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Evaluation and Validation of Carvedilol in Bulk and Pharmaceutical Dosage Forms

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Quality may be described as the character that determines the degree of excellence. A good quality medication is anything that meets the product specifications, can be purchased safely, and can be used confidently for the purpose for which it was designed.To obtain a high quality medication, the manufacturing process for producing a drug should have quality integrated into it. Analytical chemistry is the discipline that seeks ever better methods of assessing the chemical composition of natural and manmade materials.
Aims and Objective: Evaluation and validation of carvedilol in bulk and pharmaceutical dosage forms.
Material and Methods: preparation of standard stock solution and preparation of sample solution as per standard protocol.
Result: In the RP-HPLC method, a wavelength of 242 nm was retained and the retention time was found to be 2.9 with optimised conditions. Carvedilol showed linearity in the range of 15.62 - 93.75µg/ml. where the peak shape was symmetrical and a good correlation coefficient value was obtained.
Conclusion: RP-HPLC, HPTLC, UV spectroscopy were found to be sensitive, precise, and accurate. However these three methods can be used for the routine analysis of carvedilol from formulation.

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Keywords: Validation; carvedilol; pharmaceutical; dosage.

1. INTRODUCTION

Quality can be defined as the character, which defines the grade of excellence. A good quality drug is something, which will meet the established product specifications, can be safely bought and confidently used for the purpose for which it is intended [1]. To get a good quality drug, the manufacturing process should have quality built into it. Analytical chemistry is the science that seeks ever improved means of measuring the chemical composition of natural and artificial materials. Analytical chemistry is a sub- discipline of chemistry that has the broad mission of understanding the chemical composition of all matter and developing the tools to elucidate such compositions [2].

Spectrophotometry is generally preferred by industries as the cost of the equipment is less and the maintenance problems are minimal. The method of analysis based on measuring the absorption of a monochromatic light by colourless compounds in the near ultraviolet path of spectrum (200-380nm) [3]. The photometric methods of analysis are based on the Bouger-Lambert Beer,s Law, which establishes that the absorbance of a solution is directly proportional to the concentration o Gaten.W.E, Instrumental method of chemical analysis, 5th edition, 33-52.f the analyte . The basic concept of functioning of a UV spectrophotometer is that light of a specific wavelength passes through a solvent-filled cell and falls on a photoelectric cell, which converts the radiant energy into electrical energy, which is measured by a galvanometer. Molecular absorption in the ultraviolet and visible region of the spectrum is dependent on the electronic structure of the molecule. The quantization of energy absorption causes electrons to be elevated from their ground state orbital to a higher energy orbital in the excited state.

1.1 Aim and Objective

Evaluation and validation of carvedilol in bulk and pharmaceutical dosage forms.

2. MATERIAL AND METHODS

2.1 Preparation of Standard Stock Solution

Weigh accurately and transfer about 62.52 mg of carvedilol into a 100 ml volumetric flask. 50 ml methanol added and sonicated to dissolve, and then make up to the volume with methanol. Pipette out 10 ml of this solution into a 100 ml volumetric flask and diluted up to the mark with mobile phase. Filtered through 0.45µ membrane filter.

2.2 Preparation of Sample Solution

Transfer the accurately weighed samples 15.62,31. 25, 46.88, 62.50, 78.13, 93.75 mg respectively into individual 100 ml flask. 50 ml methanol added and sonicated to dissolve, then make up to the volume with methanol. Pipette out 10 ml of this solution into a 100 ml volumetric flask and diluted up to the mark with mobile phase. Filtered through 0.45 µ membrane filter. Inject 10µl of blank solution and each linearity level standard solutions into the chromatographic system and measure the peak area.

The linearity of carvedilol was performed in the range of 15.62µg/ml to 93.75µg/ml (25%- 150 % of working concentration). A graph was plotted with concentration in µg/ml on x axis and peak area on y axis. Slope, y intercept, correlation coefficient (r value), were determined.

3. RESULT AND OBSERVATION

The analytical method meets the acceptance criteria for accuracy study. Hence the method is accurate for the determination of assay of carvedilol tablets [Fig 1].

HPTLC profile [Figs. 2,3]

Linearity: Aliquots of 0.1-0.5 µg/spot of standard solution of Carvedilol is applied on the plate with the help of micro liter syringe using an automatic sample applicator. The plates were developed, dried and scanned densitometrically at 254 nm. The drug peak-area was calculated for each concentration level and a graph was plotted of drug concentration against the peak area and shown in (Fig. 3). Calibration parameters are given in Table 2:5.

4. CALIBRATION CURVE OF CAR-VEDILOL

Accuracy: Accuracy of the developed method was confirmed by doing a recovery study as per ICH guidelines at three different concentration

levels (80%, 100% and 120%) by replicate analysis (n=3). Standard drug solutions were added to a preanalyzed sample solution, and then percentage of drug content was calculated. The results of the accuracy study are reported in Table 4. From the recovery study, it was clear that the method is very accurate for quantitative estimation of Carvedilol in tablet dosage form because all the statistical results were within the acceptance range (i.e., % RSD <2.0).

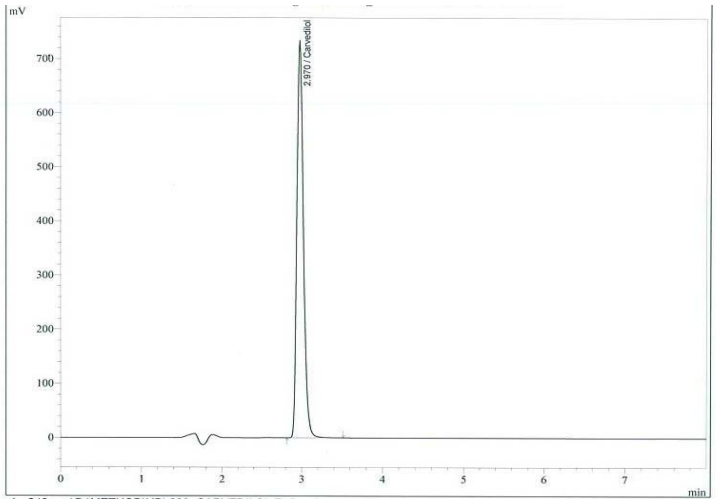


Fig. 1. RP-HPLC

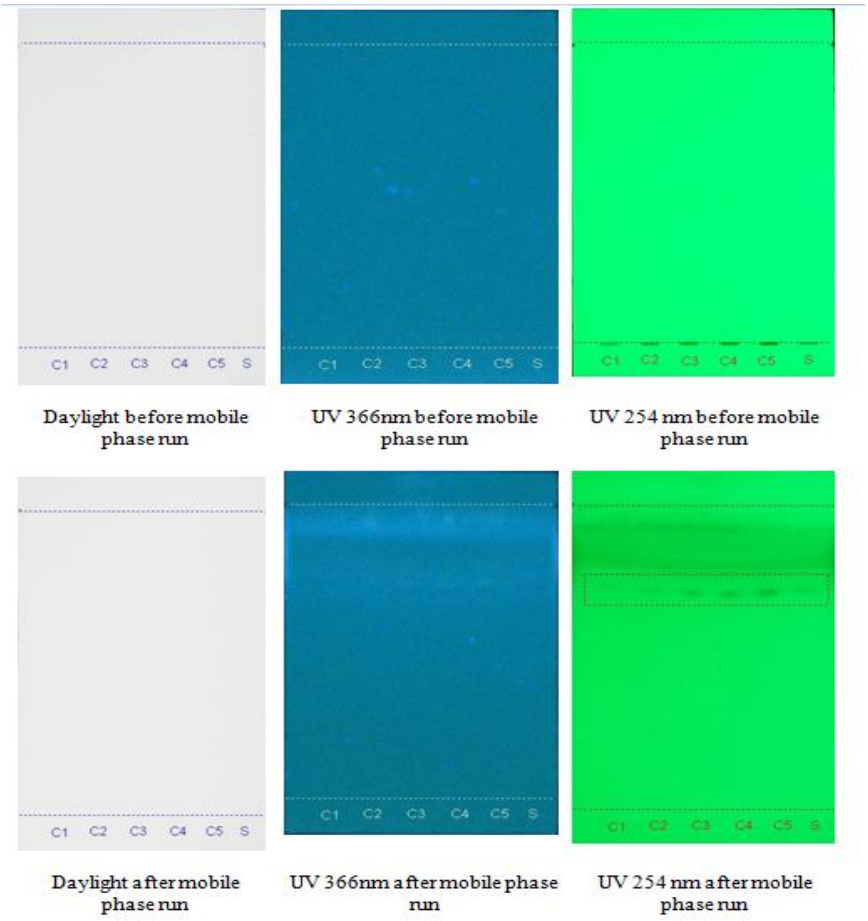
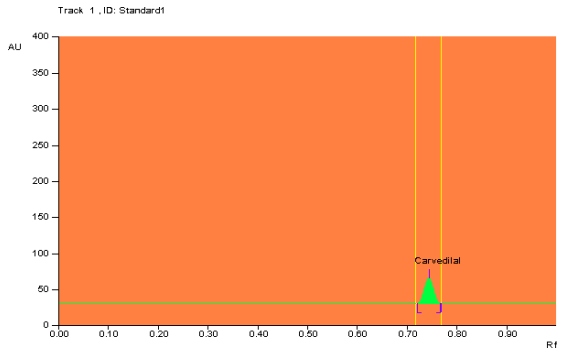
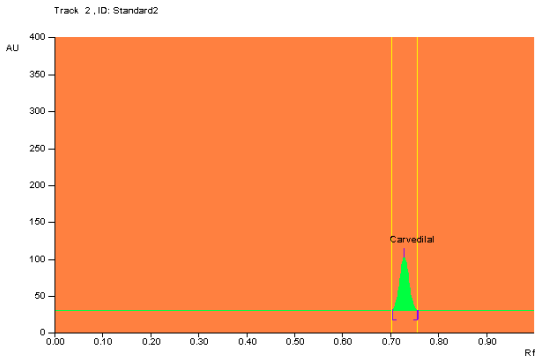


Fig. 2. HPTLC profile



Carvedilol Densitogram-0. 1µg



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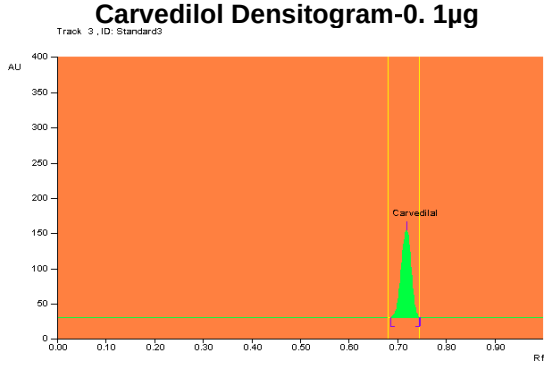

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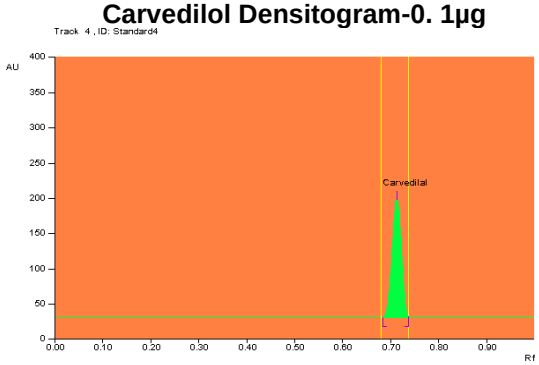

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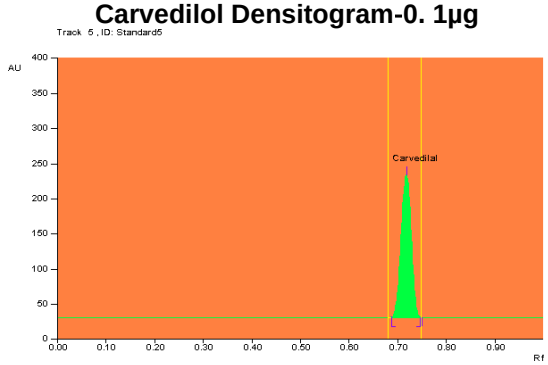
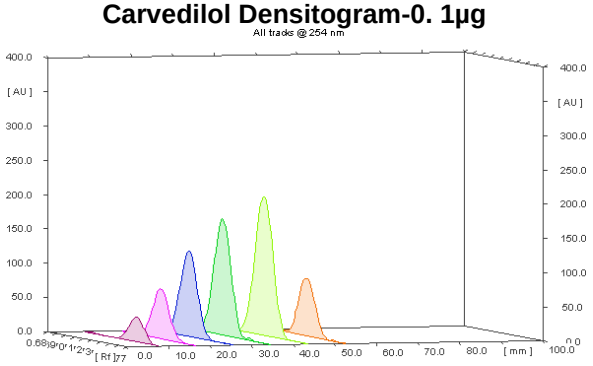
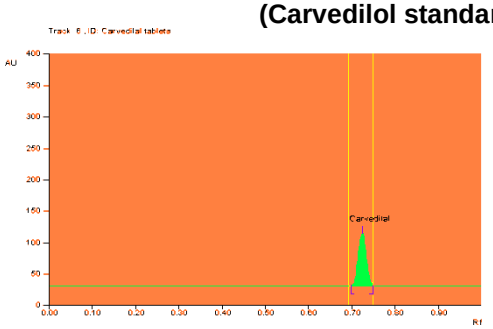


Carvedilol Densitogram-0. 1µg



3D display of Peak densitogram – All tracks (Carvedilol standards and sample) @ 254nm



Carvedilol densitogram -Sample

Fig. 3. HPTLC Densitogram

Table 1. RP-HPLC profile

Name of Drug	Retention Time	Area	Theoretical Plate	Tailing Factor
Carvedilol	2.96	4121905	5350.4	1.40

Table 2. Linearity of Carvedilol

Sl. No	Standard concentration µg/ spot	Peak Area	Peak Height
1	0.1	756.35	35.8
2	0.2	1387.96	72.4
3	0.3	2081.94	123.9
4	0.4	2775.92	168.8
5	0.5	3469.9	203.4

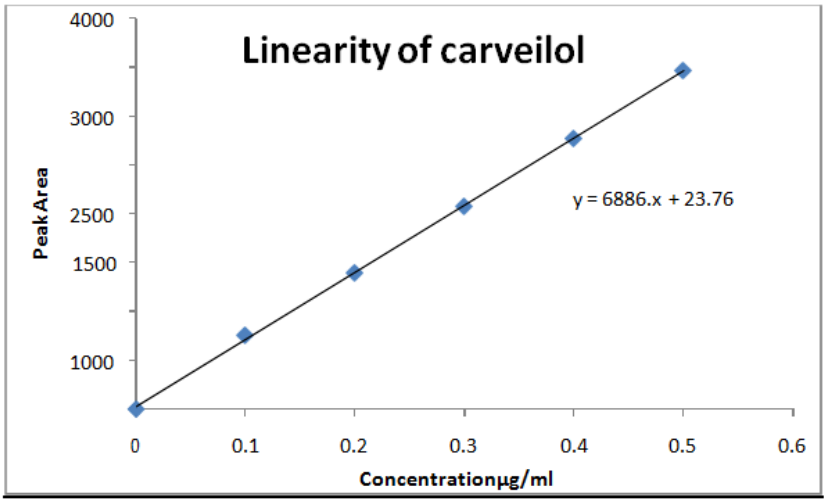


Table 3. Calibration parameters for carvedilol

Parameters	Carvedilol
Linearity Range(µg/Spot)	0.1-0.5
Slope	6886
Intercept	23.76
Regression Co-Efficient	0.999

Table 4. Recovery studies for Carvedilol (n=3)

Label claim (mg / tablet)	Recovery level (%)	Amount added (mg)	Amount recovered (mg) ± % RSD	% Recovery
25	80	20	19.96±0.42	99.82
25	100	25	24.65±0.85	98.67
25	120	30	30.45±0.59	101.5

Precision: The precision of the method (system reproducibility) was assessed by spotting 0.3µl of drug solution six times on a TLC plate, followed by development of plate and recording the peak area for 6 spots. The % RSD for peak area values of carvedilol was found to be 0.58. The results were shown in Table 6.

The method reproducibility (intra-day precision) was determined by analyzing standard solution in the concentration range of 0.1 µg/spot to 0.5 µg/spot of drug for 3 times on the same day and inter-day precision was determined by analysing corresponding standards daily for 3 day over a period of one week. The intra-day and inter-day coefficients of variation (%RSD) are in range of 0.13 to .36 and 0.30 to 0.56, respectively. The results were shown in Tables 6a, 6b.

Table 5. Precision of Carvedilol

S.No	Concentration (µg/ spot)	Peak Area
1.	0.3	2081.94
2.	0.3	2111.40
3.	0.3	2090.52
4.	0.3	2075.36
5.	0.3	2087.25
6.	0.3	2092.17
Mean	-	2089.77
Percentage Relative Standard Deviation	-	0.58

Table 6a. Intra-day precision of Carvedilol

S.No	Concentration (µg / spot)	Area	Mean	Standard Deviation	% RSD
1.	0.1	756.35			
2.	0.1	761.05	757.3	3.37	0.44
3.	0.1	754.50			
1.	0.3	2080.50			
2.	0.3	2083.72	2080.82	2.74	0.13
3.	0.3	2078.25			
1.	0.5	3469.50			
2.	0.5	3465.64	3470.32	5.13	0.14
3.	0.5	3475.82			

Table 6b. Inter-day Precision of Carvedilol

S.No	Concentration (µg / spot)	Area	Mean	Standard Deviation	% RSD
1.	0.1	757.98			
2.	0.1	754.50	758.28	3.93	0.52
3.	0.1	762.35			
1.	0.3	2081.94			
2.	0.3	2090.50	2083.56	6.28	0.30
3.	0.3	2078.25			

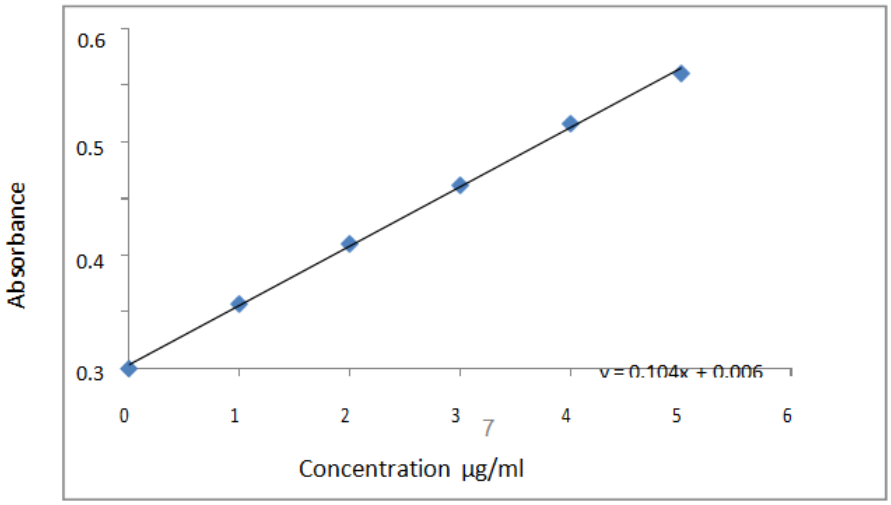


Fig. 4. Calibration Curve of Carvedilol

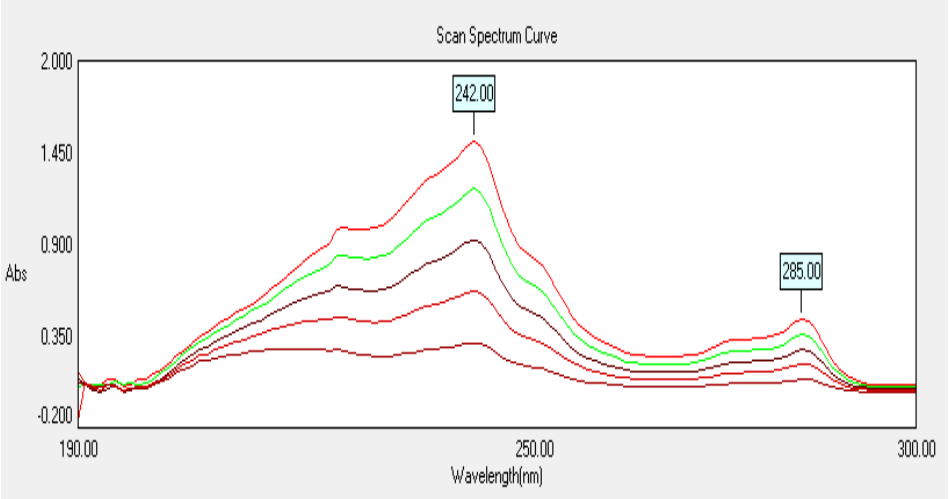


Fig. 5. UV spectrum

UV Profile: The developed method was validated in terms of linearity, accuracy and stability studies.

Linearity: In a concentration range of 1-5g/ml, carvedilol was shown to be linear. The absorbance of this solution was measured at 242 nm, and the absorbances versus concentration were plotted on a calibration graph. The value of the correlation co-efficient was found to be 0.998.

Accuracy: The accuracy, specificity, suitability and validity of the present method were satisfied by conducting percentage recovery studies. A known quantity of the drug was added to the pre-analyzed sample formulation at 50% and 100% levels. The percentage recovery and standard deviation were calculated.(Table 3).

The % recovery was calculated by using the following formula:

%Recovery = Amount of drug Amount of drug found after addition found in sample before of standard drug addition of standard drug / Amount of standard drug added × 100

Table 7. Recovery studies

Drug	Level	Amount found in µg	Actual amount Added in µg	%Recovery	% RSD
		12.30	12.22	100.6	
	50%	12.28	12.22	100.4	0.12
		12.30	12.22	100.6	
Carvedilol		24.71	24.64	100.3	
	100%	24.69	24.64	100.2	0.06
		24.70	24.64	100.2	

Stability: The drug solution was found to be stable for about three hours at room temperature. Stability data reported.

Table 8. Stability data

Concentration in µg/ml	Time (min)	Absorbance
1	0	0.113
	30	0.110
	60	0.109
	90	0.117
	120	0.112
	150	0.107
	180	0.108

Table 9. Repeatability studies

Concentration in µg/ml	Absorbance	%RSD
1	0.117	0.93
	0.118	
	0.119	
	0.117	
	0.117	
	0.116	
5	0.516	0.47
	0.513	
	0.511	
	0.510	
	0.515	
	0.511	

Table 10. Inter-day Precision

Concentration µg/ml)	Day	Absorbance	%RSD
1	1	0.116	1.02
	2	0.117	
	3	0.115	
	4	0.115	
	5	0.116	
	6	0.114	
5	1	0.512	0.40
	2	0.513	
	3	0.512	
	4	0.516	
	5	0.510	
	6	0.513	

Table 11. Intra-day Precision

Concentration µg/ml	6 times in a day	Absorbance	%RSD
1	1	0.115	
	2	0.113	
	3	0.111	
	4	0.114	
	5	0.115	1.47
	6	0.112	
5	1	0.513	
	2	0.515	
	3	0.510	
	4	0.512	
	5	0.515	0.45
	6	0.516	

5. DISCUSSION

For the estimate of carvedilol in formulation, validated analytical procedures are used. The following procedures were established for estimating carvedilol in formulation and are simple, precise, quick, and accurate. A wavelength of 242 nm was used for the RP-HPLC technique, and the mobile phase was potassium di hydrogen phosphate buffer: acetonitrile, in the ratio of (60:40). pH 3 was found to be the best condition for analysis when adjusted with formic acid at a flow rate of 1ml/min. With optimal conditions, the retention time was found to be 2.9. Carvedilol's linearity was found to be between 15.62 and 93.75 g/ml.

The peak shape was symmetrical, and the correlation coefficient value was high. The percentage label claim and recovery were tested at three distinct levels, 80 percent, 100 percent, and 120 percent. The method's appropriateness was thus established. The precision of the approach was investigated by injecting the same sample many times and calculating the standard deviation. Precision was measured on a daily and intraday basis, and the percent RSD was determined. Various mobile phases were investigated in HPTLC during the technique development stage, and the mobile phase consisting of ethyl chloroform, methanol, and toluene in the proportions of 1.5: 3:3.5 v/v/v for carvedilol was found to be the best and generated an Rf value of 0.72 for carvedilol. The drug's linearity was determined using a calibration curve and the area observed in the range of 0.1 – 0.5 g/ ml. Carvedilol has a regression coefficient of 0.999. The medications' interday precision was investigated. There was no reported interference with the formulation's additives. The accuracy parameter was subjected to recovery studies, which were published. The validated method was used to examine a tablet containing 25 mg of carvedilol, as stated on the label. The procedure that was devised was straightforward. It has a good peak as well as good Rf values. The most essential characteristic in the UV-spectroscopic technique is solubility. The solubility parameter was investigated, and methanol was chosen as the solvent because, when compared to other solvents, it provided the highest absorbance and a desirable spectral pattern. At a maximum absorbance of 242 nm, the linearity was found to be between 1 and 5 g/ml. To acquire the concentration in the linearity range, the commercial product was removed and diluted. At 242 nm, the solution was scanned and measured. Studies on percentage recovery, linearity, and stability were also conducted. The above method produced satisfactory recovery values and was determined to be stable and linear, thus it can be utilised for routine drug formulation analysis.

These methods were found to be sensitive, precise, and accurate, including RP-HPLC, HPTLC, and UV spectroscopy. These three procedures, on the other hand, can be employed for routine carvedilol analysis from formulation.

6. CONCLUSION

RP-HPLC, HPTLC should spend most of their impact on the creation and optimization of a technique as this enhances the performance of the last method. It should be simple to verify a properly designed technique. A technique should be established quickly in order to analyse preclinical samples, formulations, and commercial samples. The observations of validation factors like accuracy, accuracy, speciality, and linearity have shown that the techniques devised may be used to routinely analyse carvedillol in bulk and tablets. The results of the validation parameters met the requirements of ICH and USP and were in line with the law in BEER.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Merit W, Dean S. Instrumental method of analysis. 7th edition. 1995;75-83.
2. Sharma BK. Instrumental method of chemical analysis. 18th edition. 1994;3-12.
3. Gaten WE. Instrumental method of chemical analysis. 5th edition. 1997;33-52.

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