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Analytical method development and validation of carvedilol in bulk and tablet dosage form by using uv spectroscopic method as per ich guidelines

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ABSTRACT

A simple, sensitive, highly accurate spectrophotometric method has been developed for the determination of carvedilol in bulk and pharmaceutical tablet dosage form as per ICH Guideliness. The adequate drug solubility and maximum assay sensitivity was found in methanol. The absorbance of carvedilol was measured at 241 nm in the wavelength range of 200-400 nm. Beer's law was obeyed in the concentration range of 10-60 µg/mL, in the linearity study regression equation was found to be y = 0.183X-0.009& correlation coefficient was found to be 0.999. This method was Rugged and Robust in different testing criteria, LOD and LOQ was found to be 0.33 µg / ml & 1 µg / ml respectively. Accuracy study was done in 3 different concentration levels 50, 100, 150% & % recovery of the method was found to be 101.0%, 100.5%, 100.4% respectively in 3 different levels & mean recovery was 100.6%, so method was accurate. Results of all validation parameter were within the limit as per ICH guideline. Results of percentage recovery shows that the method was not affected by the presence of common excipients. The proposed method has been successfully used for the analysis of the drug in pure and its tablet dosage forms. Easily and the method was precise accurate to perform in future

Keywords: Carvedilol, Methanol, UV spectrophotometric estimation, Method development, Validation

INTRODUCTION

Carvedilol is a Antihypertensive, molecular formula $C_{24}H_{26}N_2O_4$, IUPAC name 1-(9H-Carbazol-4-yloxy)-3-[[2-(2 methoxy phenoxy) ethyl] amino]-2-propanol.Mechanasim action of drug involves both a non-selective beta adrenergic receptor blocker (β1, β2) and an alpha adrenergic receptor blocker (α1). The S (-) enantiomer accounts for the beta blocking activity whereas the S (-) and R (+) enantiomer have alpha blocking activity. Reversibly binds to beta adrenergic receptors on cardiac myocytes. Inhibition of these receptors prevents a response to the sympathetic nervous system, leading to decreased heart rate and contractility.

According to literature review [3-9] there are very few method reported for the determination of Carvedilol in different Instrumental techniques, out of these methods only 1 method were reported in Single Drug by using UV spectroscopic method.

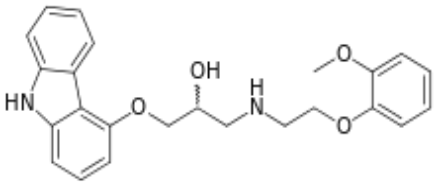


Figure: 1. Shows structure of Carvedilol

EXPERIMENTAL SECTION

Standard drugs

Carvedilol was procured from the HETERO Pharma

Chemicals and reagents

Methanol (FINER chemical LTD), Purified water (Rankem chemicals).

Instruments

UV (SHIMADZU) , UV (Elico SL-196), Sonicator (Analytical technologies).

Determination of absorption maxima by UV/Vis Spectrophotometry

Accurately weigh 100 mg of drug in to 100 ml volumetric flask. To this add 75 ml of diluent Methanol and sonicate it and further make up the volume with diluent. From this take 3 ml and make up to10ml. The solutions were scanned in the range of 200-400 nm in 1cm cell against blank

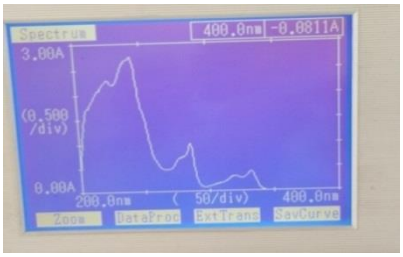


Figure: 2. Shows UV spectrum of Carvedilol

Preparation of mobile phase

Accurately measured 100 ml of Methanol, were degassed in an ultrasonic water bath for 10 minutes and then filtered through 0.45 µ nylon filter under vacuum filtration.

Diluent

Mobile phase is used as diluents

Standard preparation

Accurately weigh 25 mg of Carvedilol and transfer in to 25ml volumetric flask. Add about 10ml of solvent mixture sonicate to dissolve. Cool the solution to room temperature and dilute to volume with solvent mixture. Transfer 3ml of above solution in to a 10ml volumetric flask and make up the volume with diluents

Sample preparation

Accurately weigh 25 mg of Carvedilol powder and transfer in to 25ml volumetric flask. Add about 10ml of solvent mixture sonicate to dissolve. Cool the solution to room temperature and dilute to volume with solvent mixture. Transfer 3ml of

above solution in to a 10ml volumetric flask and make up the volume with diluent.

Optimized chromatographic conditions

- **Wavelength** - 241nm
- **Solvent** - methanol

Method validation

The following parameters were considered for the analytical method validation of Carvedilol in bulk form & tablet dosage form.

System Suitability

Chromatograph the standard preparations (6 replicate concentrations) and measure the absorbance evaluate the system suitability parameters as directed.

Accuracy

For accuracy determination, three different concentrations were prepared separately 50%, 100% and 150% for the concentration of absorbance values are recorded.

Precision

The standard solution was placed into cuvettes for six times and measured for all six concentrations absorbance values by using max in UV. The %RSD for the area of six replicate concentrations was found to be within the specified limits.

Robustness

As part of the Robustness, deliberate variations in method parameters and provides an indication of its reliability during normal usage. Wavelength was varied between plus or minus to the solutions were made in triplicates and were analyzed the

%RSD is determined.

Linearity and range

Linearity of the analytical method for assay by placing the linearity solutions prepared in the range of 10µg to 60µg of test concentration, into the cuvettes, covering minimum 6 different concentrations.

RESULTS AND DISCUSSION

Standard preparation

Accurately weigh 25 mg of Carvedilol and transfer in to 25ml volumetric flask. Add about 10ml of solvent mixture sonicate to dissolve. Cool the solution to room temperature and dilute to volume with solvent mixture. Transfer 3ml of above solution in to a 10ml volumetric flask and make up the volume with diluent.

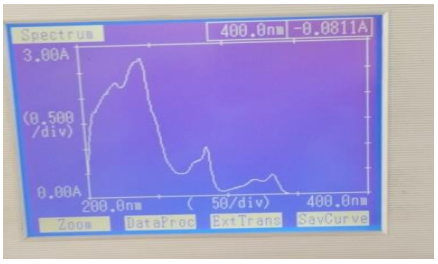


Figure: 3. Shows UV absorption spectrum of carvedilol standard

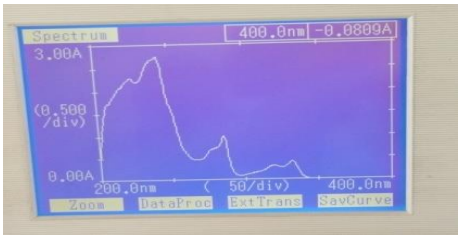


Figure: 4. Shows UV absorption spectrum of carvedilol sample

Validation

Accuracy

Average recoveries of Carvedilol are 101.0%, 100.5%, 100.4%, at 50%, 100% & 150% concentrations level respectively. The percentage recoveries of the drug is within the limits 99-102%. So the method is accurate, accuracy data for carvedilol are presented in

Table: 1 .Shows Accuracy results of Carvedilol

Concentration level	Amount added (mg)	Amount found(mg)	%recovery	Average % recovery
	12.5 mg	12.6 mg	101.5%	101.0%
	12.5 mg	12.62 mg	101.02%	
50%	12.5 mg	12.56 mg	100.5%	
	25 mg	25 mg	100.0%	100.5%
	25 mg	25.1 mg	100.5%	
100%	25 mg	24.85mg	99.4%	
	37.5 mg	37.6 mg	100.3%	100.4%
	37.5 mg	37.8 mg	101%	
150%	37.5 mg	37.5 mg	100%	

Result: The accuracy for the average of triplicate in each concentration samples are within the limit.

Table: 2. Shows % Recovery of Carvedilol

Amountadded (mg)	Amount found(mg)	Average% recovery
25mg	**50.2**	**100.6%**

Precision

Precision are summarized in **Table No: 3**, respectively. The %RSD values for Precision was less than 2.0%, which indicates that the proposed method is precise.

Table: 3.Shows Precision Results of Carvedilol

Concentration (µg/ml)	Absorbance of Carvedilol
30	0.617
30	0.618
30	0.617
30	0.617
30	0.615
30	0.617
Mean	**0.61683333**
SD	**0.000983192**
%RSD	**0.15939346**

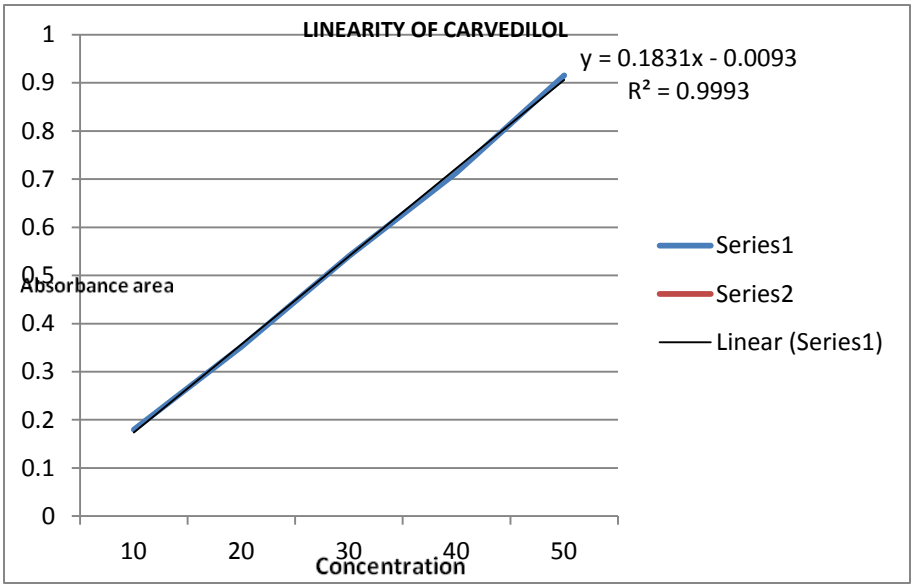
Linearity

The response was found linear over a concentration range of 10-60 µg/mL of Carvedilol. The correlation co-efficient were found to be 0.999 for Carvedilol**.** So the method is linear, data is presented in **Table: 4.** Linearity curve of Carvedilol is given in figure: 3

Table: 4. Shows linearity results of Carvedilol

S. No	Linearity Level	Concentration	Absorbance
1	I	10µg	0.18
2	II	20µg	0.352
3	III	30µg	0.54
4	IV	40µg	0.712
5	V	50µg	0.915
Correlation Coefficient			0.999
Intercept			0.183x-0.009
Slope			0.009
Linearity Range		10-50	

Figure: 5. Shows Calibration graph of Carvedilol



ROBUSTNESS

The Robustness of the method was determined by making slight changes in the experimental conditions such as change in the wavelength.

Table: 5. Shows Results of Robustness

S.No	Parameter Name	Average Results Obtained in 6 units		
		Mean	**Carvedilol drug in mg**	**Carvedilol drug in %**
1	Robust wavelength 239 nm	0.614	98.72	99.4
2	Robust wavelength 240 nm	0.615	99.24	100
3	Robust wavelength 241 nm	0.617	100.0	100.5
4	Robust wavelength 242 nm	0.615	99.61	100.3
5	Robust wavelength 243nm	0.612	98.13	100.1
		Mean		100.06
		Standard deviation		0.41
		%RSD		0.40

Limit of Detection (LOD) & LOQ

The detection limit is determined by the analysis of samples with known concentration of analyte and by establishing that minimum level at which the analyte can reliably detected , The LOD are calculated from the calibration curve by formula LOD = 3.3 x SD/ b The quantification limit is generally determined by the analysis of sample with known concentrations of analyte and by establishing the minimum level at which the analyte can be quantified with acceptable accuracy and precision, The LOQ are calculated from the calibration curve by formula LOQ = 10 x SD/ b

Table: 6. Shows LOD & LOQ results of Carvedilol

Parameter	Carvedilol
LOD	0.33µg/ml
LOQ	1µg/ml

Table: 7. Shows summary of validation parameter Results

S.NO	Parameter	Acceptance criteria	UV. Visible Spectroscopy
1	%Recovery	98-102%	100.6%
2	Linearity range((µg/ml)	-	10-60µg/ml
3	Correlation coefficient	NLT 0.999	0.999
4	Precision	%RSD(NMT 2%)	0.159
5	Intermediate precision	%RSD(NMT 2%)	0.132
6	Robustness	%RSD (NMT 2%)	0.40
7	LOD	-	0.33µg/ml
8	LOQ	-	1µg/ml

CONCLUSION

Method development & validation of Carvedilol was done by Uv-Visible spectroscopic method. The estimation was done by using mobile phase as methanol. The linearity range of Carvedilol was found to be 10-60 µg/ml. Correlation coefficient value was 0.999, values of % RSD was 0.15 which is within the limit. These results show the method is accurate, precise& sensitive. The spectroscopic method is more rapid. The proposed method is successfully applied to the bulk and tablet dosage form. The method was found to be having suitable application in routine laboratory analysis with high degree of accuracy and precision.

Acknowledgement

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