Academic Sciences Asian Journal of Pharmaceutical and Clinical Research

Vol 6, Suppl 2, 2013 ISSN - 0974-2441

Research Article

DEVELOPMENT AND VALIDATION OF NEW ANALYTICAL METHODS FOR THE ESTIMATION OF CARVEDILOL IN BULK AND PHARMACEUTICAL DOSAGE

Y.NIRUPA RANI*, B.V.V RAVI KUMAR, SMITAPADMA MOHANTY

Department of Pharmaceutical Analysis, School of Pharmaceutical Education And Research, Berhampur University, Odisha, India,
Email: ynirupa1991@gmail.com

Received: 16 February 2013, Revised and Accepted: 11 March 2013

ABSTRACT

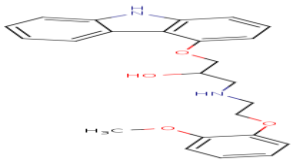
Aim of present research work is to develop and validate simple, sensitive and specific spectrophotometric method for the determination of Carvedilol, an alpha adrenergic receptor blocker, anti hypertensive drug in pure form and in pharmaceutical formulations by UV visible spectroscopic methods. The developed method was validated with respect to linearity, accuracy, precision and specificity.
The adequate drug solubility and maximum sensitivity was found in chloroform. The λ_{max} or the absorption maxima of the drug was found to be 286 nm. The calibration range was studied from 50% -150% and correlation was found to be R^2 = 0.998 which was within the limits of ICH guidelines. The objective of proposed work is to analyze and evaluate an analytical method and to compare with validation report generated for the developed method. Second objective of this research work is setting up of initial UV and chromatographic conditions for the assay of Carvedilol in pure and pharmaceutical dosage forms. It also helps in undertaking solubility studies and analytical studies of Carvedilol in order to develop initial UV and chromatographic conditions.
No interference was found from excipients at the selected wavelength and analysis conditions. The method was found to be simple, accurate, precise, economical and robust.

Keywords: Carvedilol, λmax, ICH guidelines, UV-VIS spectroscopy.

INTRODUCTION

Carvedilol[4] an anti hypertensive drugs decreases systemic vascular resistance via its alpha adrenergic receptor blocking properties. Carvedilol and its metabolite BM-910228 (A less potent beta blocker, but more potent antioxidant) have been shown to restore the inotropic responsiveness to Ca^{2+} in OH^- free radical-treated myocardium. Therefore, Carvedilol and its metabolites may be beneficial in chronic heart failure. Carvedilol and its metabolite also prevent OH^- radical induced decrease in sarcoplasmic reticulum $Ca2^+$-ATPase activity. Therefore, Carvedilol and its metabolites may be beneficial in chronic heart failure.

Chemical Structure



[3-(9H-carbazol-4-oxy)-2-hydroxypropyl][2(2methoxyphenox) ethyl] amine

Carvedilol having formula ($C_{24}H_{26}N_2O_4$) and molecular weight (406.474) is 98% protein bound drug has a half life of 24 hours[4].

The literature survey revealed that there are so many methods for the estimation of carvedilol in bulk drug and pharmaceutical formulations. Dr. C.Theivarasu et al. [5] reported the UV Spectrophotometric determination of Carvedilol in pharmaceutic al formulation. Patel Satish .A et al [6] reported validated Spectrophotometric methods for determination of carvedilol in tablets. Navneet Verma et al [7] reported simultaneous spectroscopic determination of carvedilol in its dosage form. Suddhasattya Dey et al. [10] reported analytical method development & validation of carvedilol by HPLC in bulk and dosage form and BN Suhagia et al. [8] reported on RP-HPLC and HPTLC methods for the estimation of carvedilol in bulk drug and pharmaceutical formulations. The purpose of this study was to improve the validated method with UV spectrophotometer for the determination of Carvedilol in the pure and tablet dosag forms according to ICH guidelines [11].

EXPERIMENTAL PROCESS

A simple, sensitive, accurate and rapid UV Spectrophotometric method has been developed in chloroform or the estimation of Carvedilol in bulk and its pharmaceutical formulations. The λ_{max} was found to be 286nm. It obeys Beer-Lambert's law in the concentration range of 1 – 50 µg/ml. The method was validated for its precision and accuracy according to ICH guidelines.

MATERIALS AND METHODS

Solvent used: Chloroform was used as solvent.
Instruments/Apparatus used: UV-Visible spectrophotometer (Shimadzu1800)0), Electronic
Balance (Denver), Ultra Sonicator (Enertech).

OPTIMIZATION

Scanning and determination of maximum wavelength (λ_{max})

In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, different solutions of the drugs in Chloroform were scanned using spectrophotometer within the wavelength region of 200 – 400 nm against Chloroform as blank. The resulting overlay spectrum was shown in UV absorbance spectra of Carvedilol in chloroform (20 µg/ml)

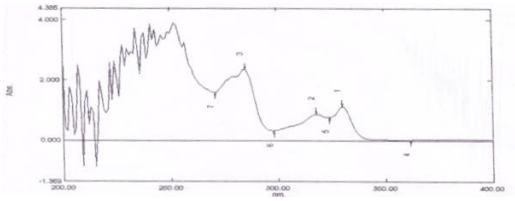


Figure 1:UV Absorption Spectrum of Carvedilol in Chloroform

METHOD

Preparation of Stock Solutions

Standard stock solution was prepared by dissolving 10 mg of drug in 10ml ml Chloroform of to get concentration of 1mg/ml (1000 µg/ml) solutions.

Preparation of Working Standard Solutions and construction of standard graph

The prepared stock solution was further diluted with Chloroform to get working standard solution of 100 µg/ml of Carvedilol. Different aliquots of Carvedilol were taken and diluted with Chloroform in 10ml Volumetric Flask. The absorbance was measured at 286 nm (λ_{max}), against reagent blank. The results were shown in Table 1. A standard graph was plotted by taking concentration of the drug on x-axis and the corresponding absorbance on y-axis and was shown in [Fig. 2].

Table 1: Linearity at 286nm

Conc. (µg/ml)	Absorbance
1	0.179
2	0.284
5	0.499
10	0.785
15	0.958
30	1.789
50	2.799

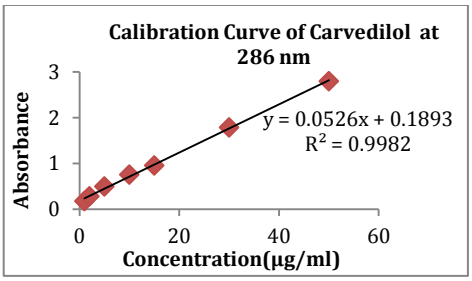


Figure 2: Calibration curve of Carvedilol at 286nm

Table 2: OPTICAL CHARACTERISTICS OF THE PROPOSED METHOD

λmax in 286nm	
Sandell's sensitivity (µg/ml/0.001 absorbance)	0.0000572
M.E.C.(ε)(1 $mole^{-1}.cm^{-1}$)	2.001×10^5
% Relative Standard Deviation	0.2504
%Range of error	
0.05 confidence limits	0.048284
0.01 confidence limits	0.07180
Regression equation(Y)	Y=0.052x+0.189
Slope(a)	0.052
Intercept(b)	0.189
Correlation coefficient	0.998

Table 3: PERCENTAGE DRUG RECOVERY

			UV- method*		
Formulation	**Wavelength (nm**	**Labelled Amount (mg**	**Mean ± SD(amount mg recovered)**	**%Drug recovered**	**% RSD**
Cardivas	286	25	24.005±0.003	96.02	0.125

*** Each value is average of three determinations ± standard deviation.**

Table 4: Precision at 286 nm

Conc.(µg/ml)	Absorbance	StatisticalAnalysis
20	1.153	Mean=1.153
20	1.158	Standard deviation ±0.002449
20	1.153	%RSD=0.2167
20	1.156	
20	1.152	
20	1.156	

Table 5: Accuracy at 286nm

Sample ID	Concentration (µg/ml)		%Recovery of Pure drug	Statistical Analysis	
	Pure drug	Formulation			
S_1 : 80 %	8	10	98.8	Mean	98.8
S_2 : 80 %	8	10	98.5	SD	0.7754
S_3 : 80 %	8	10	99.35	% RSD	0.7848
S_4 : 100 %	10	10	96.02	Mean	95.9
S_5 : 100 %	10	10	95.7	SD	0.2687
S_6 : 100 %	10	10	96.2	% RSD	0.2801
S_7 : 120 %	12	10	98.4	Mean	98.6

S_8 : 120 %	12	10	99.16	SD	0.4589
S_9 : 120 %	12	10	98.34	% RSD	0.4654

ESTIMATION OF CARVEDILOL IN COMMERCIAL FORMULATIONS

METHOD

For analysis of commercial formulations, 3 tablets were accurately weighed the contents of the tablets were taken. The powder equivalent to 103 mg of Carvedilol was taken in a 100 ml volumetric flask, containing 70 ml of chloroform and sonicated for 30 minutes. The volume was made up to 100 ml with chloroform and filtered to get a solution of concentrations 100 µg/ml. This was further diluted with chloroform to get a concentration within the linearity range and the absorbance was measured against the blank at 286 nm and the results were shown in Table 3.

VALIDATION

Precision

The precision of the proposed method was as certained by actual determination of six replicates of fixed concentration of the drug within the Beer's range and finding out the absorbance by the proposed method. From this absorbance, mean, standard deviation, % RSD was calculated. The readings were shown in Table 4.

Accuracy

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of bulk samples of Carvedilol within the linearity range were taken and added to the pre-analyzed formulation of concentration 10µg/ml. From that percentage recovery values were calculated. The results were shown in Table 5.

RESULTS AND DISCUSSION

From the optical characteristics of the proposed method, it was found that Carvedilol obeys linearity within the concentration range of 01-50 µg/ml. From the results shown in Table 2, it was found that the % RSD is 0.2801(286nm) which is less than 2 %, which indicates that the method has good reproducibility. From the results shown in accuracy Table , it was found that the percentage recovery values of pure drug from the preanalyzed solution of formulation were in between 96.2-99.35%, at the wavelength 286nm which indicates that the proposed method is accurate and also reveals that the commonly used excipients and additives in the pharmaceutical formulations were not interfering in the proposed method.

CONCLUSION

The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routine determination of Carvedilol in pure samples and pharmaceutical formulations.

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