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Research Article

HPLC Method Development and Validation for Estimation of Ivabradine and Carvedilol Bulk and Dosage Form by using QBD Approach

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ABSTRACT

Attempts were made to develop an RP-HPLC method for the simultaneous estimation of Carvedilol & Ivabradine from Tablet. For the RP Agilent Tech. Gradient System with Auto injector, UV (DAD) & Gradient Detector Reverse Phase (Waters) C18 column (4.6mm x 100mm; 2 μ m), a 20 μ l injection loop and UV730D Absorbance detector and running chemstation 10.1 software. RP-HPLC method was developed by implementing QbD methodology on analytical column- Reversed Phase Agilent C18 (250mm \times 4.6mm \times 5 μ m), with mobile phase Methanol: (0.1% OPA) Water (42.4:57.6 v/v). The flow rate used was 0.6 mL /min, and UV detection was carried out at 275 nm. The retention time for Carvedilol & Ivabradine was found to be 5.282 min & 6.808 min respectively. Systematic approach was utilized to develop an efficient and robust method which includes beginning with the determination of target profile characteristics, risk assessment, design of experiment and validation. The study was done by using 22 full fraction response surface designs. In this study interaction of 2 factors; flow rate, mobile phase composition at 2 levels. Method Operable Design Region (MODR) was developed to achieve the region of operation for drug and Ivabradine. The proposed HPLC method has also been evaluated for accuracy, precision and robustness and proved to be convenient and effective for the quality control of Carvedilol & Ivabradine.


INTRODUCTION

Quality is the heart of pharmaceutical industry. Quality is one of the fundamental criteria in

addition to safety and efficacy for any entity to be qualified and approved as a drug. For ensuring consistency of performance of pharmaceutical products and systems, the recent emphasis has

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been on building the quality rather than merely testing it. This philosophy forms the basis of Quality by Design (QbD). It is a practical implementation of some underlying concepts and principles outlined by the FDA's Pharmaceutical CGMPs for the twenty first century and Quality by Design (QbD) initiatives. [1] ICH Q9 on quality risk management develops the principles and some of the tools of quality risk management for assessment, control, communication, and review of the risks of the quality of the medicinal product.[2,3] QbD is defined as "a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management".[4] The separation criterion S was recently introduced and was defined as the difference between the retention times measured at the beginning of the second peak and at the end of the first peak of the critical pair. Moreover, even if S and RS are highly correlated, computation of S is easier and its associated uncertainty is lower. [5] An experimental design is an experimental set-up to simultaneously evaluate several factors at given numbers of levels in a predefined number of experiments [6]

Regulatory Aspects Of QBD

ICH guideline: QbD ultimately helps to implement Q8 and Q9. Recently, the US Food and Drug Administration introduced quality by design (QbD) as a fundamental pharmaceutical quality model to be considered in the development of pharmaceutical products and processes [7]. FDA Perspective: QbD leads to the establishment of the Design Space (DS), defined as the multidimensional combination and interaction of input variables and process parameters that have been demonstrated to provide assurance of quality. According to this definition, DS should be

characterized by multivariate techniques; therefore, the use of Design of Experiments (DoE) has emerged as a fundamental activity for implementing QbD[7].

Element Of QBD In Analytical Method

Analytical Target Profile (ATP)

The Analytical Target Profile (ATP) is a set of criteria that define what will be measured (e.g. the level of a specified impurity) and the performance criteria to be achieved by the measurement (e.g. accuracy, precision and range), but without specifying the method itself. [8]

Critical Quality Attribute (CQA)

CQA is a physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality [9]

Method Design

Method design is prepared for appropriate availability of material and setting various experimental conditions. In this the reagents required are made available. Regional and geographical conditions are taken into consideration. Feasibility of instruments is checked and experimental design is prepared [10]. Method design may be repeated or modified as and when required throughout the life cycle. Thorough understanding of design intent will form a better Method design [11]

Critical Process Parameters (CPP)

Critical Process Parameters (CPPs) are defined as parameters whose variability have an impact on a CQA and therefore should be monitored or controlled to ensure the process produces the

desired quality, and this statement can be fit perfectly to analytical method [12]

Name of Drug	Drug Supplier
Carvedilol	Swapnroop drug and pharmaceutical
Ivabradine	Swapnroop drug and pharmaceutical

MATERIAL AND METHODS

Materials/ Chemicals:

List of reagents & chemicals used

Drug and Drug Supplier

Sr. No.	Name of chemicals	Manufacturer.
1	Acetonitrile (HPLC grade)	Merck Ltd., India
2.	Ethanol (HPLC grade)	Merck Ltd., India
3.	0.1% OPA (HPLC grade)	Merck Ltd., India
4.	water (HPLC grade)	Merck Ltd., India

Instruments and Equipment's

	Name of Instrument	Company Name
1	HPLC Instrument	Agilent Tech. Gradient System with Auto injector
2	UV-Spectrophotometer	Analytical Technologies Limited
3	Column(C ₁₈)	AgilentC ₁₈ (250mmX 4.6mm,5µm)
4	pH meter	VSI pH meter (VSI 1-B)
5	Balance	WENSAR™ High Resolution Balance.
6	Sonicator	Ultrasonics' electronic instrument

Experimental WORK

Result of different trials

High Performance Liquid Chromatography (Hplc)
Method for Analysis of Carvedilol and Ivabradine

Fig. No.	Column used	Mobile phase, Flow Rate and Wavelength	Inj. Vol.	Observation	Conclusion
1	C ₁₈ (AGILENT) (250×4.6mm, 2µ)	50% Methanol: 50% buffer 275 nm, Flow rate 0.7ml.	20 µl	Sharpe peaks were not obtained	Hence rejected
2.	C ₁₈ (AGILENT) (250×4.6mm, 2µ)	60%Methanol: 40% Buffer 275 nm, Flow rate 0.7ml.	20 µl	Sharpe peaks were not obtained	Hence rejected
3	C ₁₈ ((AGILENT)(250×4.6mm, 2µ)	45 % Methanol: 55% Water (0.1% OPA) 275 nm, Flow rate 0.7ml.	20 µl	Sharpe and resolved peaks was obtained	Hence selected
4	C ₁₈ (AGILENT)(250 ×4.6mm, 2µ)	80% Methanol 20% Water (0.1% OPA) 275 nm, Flow rate 0.7ml.	20 µl	Sharpe peaks were not obtained	Hence rejected
5	C ₁₈ (AGILENT)(250×4.6mm, 2µ)	60%Methanol :40% Water (0.1% OPA)-275 nm , Flow rate 0.7ml	20 µl	Sharpe peaks were not obtained	Hence rejected
6	C ₁₈ (AGILENT)(250×4.6mm, 2µ)	90%ACN :10% Water (0.1% OPA)-275 nm , Flow rate 0.7 ml	20 µl	Sharpe peaks were not obtained.	Hence rejected



7	C ₁₈ (AGILENT)(250×4.6mm, 2μ)	50% ACN :50% Water (0.1% OPA)-275 nm , Flow rate 0.6 ml	20 μl	Sharpe peaks were not obtained	Hence rejected
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DOE Table central composite design (CCD)

	Factor 1	Factor 2
Run	A: Mobile Phase	B: Flow Rate
	%	ML/MIN
1	40	0.7
2	40	0.7
3	40	0.7
4	40	0.558579
5	40	0.7
6	35	0.6
7	40	0.7
8	45	0.6
9	45	0.8
10	32.9289	0.7
11	35	0.8
12	40	0.841421
13	47.0711	0.7

Chromatographic conditions (HPLC) details used during method Development.

1.	HPLC	Agilent Tech. Gradient System with Auto injector
2.	Software	Chemstation 10.1
3.	Column	(Agilent) C18 column (4.6mm x 250mm)
4.	Particle size packing	5 μm
5.	Stationary phase	C18 (Agilent)
6.	Mobile Phase	Methanol: water (0.1 % OPA) 42.4:57.6%V/V
7.	Detection Wavelength	275 nm
8.	Flow rate	0.6 ml/min
9.	Temperature	Ambient
10.	Sample size	20 μl
11.	Ph	3.2
12.	Run Time	15 min
13.	Filter paper	0.45 μm

Preparation of linearity solution: A series of standard preparations of working standard of were prepared.

Carvedilol standard stock solution: (Stock I)

6 mg of Carvedilol (CVD) - dissolved Methanol in a 10ml volumetric flask -volume made up to 10.0 ml to produce a solution of 600 ug/ml.

Ivabradine standard stock solution: (Stock II)

10 mg of Ivabradine (IBD) - dissolved in Methanol in 10 ml volumetric flask -volume made up to 10.0 ml to produce a solution of 1000 ug/ml.

Table of Linearity

Concentration (µg/mL)	
Carvedilol	Ivabradine
6	10
12	20
18	30
24	40
30	50

Table of Accuracy

Sample	Amount Added (mg)	
	Carvedilol	Ivabradine
Accuracy 80%	4.8	4
Accuracy 100%	6	5
Accuracy 120%	7.2	6

Detection Limit

Based on the S.D. of the response and the slope of calibration curve, the detection limit (DL) was calculated as, $DL = 3.3\sigma/s$

Where,

σ = the S.D. of the y-intercepts of regression lines.

S = the slope of the calibration curve.

Quantitation Limit

Based on the S.D. of the response and the slope of calibration curve, the quantitation limit (QL) was calculated as, $QL = 10 \sigma/s$

Where,

σ = the S.D. of the y-intercepts of regression lines.

S = the slope of the calibration curve.

RESULT AND DISCUSSION

Preliminary studies on Carvedilol and Ivabradine.

Melting point:

Drug	Melting point
Carvedilol	113-119 °C
Ivabradine	194-196°C

Solubility:

Carvedilol

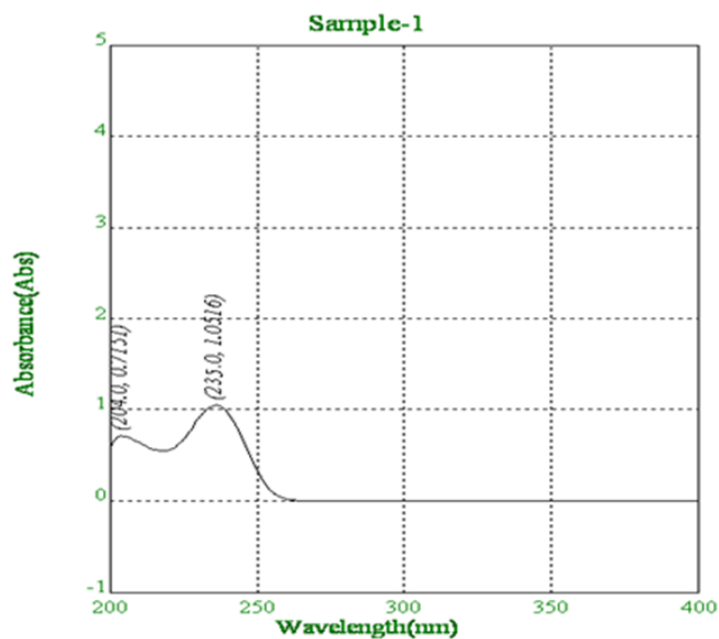
Solvents	Observation	Inference
Water	Sparingly soluble	Very slightly soluble
Methanol	Soluble	soluble
Ethanol	Freely soluble	Soluble

Ivabradine

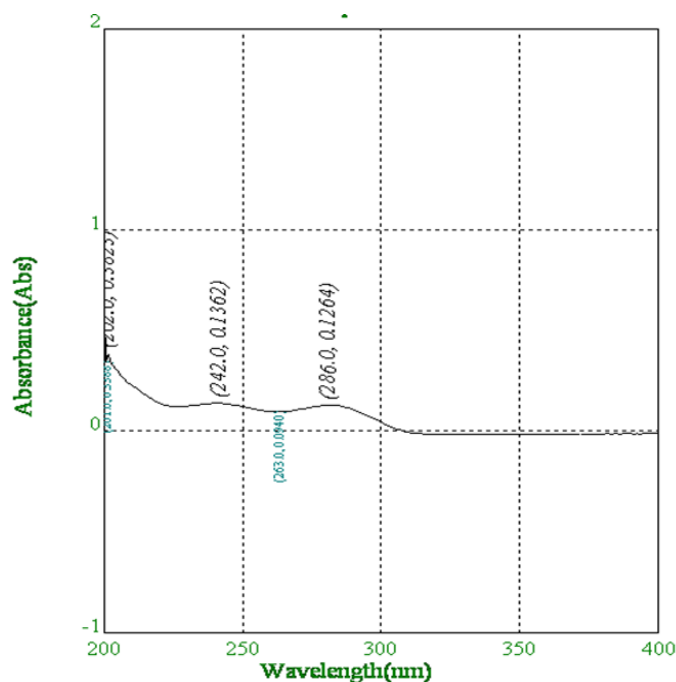
Solvents	Observation	Inference
Water	Sparingly soluble	Very slightly soluble
Methanol	Soluble	Soluble
Ethanol	Freely soluble	Soluble
Ethyl Acetate	Insoluble	Insoluble

UV Spectroscopy

UV absorption of 6 and 10 µg/mL solution of Carvedilol and Ivabradine in Methanol was generated and absorbance was taken in the range of 200-400 nm. 235 nm and 286nm, λ_{max} of Carvedilol and Ivabradine in Methanol was found to be 235 nm and 286 nm respectively.



UV Spectrum of Carvedilol



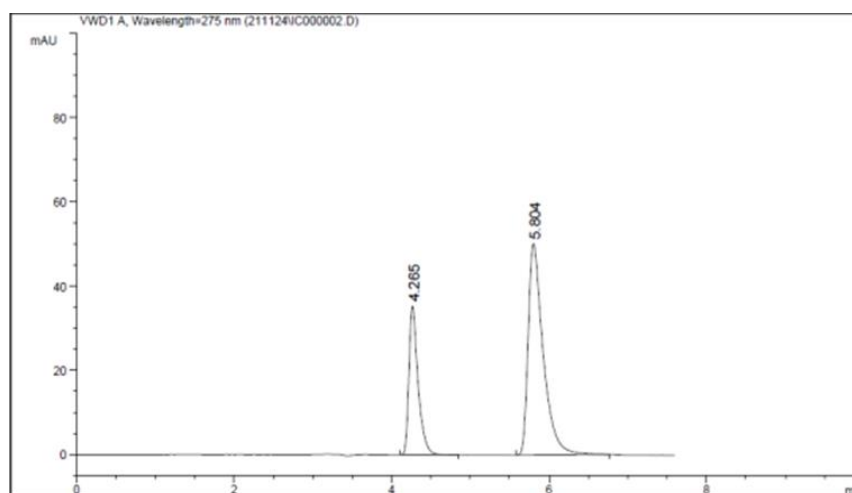
UV spectrum of Ivabradine

Chromatographic behaviour of Carvedilol and Ivabradine mobile phase of various compositions.

Fig. No.	Column used	Mobile phase, Flow Rate and Wavelength	Inj. Vol.	Observation	Conclusion
1	C ₁₈ (AGILENT)(250 ×4.6mm, 2μ)	50% Methanol: 50% buffer 275 nm, Flow rate 0.7ml.	20 μl	Sharpe peaks were not obtained	Hence rejected

2.	C ₁₈ (AGILENT)(250 ×4.6mm, 2μ)	60%Methanol: 40% Buffer 275 nm, Flow rate 0.7ml.	20 μl	Sharpe peaks were not obtained	Hence rejected
3	C ₁₈ ((AGILENT)(250×4.6mm, 2μ)	45% Methanol: 55% Water (0.1% OPA) 275 nm, Flow rate 0.7ml.	20 μl	Sharpe and resolved peaks was obtained	Hence selected
4	C ₁₈ (AGILENT)(250 ×4.6mm, 2μ)	80% Methanol 20% Water (0.1% OPA) 275 nm, Flow rate 0.7ml.	20 μl	Sharpe peaks were not obtained	Hence rejected
5	C ₁₈ (AGILENT)(250×4.6mm, 2μ)	60%Methanol :40% Water (0.1% OPA)-275 nm , Flow rate 0.7ml	20 μl	Sharpe peaks were not obtained	Hence rejected
6.	C ₁₈ (AGILENT)(250×4.6mm, 2μ)	90%ACN :10% Water (0.1% OPA)-275 nm , Flow rate 0.7 ml	20 μl	Sharpe and resolved peaks was obtained	Hence selected
7	C ₁₈ (AGILENT)(250×4.6mm, 2μ)	50% ACN :50% Water (0.1% OPA)-275 nm , Flow rate 0.7 ml	20 μl	Sharpe peaks were not obtained	Hence rejected

Chromatogram of Final Trial:



Representative Chromatogram of Carvedilol and Ivabradine using 45 % Methanol+ 55 0.1% OPA - 275 nm- 0.7 ML- 20 MCG as mobile phase.

Chromatogram of Carvedilol and Ivabradine using 45% Methanol+ 55 % 0.1% OPA

Sr. No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.265	283.32419	7639	0.59	-
2	5.804	660.48065	5209	0.52	5.94

High Performance Liquid Chromatography (Rp-hplc) Method for Analysis of Carvedilol and Ivabradine:

Chromatogram of QBD Trial-1

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.736	219.17020	5523	0.69	-
2	6.379	974.44336	6958	0.71	5.85



Chromatogram of QBD Trial-3

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.231	218.98126	5550	0.68	-
2	6.376	973.15372	6935	0.72	5.83

Chromatogram of QBD Trial-4

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	6.027	281.07898	5915	0.68	-
2	8.085	1251.35791	7334	0.72	5.95

Chromatogram of QBD Trial-5

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.734	219.11046	5642	0.68	-
2	6.366	974.35797	7104	0.71	5.88

Chromatogram of QBD Trial-6

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.949	251.18285	4590	0.67	-
2	8.801	1147.20679	6347	0.70	7.18

Chromatogram of QBD Trial -7

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.735	219.40160	5540	0.69	-
2	6.377	974.16626	6926	0.71	5.85

Chromatogram of QBD Trial-8

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.159	260.40240	6409	0.68	-
2	6.472	1144.22437	7723	0.70	4.75

Chromatogram of QBD Trial-9

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	3.848	194.35286	5824	0.68	-
2	4.838	855.53400	6941	0.70	4.56

Chromatogram of QBD Trial-10

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.454	215.14786	4962	0.71	-
2	8.456	986.01636	7006	0.76	8.40

Chromatogram of QBD Trial-11

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.553	188.25652	5219	0.71	-
2	6.733	857.96375	6876	0.74	7.55

Chromatogram of QBD Trial-12

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	3.939	182.91982	5471	0.69	-
2	5.304	813.2002	6775	0.72	5.79

Chromatogram of QBD Trial-13

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	4.301	223.04071	6221	0.68	-
2	5.285	979.24805	7034	0.70	4.18

Statistical data analysis (DOE).

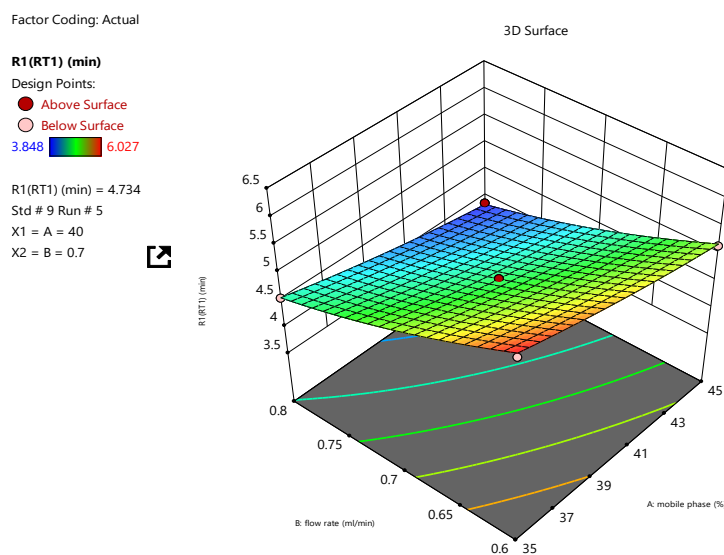
The layout of actual design of DOE with the subsequent response results are shown in table

	Factor 1	Factor 2	Response 1	Response 2	Response 3
Run	A: Mobile Phase	B: Flow Rate	R1(RT1)	R2(AREA1)	R3(TP1)
	%	ML/MIN	MIN	AUC	TP
1	40	0.7	4.736	219.1702	5523
2	40	0.7	4.737	219.4483	5524
3	40	0.7	4.731	218.9812	5550
4	40	0.558579	6.027	281.0789	5915
5	40	0.7	4.734	219.1104	5642
6	35	0.6	5.949	251.1828	4590
7	40	0.7	4.735	219.4016	5540
8	45	0.6	5.159	260.4024	6409
9	45	0.8	3.848	194.3528	5824
10	32.9289	0.7	5.454	215.1478	4962
11	35	0.8	4.555	188.2565	5219
12	40	0.841421	3.939	182.9198	5471
13	47.0711	0.7	4.301	223.0407	6221

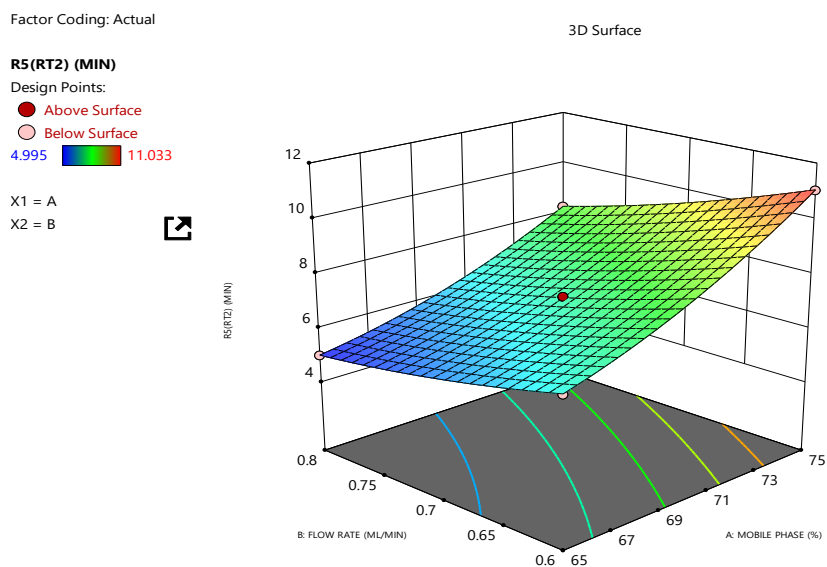
Layout of Actual Design of DOE of Carvedilol

	Factor 1	Factor 2	Response 5	Response 6	Response 7	Response 8
Run	A: Mobile Phase	B: Flow Rate	R5(RT2)	R6(AREA2)	R7(TP2)	R8(TF2)
	%	ML/MIN	MIN	AUC	TP	TF
1	40	0.7	6.379	974.4433	6958	0.71
2	40	0.7	6.374	976.1696	6947	0.71
3	40	0.7	6.376	973.1537	6935	0.71
4	40	0.558579	8.085	1251.3579	7334	0.72
5	40	0.7	6.366	974.3579	7104	0.72
6	35	0.6	8.801	1147.2067	6347	0.71
7	40	0.7	6.377	972.1662	6926	0.70
8	45	0.6	6.472	1144.2243	7723	0.71
9	45	0.8	4.838	855.5340	6941	0.70
10	32.9289	0.7	8.456	986.0163	7006	0.70
11	35	0.8	6.733	857.96	6876	0.76
12	40s	0.841421	5.304	813.2002	6775	0.74
13	47.0711	0.7	5.285	979.2480	7034	0.72

Layout of Actual Design of DOE of Ivabradine 3D Diagram for DOE of RT of Carvedilol against Mobile phase and Flow rate.



3D Diagram for DOE of RT of Ivabradine against Mobile phase and Flow rate



Optimization solution:

Analytical column: Agilent C18 Column 250 mm x 4.6mm, 5µm particle size).

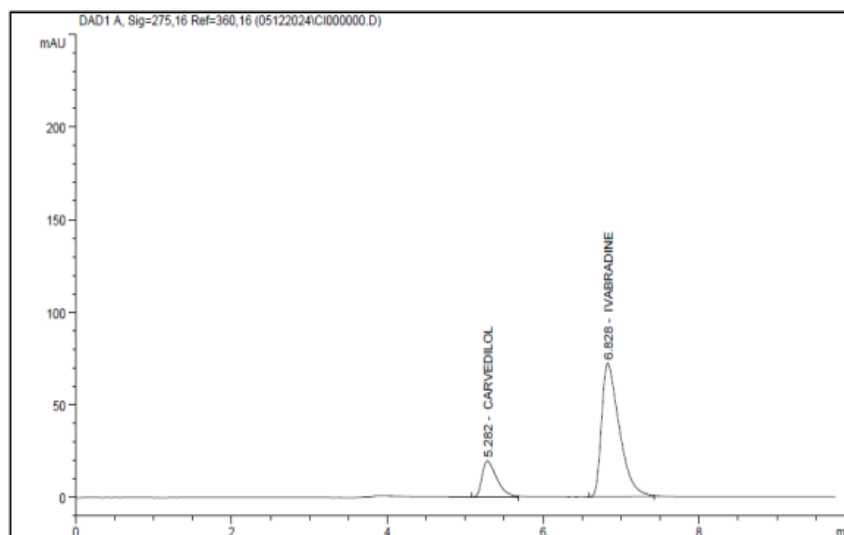
Injection volume: 20µl

Flow rate: 0.6 ml/min

Mobile phase: Methanol+0.1% OPA (42.4+57.6 % v/v)

Detection: 275 nm

Run Time: 15 min



Chromatogram of standard Combination of Carvedilol and Ivabradine

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.282	245.04359	3952	0.91	-
2	6.828	1086.31421	4484	0.90	4.15

Calibration experiment

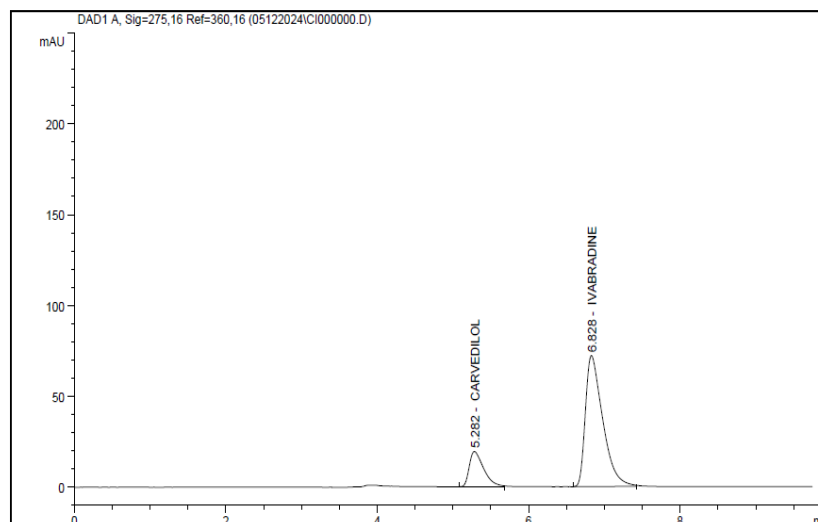
Linearity data for Carvedilol

Method	Conc. µg/ml	Peak area(µV.sec)		Average peak area (µV.sec)	S.D. of Peak Area	% RSD of Peak Area
		1	2			
RP-HPLC Method	6	245.0400	245.8873	245.4637	0.60	0.24
	12	453.7372	453.4337	453.5855	0.21	0.05
	18	668.6567	667.5858	668.1213	0.76	0.11
	24	861.3100	861.9387	861.6244	0.44	0.05
	30	1090.4133	1102.5859	1096.4996	8.61	0.78
Equation		$y = 35.16 x - 32.02$				
R ²		0.999				

Linearity data for Ivabradine

Method	Conc. µg/ml	Peak area(µV.sec)		Average peak area (µV.sec)	S.D. of Peak Area	% RSD of Peak Area
		1	2			
RP-HPLC Method	10	1086.3100	1086.6042	1086.46	0.21	0.02
	20	1995.6126	1994.2733	1994.94	0.95	0.05
	30	2952.5422	2950.2927	2951.42	1.59	0.05
	40	3781.6247	3788.5730	3785.10	4.91	0.13
	50	4802.4902	4841.2255	4821.86	27.39	0.57
Equation		$y = 92.61x + 149.6$				
R ²		0.999				

Linearity

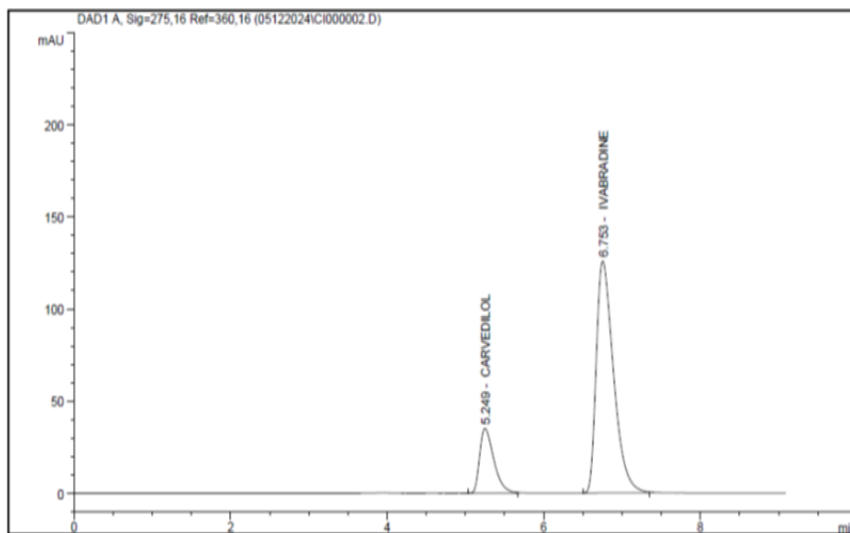


Chromatogram of Linearity (6+10 mcg)

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.282	245.04359	3952	0.91	-

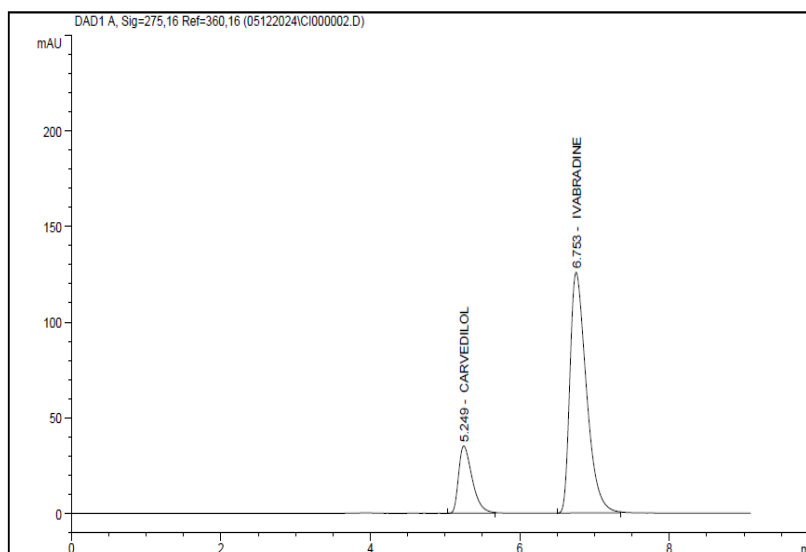


2	6.828	1086.31421	4484	0.90	4.15
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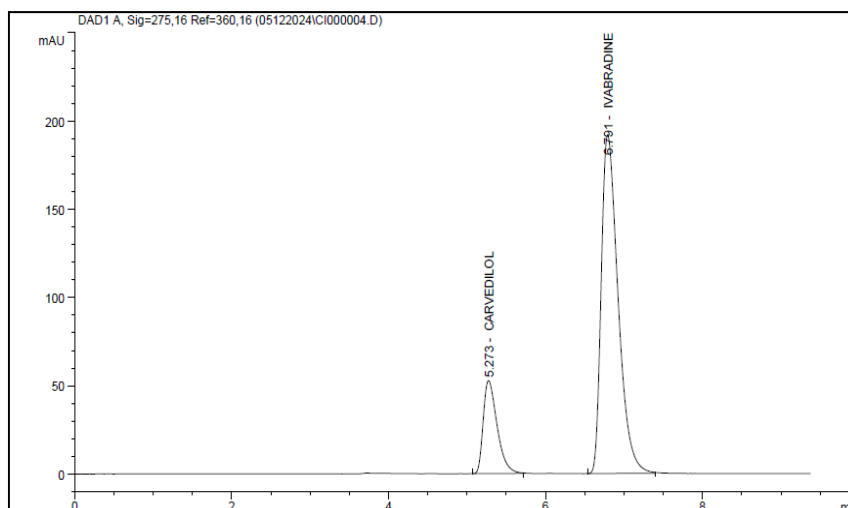
Chromatogram of Linearity (12+20 mcg)

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.249	453.73721	4278	0.97	-
2	6.753	1925.61267	4822	0.96	4.23



Chromatogram of Linearity (12+20 mcg)

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.249	453.73721	4278	0.97	-
2	6.753	1925.61267	4822	0.96	4.23



Chromatogram of Linearity (18+30 mcg)

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.273	668.65674	4527	0.98	-
2	6.791	2952.54224	5071	0.97	4.36

Accuracy: -

Each 2 reading for 80%.

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.363	411.22888	7243	0.96	-
2	6.940	1810.59497	8036	0.97	5.61

Each 2 reading for 100%.

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.364	452.70288	4021	0.70	-
2	6.943	1994.25598	8451	0.96	5.78

**Statistical Validation of Recovery Studies
Carvedilol and Ivabradine**

Level of Recovery (%)	Drug	Mean % Recovery	Standard Deviation*	% RSD
80%	CVD	99.57	0.17	0.18
	IBD	99.55	0.51	0.51
100%	CVD	99.41	0.01	0.01
	IBD	99.10	0.12	0.12
120%	CVD	99.50	0.12	0.12
	IBD	100.44	0.08	0.08

System suitability parameters

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.328	607.65833	6690	0.96	-
2	6.874	2639.12280	7884	0.98	5.41

Chromatogram of System suitability -1(18+30 mcg)

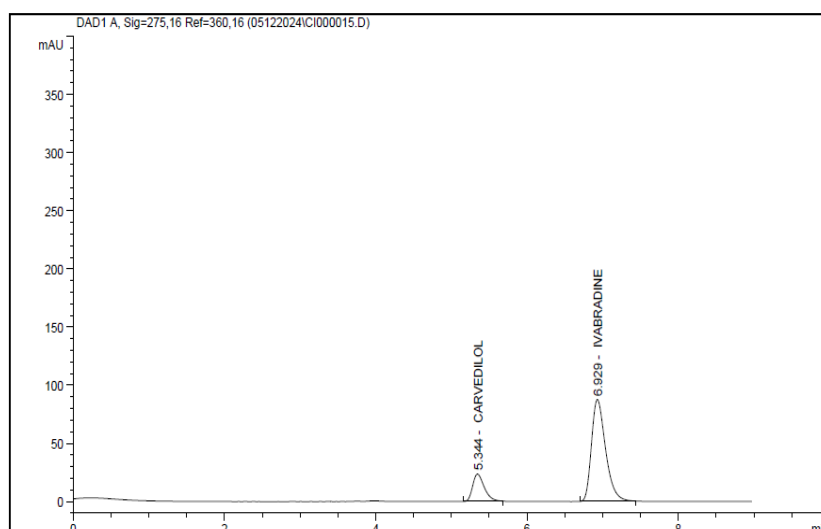
No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	3.738	958.41102	4042	0.68	-
2	6.114	1883.14587	5094	0.92	8.08

Chromatogram of System suitability No- 2 (18+30mcg)

Method	Concentration of Carvedilol and Ivabradine (mg/ml)	Peak area	Amount found (mg)	% Amount found
RP-HPLC Method for DAPA	18	607.6583	18.19	101.06
	18	607.4635		
		Mean	18.19	101.06
		SD	0.10	
		%RSD	0.02	
RP-HPLC Method for LINA	30	2639.122	30.09	100.32
	30	2636.112	30.10	100.35
		Mean	2637.46	100.32
		SD	1.53	
		%RSD	0.06	

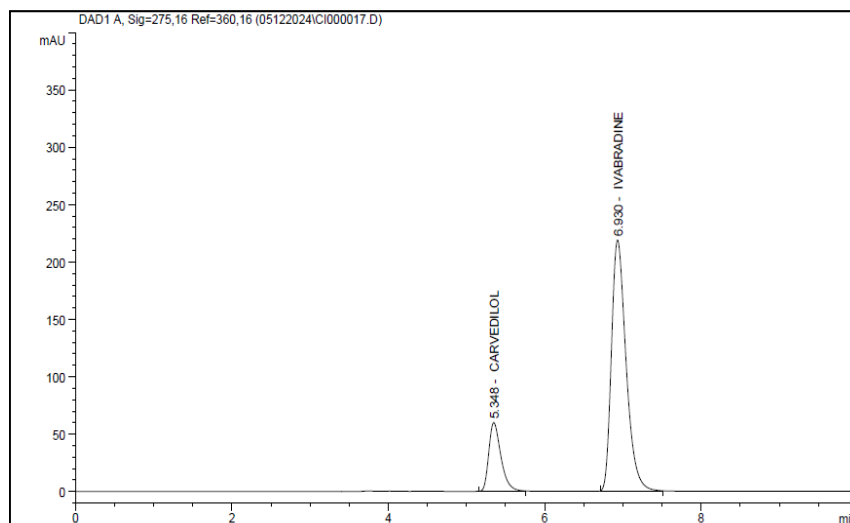
Repeatability studies on RP-HPLC for Carvedilol and Ivabradine Chromatogram of intraday Precision (6+10 mcg)

Precision: - Chromatogram of Intraday Precision



No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.344	245.69852	6054	0.95	-
2	6.929	1089.52417	7116	0.97	5.25

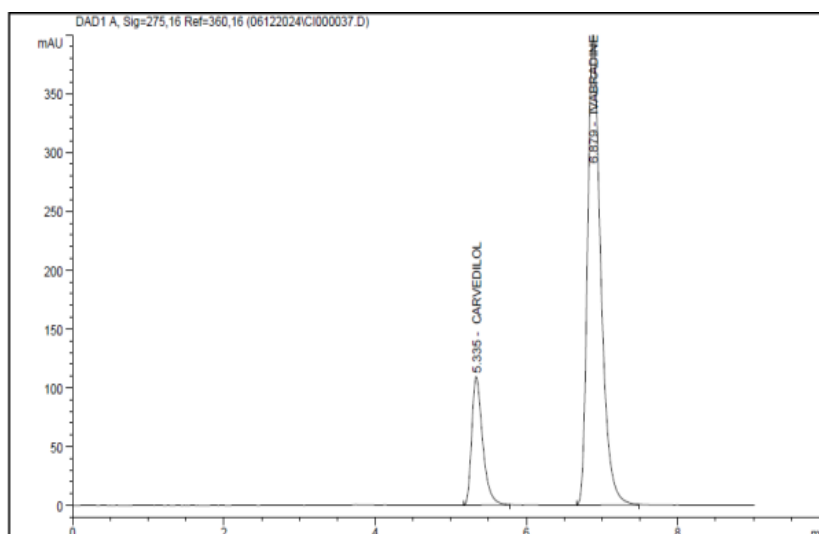
Chromatogram of intraday Precision (18+30 mcg)



No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.321	668.23785	6671	0.94	-
2	6.864	2959.35425	7860	0.96	5.40

Chromatogram of interday Precision (30+50 mcg)





No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.335	1102.31042	7167	0.93	-
2	6.879	4852.31543	8296	0.95	5.56

Result of Intraday and Inter day Precision studies on RP-HPLC for Carvedilol and Ivabradine

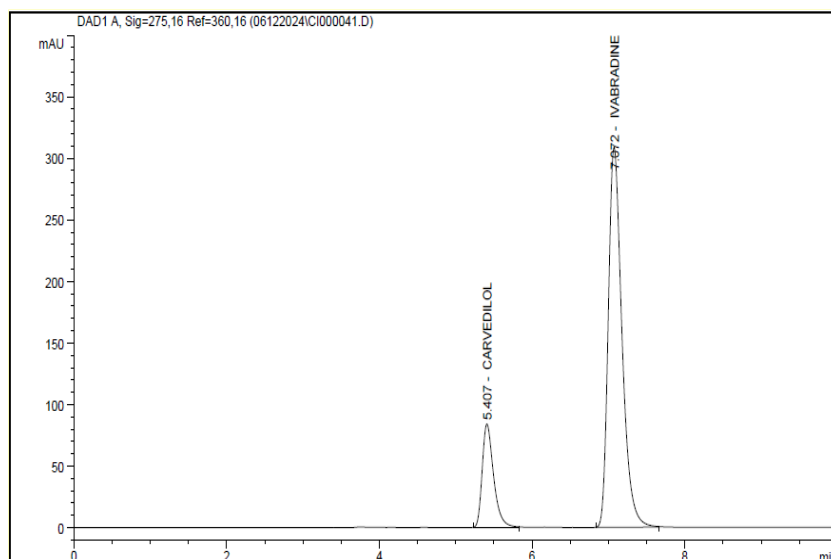
Drug	Conc ⁿ (µg/ml)	Intraday Precision		%	Interday Precision		%
		Mean± SD	%Amt Found	RSD	Mean± SD	%Amt Found	RSD
CVD	6	245.43± 0.39	101.16	0.16	246.54± 0.51	101.69	0.21
	18	667.43±0.65	100.40	0.10	668.76±0.74	100.61	0.11
	30	1088.1±3.61	100.13	0.33	1102.64±0.47	101.50	0.04
IBD	10	1089.5±0.08	101.50	0.08	1085.69±0.17	101.08	0.02
	30	2949.7±1.04	100.79	0.04	2958.98±0.53	101.12	0.02
	50	4779.4±14.3	99.99	14.3	4853.52±1.71	101.59	0.04

Mean of each 3 concentration they have 2 reading

Mobile phase change (41% MEOH, 58 % 0.1%OPA)

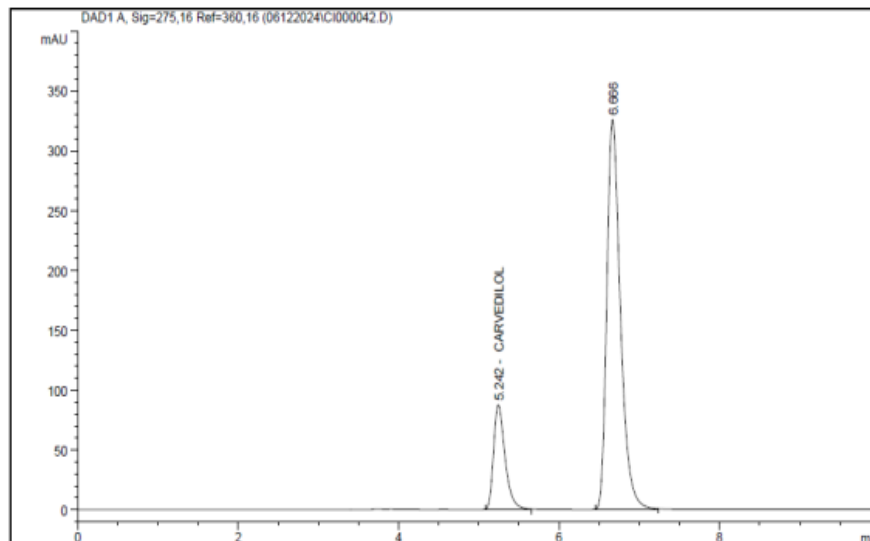
Robustness:





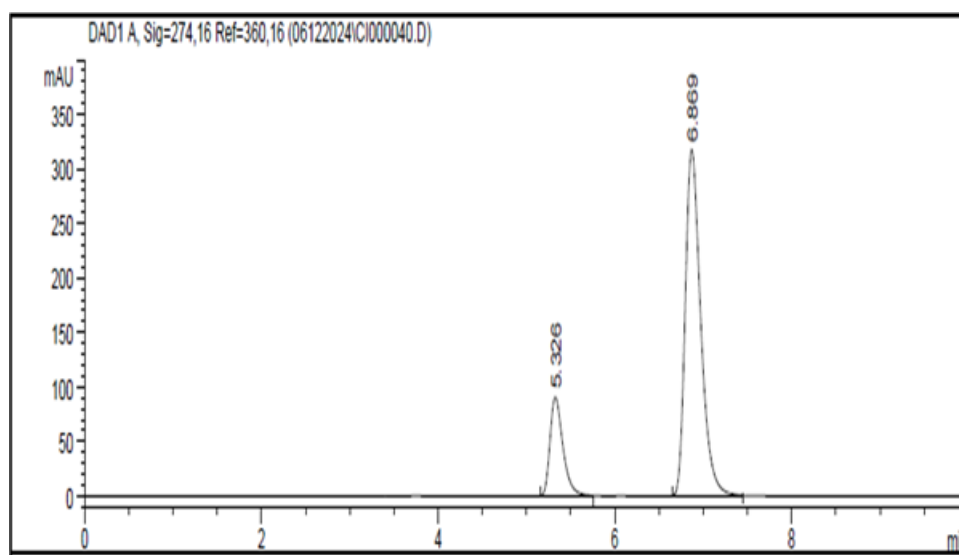
No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.407	868.88885	6889	0.95	-
2	7.072	3839.80762	8144	0.98	5.79

Mobile phase change (43% MEOH, 56 % 0.1%OPA)



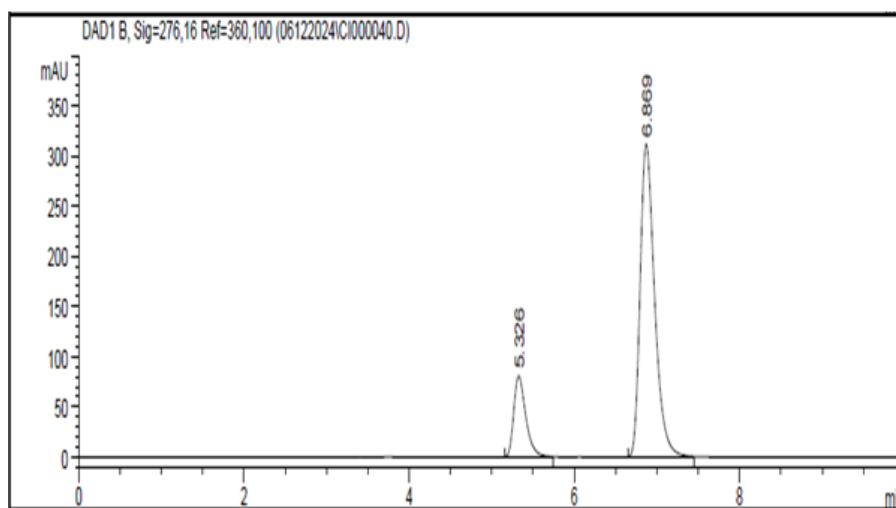
No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.242	874.02655	7077	0.95	-
2	6.666	3832.49756	7987	0.97	5.19

Wavelength change 274 nm



No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.326	926.38062	6983	0.95	-
2	6.869	3867.30127	7872	0.96	5.46

Wavelength change 276 nm



No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.326	824.90552	6983	0.95	-
2	6.869	3796.69238	7872	0.97	5.46

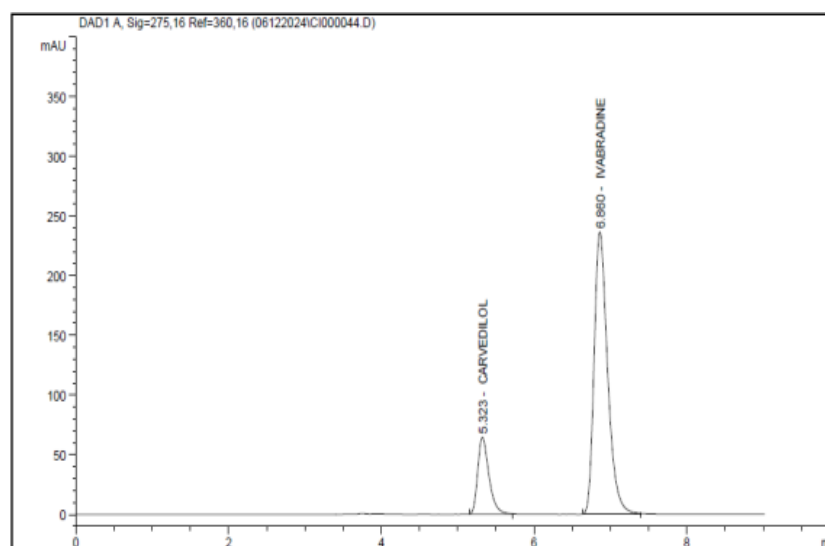
Result of Robustness Study of Carvedilol

Parameters	Conc.(µg/ml)	Amount of detected (mean ±SD)	%RSD
Chromatogram of comp change 41.4 Meoh +58.6 WATER	24	867.7±1.69	0.19

Chromatogram of comp change 43.4 MEOH + 56.6 WATER	24	872.63±1.97	0.23
Chromatogram of comp change wavelength change 274 nm	24	925.5±1.32	0.14
Chromatogram of comp change wavelength change 276 nm	24	826.28±1.95	0.24

Result of Robustness Study of Ivabradine

Parameters	Conc.(µg/ml)	Amount of detected (mean ±SD)	%RSD
Chromatogram of comp change 41.4 Meoh +58.6 WATER	40	3841.1±1.78	0.05
Chromatogram of comp change 43.4 MEOH + 56.6 WATER	40	3831.03±2.07	0.05
Chromatogram of comp change wavelength change 274 nm	40	3869.0±2.37	0.06
Chromatogram of comp change wavelength change 276 nm	40	3798.01±1.86	0.05



Result Chromatogram of Marketed Formulation (18+30 mcg)

No.	RT [min]	Area[mV*s]	TP	TF	Resolution
1	5.323	609.8725	6823	0.96	-
2	6.860	2610.21680	7852	0.98	5.41

REFERENCES



1. Trivedi B., Quality by design (QbD) in pharmaceuticals. *Int J Pharm a Pharm Sci* 4(1), 17-29.
2. ICHQ9, Quality Risk Management, 2005
3. Serena O., Sergio P., Andra F, Application of quality by design to the development of analytical separation methods. *Anal Bioanal Chem.* 2012.
4. US Food and Drug Administration (FDA), Department of Health and Human Services, Pharmaceutical Quality for the 21st Century A Risk-Based Approach Progress Report, (2013)
5. Rozet E., Lebrun P., Debrus B., Boulanger B., Hubert P., 2013. Design Spaces for analytical methods. *Trends in Analytical Chemistry* 42, 157-167.
6. Monks, K.E., Rieger, H.J., Molnar, I. Expanding the term “Design Space” in high Performance liquid chromatography (I). *J. Pharm. Biomed. Anal.* 2011, 56 (5), 874879.
7. Serena O., Sergio P., Andra F, Application of quality by design to the development of analytical separation methods. *Anal Bioanal Chem.* 2012.
8. Bhutani H., Kurmi M., Singh S., Beg S., Singh B., 2014. Quality by Design (QbD) in Analytical Sciences: An Overview. *Pharma Times* 46 (08), 71-75.
9. Rozet E., Lebrun P., Debrus B., Boulanger B., Hubert P., 2013. Design Spaces for analytical methods. *Trends in Analytical Chemistry* 42, 157-167.
10. Molnar I., Rieger H.J., Monks K.E., 2010. Aspects of the “Design Space” in high pressure chromatography method Development. *J Chrom Anal* 1217, Liquid 3193–3200.
11. Monks, K.E., Rieger, H.J., Molnar, I. Expanding the term “DesignS pace” in high Performance liquid chromatography (I). *J. Pharm. Biomed. Anal.* 2011, 56 (5), 874879.
12. Sangshetti J. N., Deshpande M., Zaheer Z., Shinde D. B., Arote R, Quality by design approach: Regulatory need. *Arab J Chem*, 2014, 1-14.

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