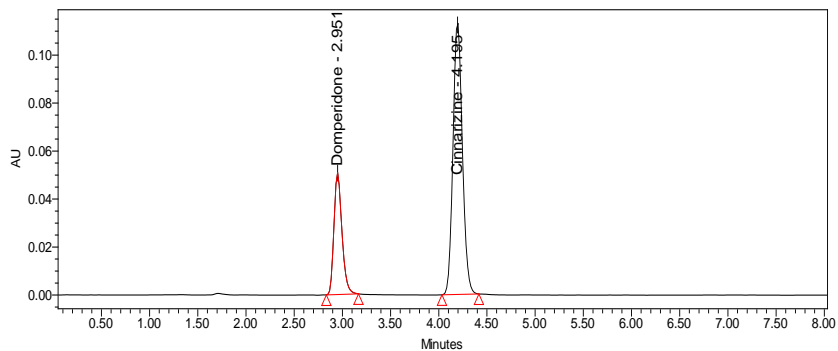
Acceptance criteria:

Correlation Coefficient should be not less than 0.9990.

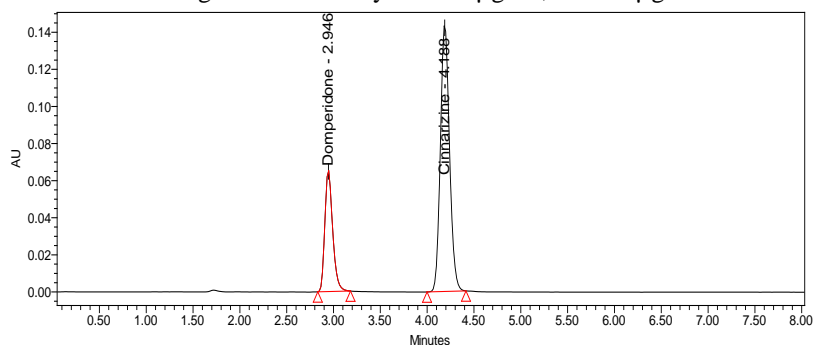
% of y- Intercept should be ± 2.0 .

% of RSD for level 1 and Level 6 should be not more than 2.0%.

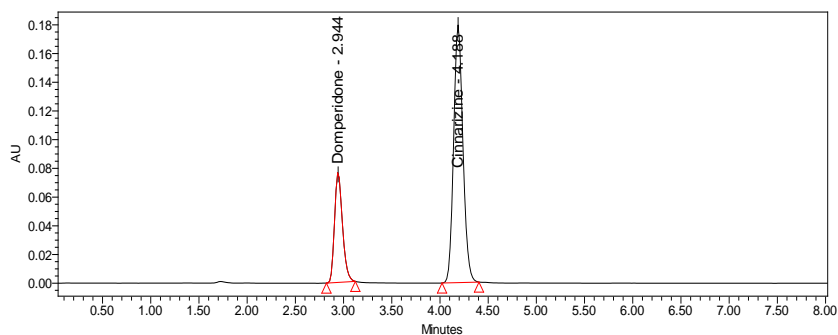
Chromatograms of linearity:Chromatogram for linearity dom-18 $\mu\text{g/ml}$; cinn-24 $\mu\text{g/ml}$ Chromatogram for linearity dom-24 $\mu\text{g/ml}$; cinn-32 $\mu\text{g/ml}$



Chromatogram for linearity dom-30µg/ml; cinn-40µg/ml



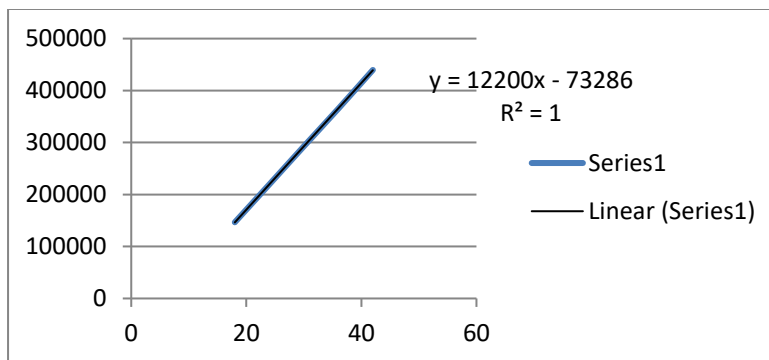
Chromatogram for linearity dom-36µg/ml; cinn-48µg/ml



Chromatogram for linearity dom-42µg/ml; cinn-56µg/ml

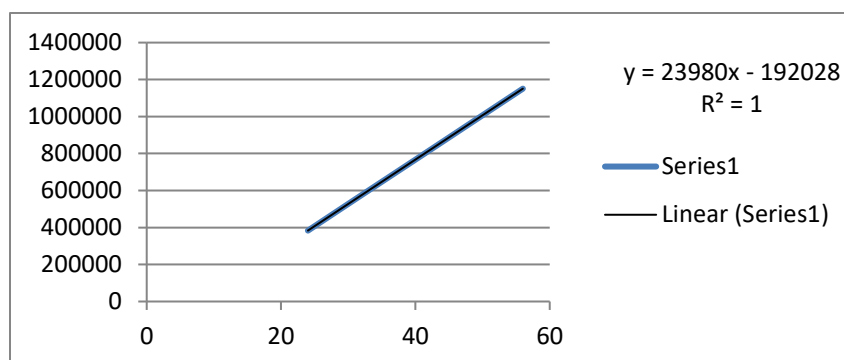
Concentration(µg/ml)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
18	146533	219819	18.01795	100.0997
24	219471	292757	23.99648	99.98531
30	292670	365956	29.99639	99.98798
36	365232	438518	35.9441	99.84472
42	439650	512936	42.04393	100.1046
Slope =12200	y-intercept= - 73286		Correlation coefficient=1	

(a) Data of Linearity for domperidone



Linearity plot for domperidone

Concentration($\mu\text{g/ml}$)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
24	383277	575305	23.9910342	99.96264
32	575809	767837	32.01989158	100.0622
40	766960	958988	39.9911593	99.9779
48	958987	1151015	47.99895746	99.99783
56	1150903	1342931	56.00212677	100.0038
Slope = 23980		y-intercept = -192028		Correlation coefficient=1

(b)Data of Linearity of Cinnarizine
Linearity plot for Cinnarizine

Observation: Correlation Coefficient was found to be 1 hence the method was found to be linear.

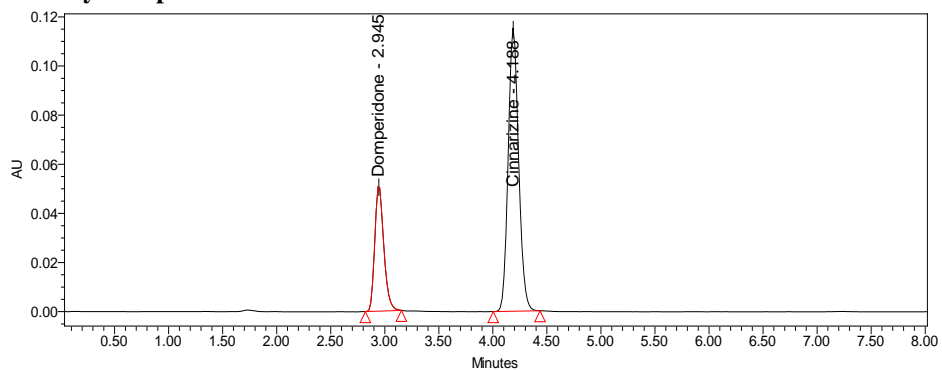
System precision:

Repeatability:

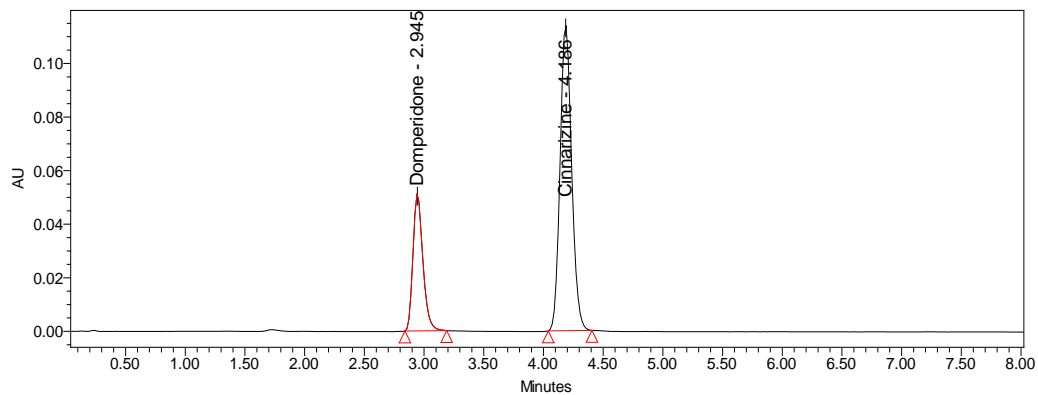
System precision: Standard solution prepared as per test method and injected five times. **Acceptance Criteria:** The % Relative Standard Deviation Of Individual Domperidone and Cinnarizine, From The five Units Should Be Not More Than 2.0%.

The Individual Assays Of Domperidone And Cinnarizine Should Be Not Less Than 98% And Not More Than 102.0%.

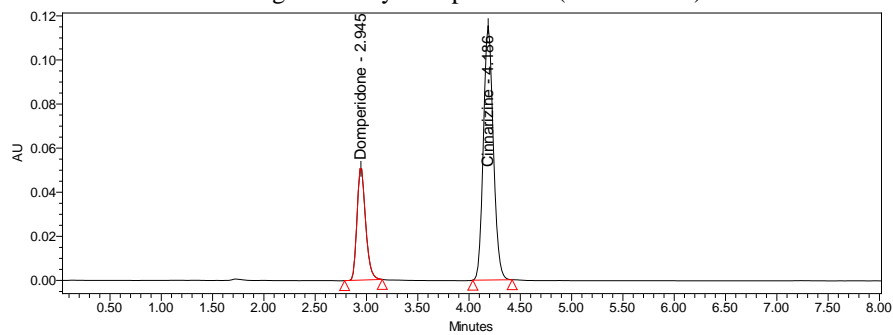
Chromatograms for System precision:



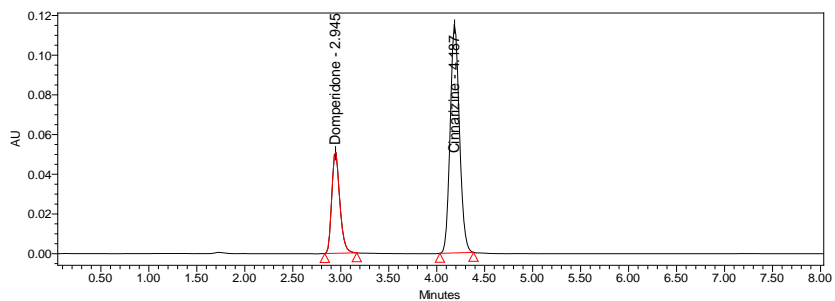
Chromatogram for system precision



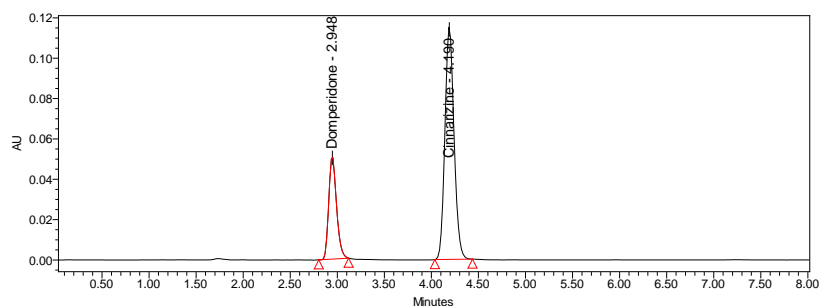
Chromatogram for system precision (standard-- 2)



: Chromatogram for system precision



Chromatogram for system precision



Chromatogram for system precision

Injections(30µg/ml)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	292483	365769	29.98107	99.93689
2	292026	365312	29.94361	99.81202
3	292954	366240	30.01967	100.0656
4	292443	365729	29.97779	99.92596
5	292228	365514	29.96016	99.86721
Mean	292426.8			99.92153
SD	346.9592			0.094798
%RSD	0.118648			0.094872

(a) Data of Repeatability (System precision) for Domperidone

Injections(40 µg/ml)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	766771	958799	39.98328	99.95819
2	766471	958499	39.97077	99.92692
3	766714	958742	39.9809	99.95225
4	766488	958516	39.97148	99.92869
5	766570	958598	39.9749	99.93724
Mean	766602.8			99.94066
SD	134.4273			0.014015
%RSD	0.017535			0.014023

(b) Data of Repeatability (System precision) for Cinnarizine

Observation:

The % Relative Standard Deviation of Individual Domperidone and Cinnarizine, from five units was found to be Not More Than 2.0%.

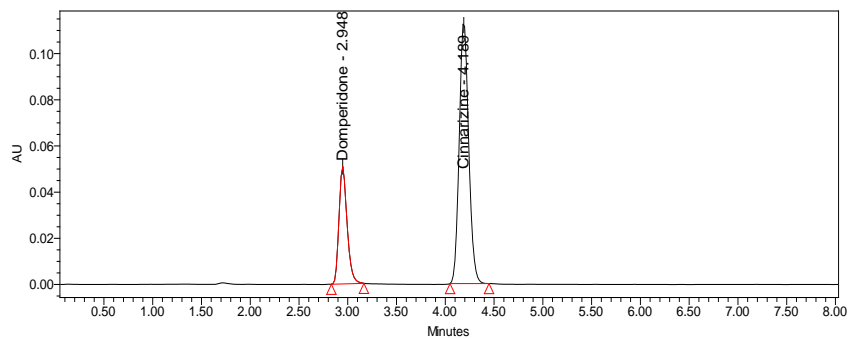
The Individual Assays of Domperidone and Cinnarizine were found to be Not Less Than 98% And Not More Than 102.0%.

Intermediate precision:

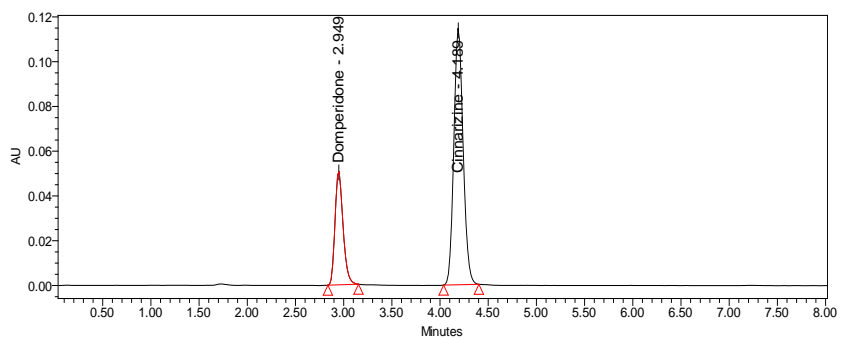
A study was conducted by two analysts as per test method

Acceptance criteria:

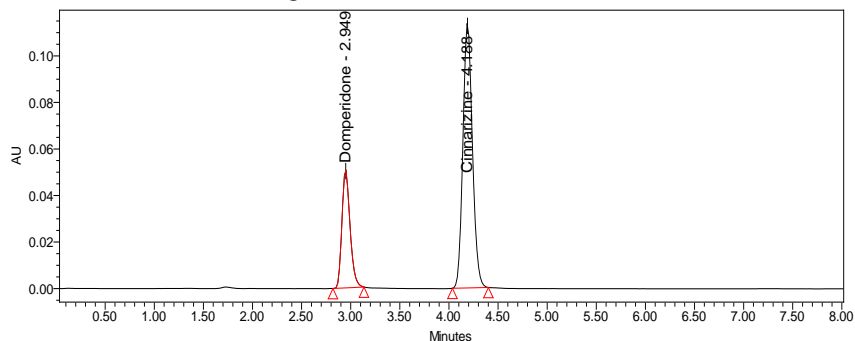
The individual assays of domperidone and cinnarizine should be not less than 98% and not more than 102% and %RSD of assays should be NMT2.0% by both analysts.

Chromatograms for Intermediate Precision:

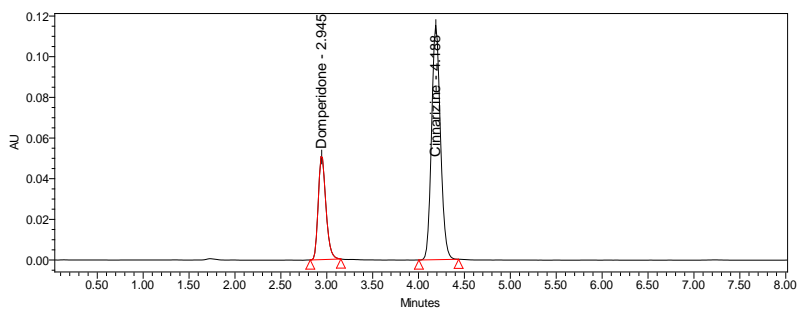
Chromatogram for Intermediate Precision-1



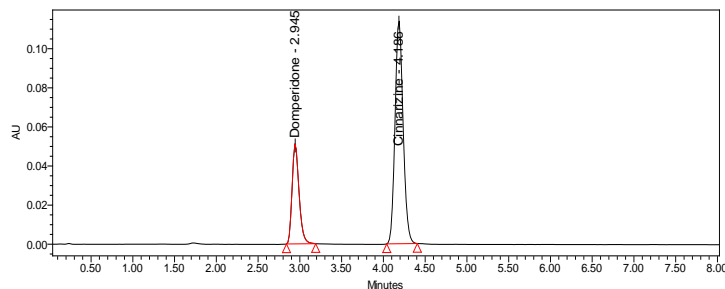
Chromatogram for Intermediate Precision-2



Chromatogram for Intermediate Precision-3



Chromatogram for Intermediate Precision-4



Chromatogram for Intermediate Precision-5

Injections(30 μ g/ml)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	292635	365921	29.99352	99.97842
2	292853	366139	30.01139	100.038
3	292953	366239	30.01959	100.0653
4	292885	366171	30.01402	100.0467
5	292362	365648	29.97115	99.90383
Mean	292737.6			100.0064
SD	241.3727			0.065949
%RSD	0.082454			0.065945

(a): Data of Intermediate precision for Domperidone

Injections(40 μ g/ml)	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	766662	958690	39.97873	99.94683
2	766952	958980	39.99083	99.97706
3	766634	958662	39.97756	99.94391
4	766364	958392	39.96631	99.91576
5	766413	958441	39.96835	99.92087
Mean	766605			99.94089
SD	234.2243			0.024419
%RSD	0.030553			0.024433

Data of Intermediate precision for Cinnarizine

OBSERVATION:

The individual assays of domperidone and cinnarizine were to be not less than 98% and not more than 102% and %RSD of assays were found to be NMT2.0% by both analysts.

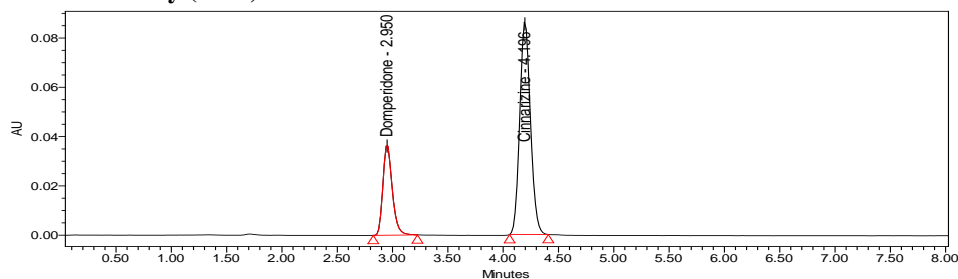
Accuracy:

A study of accuracy was conducted. Drug assay was performed in triplicate as per test method with equivalent amount of domperidone and cinnarizine into each volumetric flask for each spike level to get

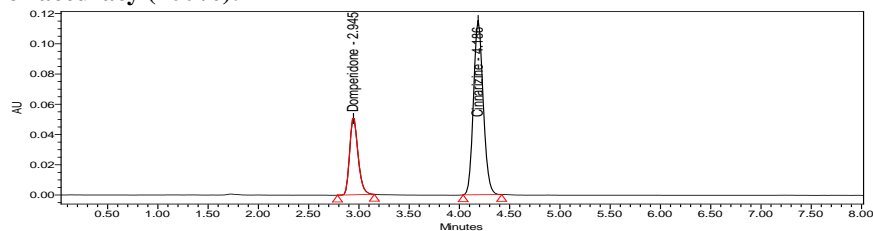
the concentration of domperidone and cinnarizine equivalent to 80%, 100%, and 120% of the labeled amount as per the test method. The average % recoveries of domperidone and cinnarizine were calculated.

Acceptance criteria:

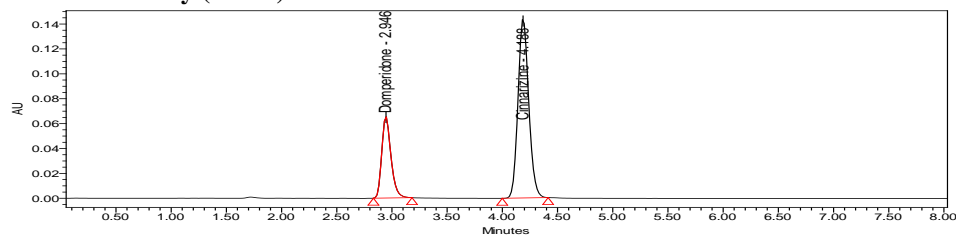
The mean % recovery of the domperidone and cinnarizine at each spike level should be not less than 98.0% and not more than 102.0% for both the drugs separately.

Chromatograms for accuracy (80%):

Chromatogram for standard-1

Chromatograms for accuracy (100%):

Chromatogram for standard-1

Chromatograms For Accuracy (120%):

Chromatogram for standard-1

Concentration % of spiked level	Amount added ($\mu\text{g/ml}$)	Amount found ($\mu\text{g/ml}$)	% Recovery	Statistical Analysis of % Recovery	
				MEAN	SD
80%	24	23.99647541	99.98531	99.98577	
80%	24	23.99663934	99.986		0.000394
80%	24	23.99663934	99.986		0.000394
100 %	30	30.02278689	100.076	100.0181	
100 %	30	30.01696721	100.0566		0.083931
100%	30	29.97655738	99.92186		0.083916
120%	36	35.94409836	99.84472	99.84517	
120%	36	35.9442623	99.84517		0.000455
120%	36	35.94442623	99.84563		0.000456

accuracy for domperidone

Concentration % of spiked level	Amount added ($\mu\text{g/ml}$)	Amount found ($\mu\text{g/ml}$)	% Recovery	Statistical Analysis of % Recovery	
80% Injection 1	32	32.019891	100.0622	MEAN	100.062
80% Injection 2	32	32.020016	100.0626		
80% Injection 3	32	32.019974	100.0624		
				%RSD	0.00019
100 % Injection 1	40	39.95972	99.89929	MEAN	99.9292
100 % Injection 2	40	39.97769	99.94422		
100% Injection 3	40	39.97769	99.94422		
				%RSD	0.02596
120% Injection 1	48	47.99896	99.99783	MEAN	99.9976
120% Injection 2	48	47.99883	99.99757		
120% Injection 3	48	47.99887	99.99765		
				%RSD	0.00013

accuracy for cinnarizine

observation:

The mean % recovery of the domperidone and cinnarizine at each spike level were found to be not less than 98.0% and not more than 102.0% for both the drugs separately.

Ruggedness:

System to System variability:

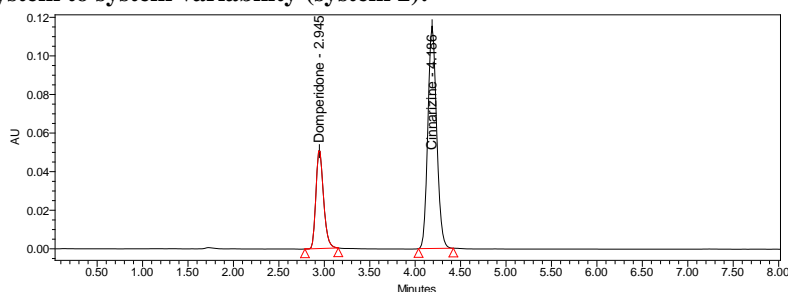
System to system variability study was conducted on different hplc systems, under similar conditions at different times. Five samples were prepared and each was analyzed as per test method.

Comparison of both the results obtained on two different hplc systems, shows that the assay test method is rugged for system to system variability.

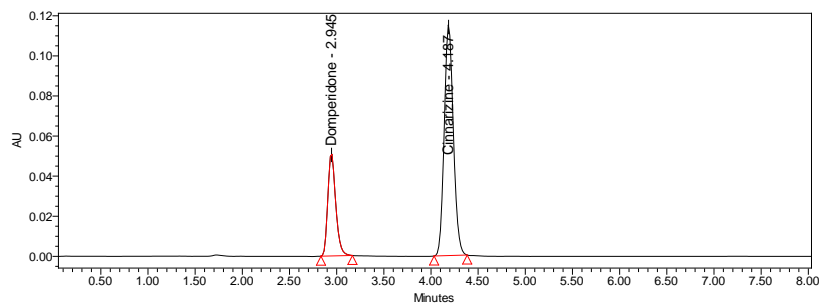
Acceptance criteria:

The % relative standard deviation of domperidone and cinnarizine from the five sample preparations should be not more than 2.0%. The % assay of domperidone and cinnarizine should be between 98.0%-102.0%.

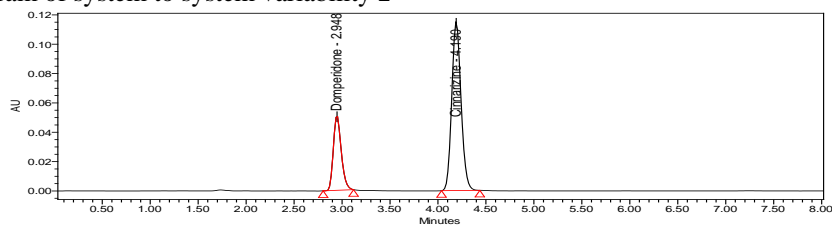
Chromatograms of system to system variability (system 2):



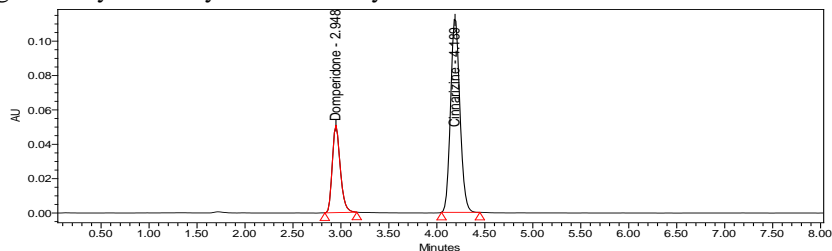
Chromatogram of system to system variability - 1



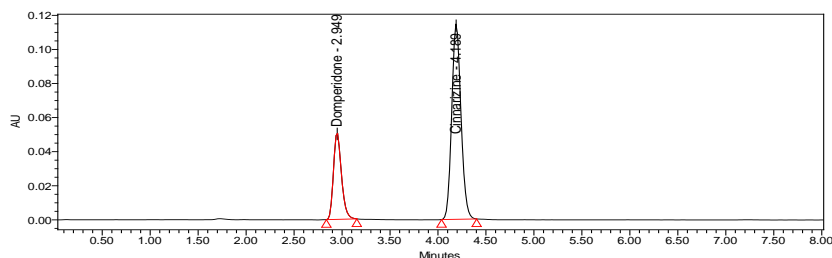
Chromatogram of system to system variability 2



Chromatogram of system to system variability - 3



Chromatogram of system to system variability - 4



Chromatogram of system to system variability - 5

Data of system to system variability (sample) Domperidone

injections	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	292670	365956	29.99639	99.98798
2	292770	366056	30.00459	100.0153
3	292212	365498	29.95885	99.86284
4	292949	366235	30.01926	100.0642
5	292892	366178	30.01459	100.0486
Mean	292698.6			99.99579
SD	292.7453			0.079985
%RSD	0.100016			0.079988

System-1

injections	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	292992	366278	30.02279	100.076
2	292921	366207	30.01697	100.0566
3	292428	365714	29.97656	99.92186
4	292853	366139	30.01139	100.038
5	292924	366210	30.01721	100.0574
mean	292823.6			100.0299
SD	226.5443			0.061897
%RSD	0.077365			0.061879

System-2

Data of system to system variability (sample) Cinnarizine:

injections	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	766960	958988	39.99116	99.9779
2	766634	958662	39.97756	99.94391
3	766196	958224	39.9593	99.89825
4	766634	958662	39.97756	99.94391
5	766951	958979	39.99078	99.97696
mean	766675			99.94819
SD	312.3316			0.032562
%RSD	0.040738			0.032579

System-1

injections	areas (y)	y-c	y-c/m (X- amount found)	% Assay
1	766206	958234	39.95972	99.89929
2	766637	958665	39.97769	99.94422
3	766637	958665	39.97769	99.94422
4	766525	958553	39.97302	99.93255
5	766905	958933	39.98887	99.97216
mean	766582			99.93849
SD	252.4896037			0.026323
%RSD	0.032937064			0.026339

System-2

Observation:

The % relative standard deviation of domperidone and cinnarizine from the five sample preparations should be not more than 2.0%. The % assay of domperidone and cinnarizine were found to be between 98.0%-102.0%.

Robustness:**Effect of variation of flow rate:**

A study was conducted to determine the effect of variation in flow rate. standard solution prepared as per the test method was injected into the HPLC system using flow rates 0.8ml/min, 1.0ml/min and 1.2ml/min. the system suitability parameters were evaluated and found to be within the limits for 0.8ml/min, 1.0ml/min and 1.2ml/min flow.

Domperidone and cinnarizine was resolved from all other peaks and the retention times were comparable

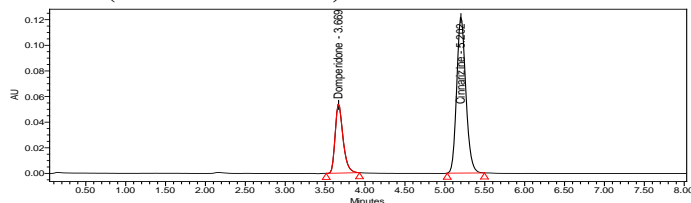
with those obtained for mobile phase having flow rates 1.0ml/min.

The system suitability should pass as per the test method at variation in flow rate. The Tailing Factor of domperidone and cinnarizine standards should be NMT 2.0 for Variation in Flow.

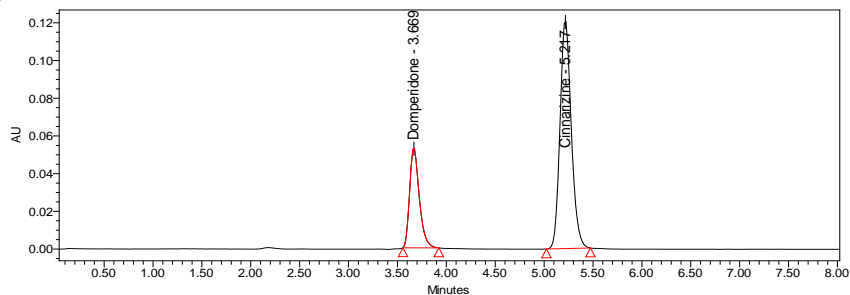
Acceptance criteria:

Chromatograms of robustness:

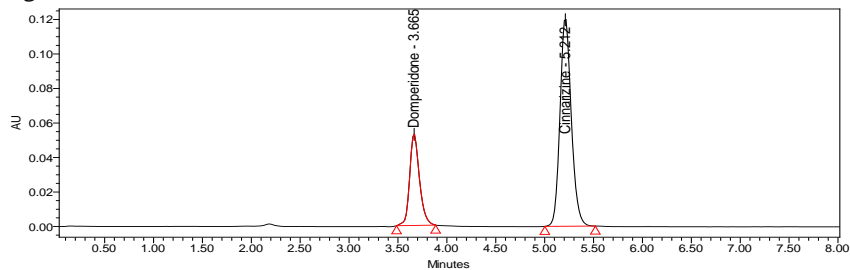
a) Effect of variation of flow rate (for 0.8 ml/min flow)



Chromatogram for robustness -1

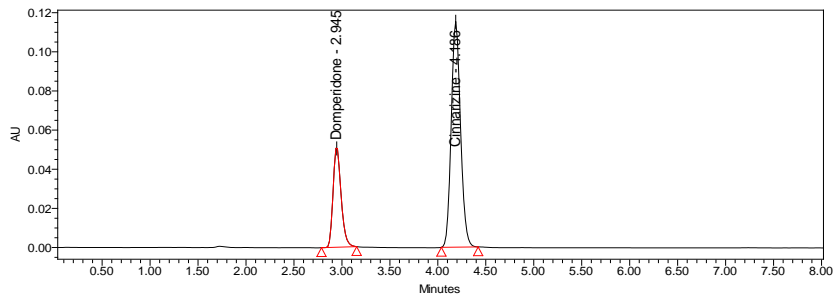


Chromatogram for robustness —2

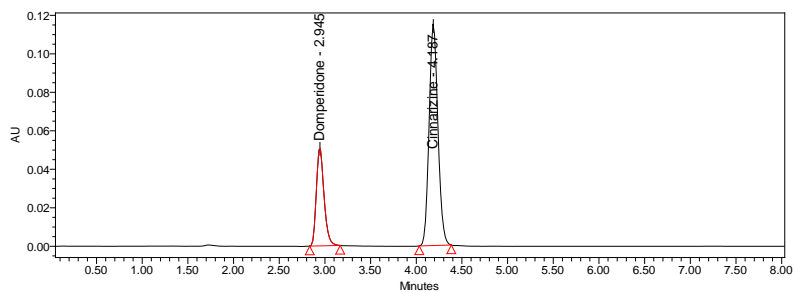


Chromatogram for robustness -- 3

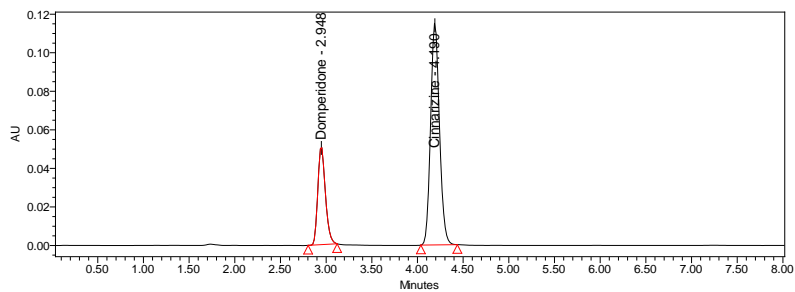
b) Chromatograms for 1ml/min



Chromatogram for robustness -1

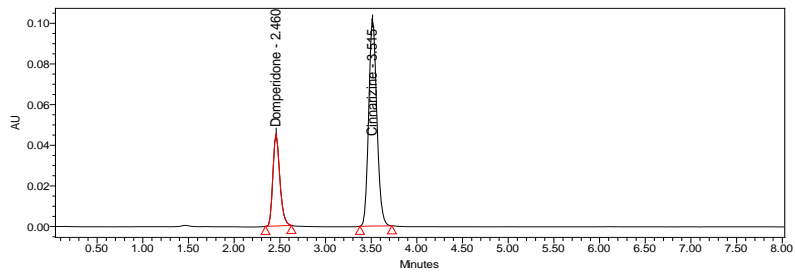


Chromatogram for robustness -2

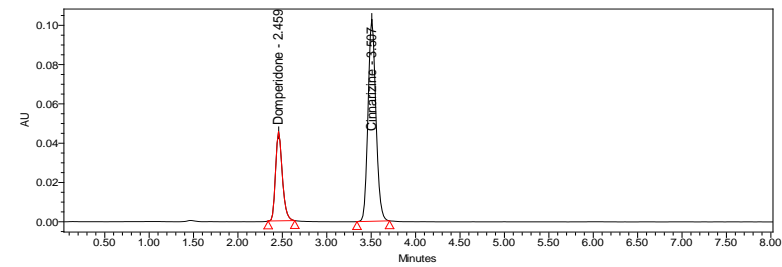


Chromatogram for robustness -3

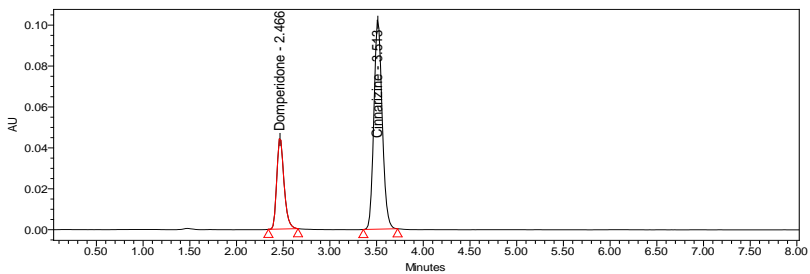
c) Chromatograms for 1.2ml/min:



Chromatogram for robustness -1



Chromatogram for robustness-2



Chromatogram for robustness- 3

Flow rate	Area	Statistical data	Tailing factor	Statistical data
0.8ml/min	369159	MEAN 367362.6667	1.321529	MEAN 1.279319
	364048	SD 2873.948909	1.322637	
	368881	%RSD 0.782319264	1.193790	
1 ml/min	292992	MEAN 292780.3 SD 307.1878 %RSD 0.104921	1.245346	MEAN 1.231116
	292921		1.239634	
	292428		1.208367	
1.2ml/min	238117	MEAN 236994.3	1.215669	MEAN 1.234445
	238605	SD 2379.678	1.236544	
	234261	%RSD 1.004108	1.251121	

Data for Effect of variation in flow rate for Domperidone

Flow rate	Area	Statistical data	Tailing factor	Statistical data
0.8ml/min	968921	MEAN 968422.3	1.159707	MEAN 1.149312
	967603	SD 715.1233	1.147903	
	968743	%RSD 0.073844	1.140327	
1 ml/min	766206	MEAN 766493.3333 SD 248.8379661 %RSD 0.032464466	1.119963	MEAN 1.119778
	766637		1.116445	
	766637		1.122927	
1.2ml/min	631130	MEAN 632290.3333	1.137367	MEAN 1.128949
	632154	SD 1234.160578	1.116291	
	633587	%RSD 0.195188905	1.133190	

Data for Effect of variation in flow rate for Cinnarizine:

Observation:

From the observation it was found that the system suitability parameters were within limit at variable flow rate since the Tailing Factor of domperidone and cinnarizine is NMT 2.0.

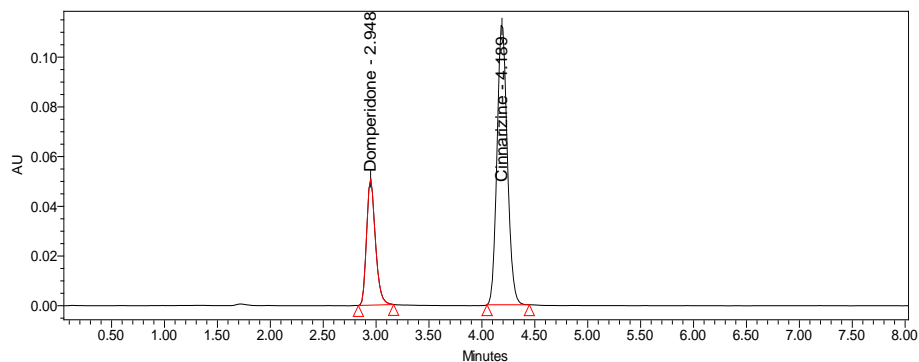
LIMIT OF DETECTION AND LIMIT OF QUANTITATION (LOD and LOQ):

From the linearity plot the LOD and LOQ are calculated:

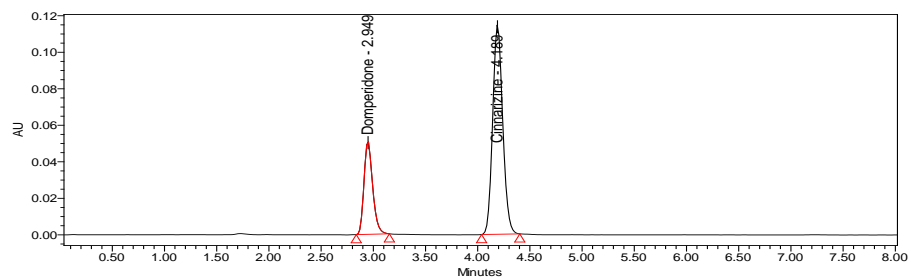
$$\text{LOD} = 3.3 * \sigma/m$$

$$\text{LOQ} = 10 * \sigma/m$$

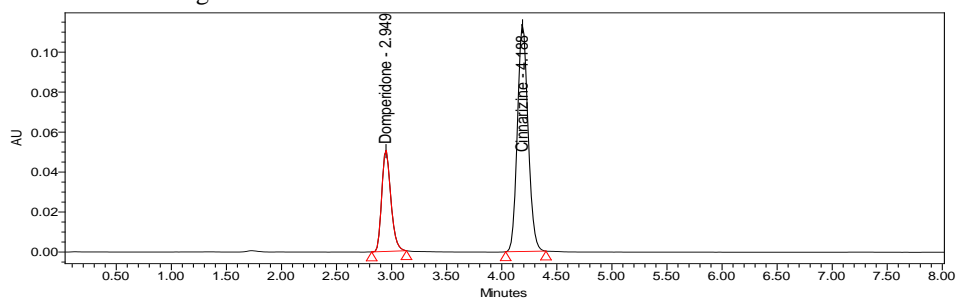
Chromatograms for LOD



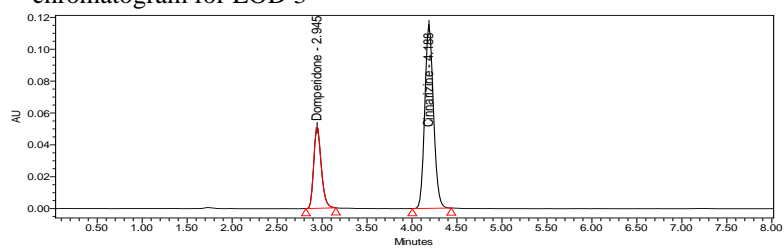
chromatogram for LOD 1



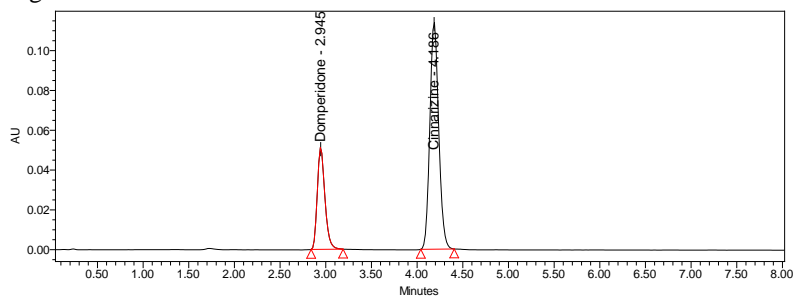
chromatogram for LOD 2



chromatogram for LOD 3



chromatogram for LOD 4



chromatogram for LOD 5

injections	Area
1	292352
2	293638
3	290428
4	296385
5	295208
Mean	293602.2
SD	2343.203
LOD	1.055929
LOQ	3.199785

LOD & LOQ for Domperidone

injections	Area
1	763937
2	768953
3	764985
4	773637
5	767692
mean	767840.8
SD	3816.094627
LOD	0.656951968
LOQ	1.990763538

LOD & LOQ for Cinnarizine

Observation:

The LOD of domperidone and cinnarizine were found to be 1.055929 and 0.656951968 respectively.

The LOQ of domperidone and cinnarizine were found to be 3.199785 and 1.990763538 respectively.

For system suitability the % RSD for the peak area of domperidone and cinnarizine were found to be 0.100016 and 0.040736 respectively. For regression coefficient for both the drugs in linearity was found to be 1, Y- intercept for domperidone and cinnarizine were found to be -73286 and -92028 respectively. The individual % assays of domperidone and cinnarizine for system precision were found to be between 98-102. The % RSD of domperidone and cinnarizine were found to be 0.094872 and 0.014023 respectively. In intermediate precision the individual % assays of domperidone and cinnarizine were found to be between 98 to 102. The % RSD of domperidone and cinnarizine of analyst 1 were found to be 0.065945 and 0.024433 respectively. The % RSD of domperidone and cinnarizine of analyst 2 were found to be 0.082395 and 0.030517 respectively. For accuracy the percentage mean recovery of 80 % domperidone and cinnarizine were found to be 99.98577 and 100.062 respectively, 100% domperidone and cinnarizine were found to be 100.0181 and 99.9292 respectively, 120 % domperidone and cinnarizine were found to be 99.84517 and 99.9976 respectively. For Ruggedness for system-1 the %RSD of domperidone and cinnarizine were found to be 0.079988 and 0.032579 respectively and % assay of domperidone and cinnarizine were found to be 99.99 and 100.07 respectively. For system-2 the %RSD of domperidone and cinnarizine were found to be 0.061879 and 0.026339 respectively and % assay of domperidone and cinnarizine were found to be 99.94

and 99.93 respectively. The LOD of domperidone and cinnarizine were found to be 1.055929 and 0.656951968 respectively. The LOQ of domperidone and cinnarizine were found to be 3.199785 and 1.990763538 respectively.

From the above data the developed RP-HPLC method for the simultaneous estimation of domperidone and cinnarizine was found to be linear, accurate, robust, accurate and precise from the above-mentioned data. Thus the developed method can be used in the routine analysis for the simultaneous estimation of domperidone and cinnarizine.

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