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Research Paper

Development and validation of Carvedilol In RP- HPLC

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ABSTRACT

The present study describes the development of a new rapid, simple, sensitive and reproducible RP-HPLC, method for the analysis of Carvedilol that offer certain advantages in its simplicity and sensitivity and applicable in routine analysis. It also describes the development of validation work as per ICH guidelines recommended by the Food and Drug Administration (FDA) of the United States. In order to develop a RP-HPLC, effective most of the effect should be spent in method development and optimization as this will improve the final method performance. A well developed method should be easy to validate. A method should be developed with the goal to analyse rapidly, the preclinical samples, formulations and commercial samples. Review of literature on drug strongly indicates that there is few method available for determination and validation of carvedilol in bulk and pharmaceutical dosage forms . Keeping in this mind we developed methods for determination and validation of carvedilol in bulk and pharmaceutical dosage forms by RP- HPLC, method with some improvements than the existing methods. The analytical procedure described for assay was specific, linear, precise, accurate, and system suitable for determination of carvedilol in bulk and pharmaceutical dosage forms. The observations of the validation parameters such as accuracy, precision, specificity, linearity, shows that the developed methods can be employed for routine analysis of bulk and tablets form of carvedilol. The result obtained from the validation parameters met the ICH and USP requirement as well as obeys BEER'S law.

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1. INTRODUCTION

HPLC is able to separate macromolecules and ionic species labile natural products, polymeric materials, and a wide variety of other high – molecular weight poly functional group. HPLC is the fastest growing analytical technique for the analysis of the drugs. It's simplicity, high specificity, and wide range of sensitivity makes it ideal for the analysis of many drugs in bothdosage forms and biological fluids[1].

In this the separation is about 100 times faster than the conventional liquid chromatography due to packing of particles in the range of 3-10µm.Modern LC uses very small particles for packing. The small particle size results in more rapid approach to the distribution equilibrium and consequently smaller plate height, so that a given length of column includes large number of plates which makes the column efficient and the peak narrow. But close packing of these small particles reduces the flow rate of the mobile phase through the packed bed (the packing said to develop high back pressure) and in order to achieve a reasonable flow rate it is necessary to apply pressure to the mobile phase. So the designation, put forth as high pressure liquid chromatography. Thus HPLC is having advantages of improved resolution, faster separation, improved accuracy, precision and sensitivity[2].

Carvedilol tablets are indicated for the treatment of mild to severe chronic heart failure of ischemic or cardio myopathic origin .usually in addition to diuretics ACE inhibitors and digitalis . They can be used alone or in combination with other antihypertensive agents especially thiazide type diuretics should not be given to patients with severe

hepatic impairment .It is a non selective β-adrenergic blocking agent with α-1 blocking activity. Carvedilol has much greater antioxidant activity than other commonly used β blockers. Tablet containing inactive ingredients as colloidal silicon dioxide, crospovidone, hypromellose, lactose monohydrate, magnesium stearate, polyethylene glycol, polysorbate, povidone, and titanium dioxide[3].

The present study describes the development of a new rapid, simple, sensitive and reproducible RP-HPLC, HPTLC, UV Spectrophotometry method for the analysis of Carvedilol that offer certain advantages in its simplicity and sensitivity and applicable in routine analysis. It also describes the development of validation work as per ICH guidelines recommended by the Food and Drug Administration (FDA) of the United States[4].

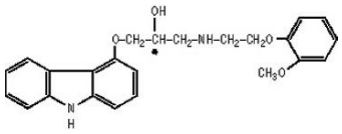

Figure no. 1 Chemical structure of Carvedilol

2. MATERIALS AND METHOD

Chemicals

S.No.	Chemicals and solvents	Manufacturer
1.	Carvedilol working standard	USP standards
2.	Acetonitrile (HPLC grade)	Rankem
3.	Methanol (HPLC grade)	Fischer scientific
4.	Potassium di hydrogen phosphate	Merck
5.	Formic acid	Merck
6.	Milli - Q/HPLC water	Merck
7	Toluene	Merck
8	Chloroform	Merck

Selection of mobile phase:

Various mobile phases were tried in different ratios for selection of mobile phase. The drug carvedilol was injected with different mobile phase at different ratios with different flow rates till a sharp peak without any interference peak containing spectrum was obtained. The different mobile phase were containing either one or the combinations of two or three of following solvents, acetonitrile, water, methanol, tetrahydrofuran[5].

Tried at different ratios no favourable results obtained. But the mobile phasecontaining potassium di hydrogen phosphate buffer : acetonitrile in the ratio 60:40 gave acceptable peak with retention time 2.97 min.

Instruments

S.NO	INSTRUMENT
1	Shimadzu uv-1700 spectrophotometer
2.	Shimadzu hplc with uv detector
3	Ymc pack pro c18 column (100 × 4.6mm, 5µ)
4	Camag hptlc instrument
5	Camag tlc scanner 3
6	Camag linnomate v automaic sampleapplicator
7	Twin-trough chamber (10 × 10 cm)
8	Ultra Sonicator
9.	Electronic balance (2mg-200gm) (Sartorius)
10.	pH Analyser

Separation using acetonitrile and water

A mobile phase consisting acetonitrile and water at different ratios were tried to achieve the separation. But it was found that carvedilol peak was merging.

Separation using methanol and water

Next trial was done by using mobile phase consisting methanol and water. Althoughdifferent ratios were tried tailing of the peak occurred.

Separation using tetrahydrofuran, acetonitrile and water

Tetrahydrofuran, acetonitrile, water composition as mobile phase were tried at differentratios peak shape was not found to be good.

Separation using potassium di hydrogen phosphate buffer and acetonitrile

Potassium di hydrogen phosphate buffer, acetonitrile composition as mobile phase weretried at different ratios. With this good symmetrical peaks were obtained. As our aim was to

S.no of insertion	Area	Shadowing factor
1	4121144	1.514
2	4111957	1.521
3	4112953	1.520
4	4135077	1.525
5	4118577	1.516
Average	4119942	1.519
SD	9286.85	
%RSD	0.23	

Table no.1 Intraday precision at 20 µg /ml

Example	Wt(mg)	Area	%assay
1	1798.25	4123717	97.51
2	1812.02	4117537	96.62
3	1825.02	4174580	97.26
4	1820.13	4152250	97.00
5	1835.14	4175261	96.74
6	1841.13	4193482	96.85
		Average	96.99
		SD	0.33
		%RSD	0.34

Table no.2 Data representing Repeatability

The testing approach included evaluating six samples from the same batch to ensure the method's precision.Each day of this study was conducted by a distinct set of analysts, each of whom used a unique set of instruments and columns. standard deviations (absolute and relative) for 6 assessment results were computed.

Reception methods

The ideal range for carvedilol concentration is between 90.0 and 110.0. The percentage of variation between the means of two analysts is 0.77, which is below the recommended maximum of 2.0%.

Sample No	Percentage of assay(w/w)	
	Analyst-I	Analyst-II
1	99.4	99.0
2	99.9	97.0
3	100.5	97.4
4	99.6	97.1
5	99.4	98.9
6	100.6	98.7
Average	99.9	98.0
%RSD	0.54	1.0

Table no.3 Data representing Ruggedness

The analytical method for the determination of the assay of carvedilol tablets is sufficiently robust if the relative standard deviation value is an acceptable percentage.

Accuracy of the System: The injection of a standard solution was repeated five times. Carvedilol's peak regions were analysed to determine their mean and relative standard deviation (RSD).

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S.no	Parameters	Normal Condtion	Higher side	Lower side
1	pH	3.0	3.2	2.8
2	Flow rate	1.0ml/min	1.2ml/min	0.8ml/min
3	wavelength	242nm	244nm	240nm

Table no.4 Data representing Robustness conditions

Not much has changed in the accepted clinical practises regarding carvedilol's definition. Methods for the genuine, specific, rapid, and specific evaluation of carvedilol in fine detail have been developed.

Analysing Carvedilol with RP-HPLC[6].

The RP-HPLC technique uses a frequency of 242 nm and a ambulant phase composed of a 60:40 mixture of potassium dihydrogen phosphate cradle and acetonitrile. The optimal conditions for this study involved a pH three solution attuned with formic corrosive and a circulation rate of 1 ml/min. With the new and improved circumstances, the estimated time for maintenance was 2.9.

The linearity of Carvedilol became visible between 16.62 and 93.75 g/ml, where the top shape became even and a cracking connection constant esteem was get.

The three extraordinary stages of reimbursement and price assurance (eighty%, one hundred%, and 120%) have been completed. The soundness of the method become in this way proven. By using a similar example and standard over and over again, the accuracy of the method was honed in. Additionally, % RSD was determined after completing the entomb day and intra day accuracy.

These method acting, RP-HPLC, were thought to be delicate, authentic, and precise. The standard carvedilol test can involve more than just these three methods[7].

4.CONCLUSION

In order to develop a RP-HPLC, effective most of the effect should be spent inmethod development and optimization as this will improve the final method performance. Awell developed method should be easy to validate. A method should be developed with the goal to analyse rapidly, the preclinical samples, formulations and commercial samples.

Review of literature on drug strongly indicates that there is few method available for determination and validation of carvedilol in bulk and pharmaceutical dosage forms . Keeping in this mind we developed methods for determination and validation of carvedilol in bulk and pharmaceutical dosage forms by RP- HPLC, method with some improvements than the existing methods[8-9].

The analytical procedure described for assay was specific, linear, precise, accurate, and system suitable for determination of carvedilol in bulk and pharmaceutical dosage forms.

The observations of the validation parameters such as accuracy, precision, specificity, linearity, shows that the developed methods can be employed for routine analysis of bulk and tablets form of

carvedilol.[10-11] The result obtained from the validation parameters met the ICH and USP requirement as well as obeys BEER'S law[12].

5.CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

6. ACKNOWLEDGEMENT

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