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Validation Of U.V Spectrophotometric Technique For Estimation Of Cardiovascular Drugs

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Abstract:

The current study's goals are to provide a quick, accurate UV absorption spectrophotometric method for measuring medicines with low water solubility, such carvedilol, in pharmaceutical formulations and to assess cavtedilol's improved solubility in the formulation. By utilising the hydrotropy principle, the aqueous solubilities of these chosen model pharmaceuticals were significantly (5 to 98 fold) increased in distilled water. Ammonium acetate (6M), potassium acetate (5M), potassium citrate (0.5 M), sodium citrate (1.25 M), and urea (8M) are some of the different hydrotropic agents that can be utilised. Sodium lauryl sulphate and Sodium hydroxide are the least expensive and safest solubilizing agent utilised here. The main goal of the current study is to use this solubilizing agent instead of more expensive organic solvents to extract and dissolve the pharmaceuticals from their dosage forms. Because sodium lauryl sulphate and Sodium hydroxide did not exhibit any absorbance at the chosen maximum wavelength for carvedilol, 241 nm and valsartan 250 nm, there was no interference with the estimation. The analysis's findings have been supported by statistical analysis and recovery studies. The suggested approach is fresh, uncomplicated, economical, accurate, secure, and exact. Recoveryinvestigations confirmed the accuracy and precision of the developed methodologies that were applied in accordance with the International Conference on Harmonisation (ICH) principles.

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide, and benzene have been employed for the solubilization of poorly water soluble drugs for spectrophotometric estimations. Drawbacks of organic solvents include higher cost, toxicity, pollution, and error, in analysis due to volatility. In the preliminary solubility studies, it was found that there was considerable enhancement in the aqueous solubilities.

KEYWORDS: Hydrotropic, Spectrophotometric estimation, Carvedilol, Sodium lauryl sulphate.

CHAPTER-I INTRODUCTION

1.0 INTRODUCTION:

Carvedilol is chemically **(±)-[3-(9H-carbazol-4-yloxy)-2-hydroxypropyl][2-(2-methoxyphenoxy)ethyl]amine.** Carvedilol (Coreg/Kredex/Dilatrend) is commonly referred to as a 'third generation beta blocker' that has a complex pharmacological profile, including non-selectivebeta-adrenergic and alpha-1 adrenergic receptor blocking actions, anti-oxidant activity and other properties. The first beta blocker to be licenced for the treatment of mild, moderate, and severe congestive heart failure is carvingilol. Having an alpha1-blocking effect and being extremely lipophilic, carvingilol is a non-selective beta-adrenoceptor antagonist that encourages peripheral vasodilation. Additionally, it has antimitogenic and free radical scavenging properties. Water does not readily dissolve carvedilol. Poorly water-soluble pharmaceuticals must be solubilized using special procedures.The literature has described a number of techniques to improve the aqueous solubilities of medications that are not very water-soluble. One of them is hydrotropic solubilization. This phenomenon occurs when a second solute is added in considerable quantities, increasing the solubility of the first solute in water. Sodium benzoate, niacinamide, sodium citrate,sodium glycinate, and urea concentrated aqueous hydrotropic solutions have been seen to increase the solubility of insoluble and hardly soluble medicines in water. In the study of pharmaceuticals that are poorly soluble in water, hydrotropic solutions can be used in place of organic solvents. The main goal of the current study is to use a solubilizing ingredient in the formulation of tablets and analytical stock solutions for a drug that is weakly water-soluble. Carvedilol is well dissolved from its dosage form, eliminating the need for an expensive organic solvent. Results of the analysis performed using the suggested method were compared to those produced using the United States Pharmacopoeial method. The sodium lauryl sulphate solubilizing hydrotropic agent and frequently used tablet excipients did not affect the spectrophotometric result at λmax 241nm. Beer's law was followed at concentrations between 5 and 30 g/ml. Statistics have been used to validate the analysis' findings. The suggested approach has the advantage of replacing expensive and hazardousorganic solvents with sodium lauryl sulphate, a less expensive chemical, without sacrificing accuracy. The suggested approach was determined to be novel, straightforward, environmentally friendly, precise, safe, reproducible, and economical, and it may be successfully used in regular examination of Carvedilol tablets.Certainly, there is further scope of 10 % sodium

lauryl sulphate as solubilizing agent for the spectrophotometric analysis of other poorly water-soluble drugs . The proposed method is the proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines.

CHAPTER-II REVIEW OF LITERATURE

LITERATURE REVIEW:-

Cyclic voltammetry is frequently utilised in an electrochemical examination of a molecule, a biological material, or an electrode surface, according to Vinod K. Gupta and colleagues in "Voltammetric techniques for the assay of pharmaceuticals—A review", Analytical Biochemistry 408 (2011) 179-196. The disciplines of environmental electrochemistry, organic chemistry, inorganic chemistry, and biochemistry all make use of it successfully. The capacity of CV to quickly observe the redox behaviour over a broad potential range is what gives it its usefulness.Additionally, various voltametric validation techniques are investigated.

Vinod V. Anuse and etal in World Journal of Pharmaceutical Research Volume 10, Issue 1, 1112-1140 used High-Performance Liquid Chromatography (HPLC), a technique where the mobile phase is pushed quickly through the column. Water was utilised as the solvent in the AUC method, and detection took place between 240 and 280 nm. For the determination of Vigabatrin, the stability indicating HPLC method was created and verified. The mobile phase included a 95:5 ACN:methanol pH3 ratio. The detection wavelength was 285 nm. The procedure was discovered to be straightforward, linear, quick, precise, accurate, repeatable, and robust. All parameters had % RSDs that were less than 2. The findings indicated that the suggested technique was effective for accurately, precisely, and quickly determining the bulk form of vigabatrin..

Permender Rathee and etal "Simultaneous estimation of amlodipine besylate and atenolol as a.p.i. and in tablet dosage forms by Vierodt's method using u.v. spectrophotometry" International Journal of ChemTech Research CODEN(USA): IJCRGG ISSN : 0974-4290 Vol.2, No.1, pp 62- 68, developed new Amlodipine besylate and atenolol were simultaneously analysed utilising a newly designed UV-Spectrophotometric method with aqueous medium as the solvent. The Vierodtmethod or simultaneous equations are the foundations of the method. Amlodipine Besylate and Atenolol were found to have max values in the solvent medium of 238.4 nm and 273.4 nm, respectively. In the range of 4.0 to 32.0 mg/ml and 20.0 to 200.0 mg/ml, respectively, the systems follow Beer's law, with correlation coefficients of 0.9984 and 0.9996 for amlodipine besylate and atenolol, respectively. The results showed that repeatability, interday precision, and intraday precision were, respectively, 0.562, 0.474, 0.456, and 0.238, 1.31, 0.337. There was no interferencefrom common tablet adjuvants. The recovery has been tested using the t-test and F-test.The method was successfully applied to the assay of Amlodipine Besylate and Atenolol in tablet formulations.

Rakesh, S. U. and etal in "HPTLC method for quantitative determination of quercetin inhydroalcoholic extract of dried flower of Nymphaea stellata Willd" International Journal of ChemTech Research 2009Vol.1No.4pp.931, In order to quantify the amount of quercetin in the dried flowers of Nymphaea stellata Willd, a sensitive and trustworthy high performance thin layerchromatographic method has been devised. On silica gel 60 F plates, the hydroalcoholic extract of

N. stellata was chromatographed using toluene: ethyl acetate: formic acid, 5: 4: 0.2 (v/v/v) as the mobile phase. Using a deuterium lamp and densitometric scanning at a wavelength of =380 nm, detection and quantification were carried out. By employing the standard addition method to conduct recovery experiments at three different levels, the accuracy of the approach was tested, and the average recovery of quercetin was determined to be 99.33%.

Gaurav Tiwari and etal in "Simultaneous Estimation of Metronidazoleand Amoxicillin inSynthetic Mixture by Ultraviolet Spectroscopy"Asian Journal of Research in Chemistry, For the simultaneous estimation of metronidazole and amoxicillin in combination dosage form, two straightforward, accurate, exact, repeatable, cost-effective, and methods have been devised.The first approach uses two analytical wavelengths for both medicines at 319 nm and 273.8 nm to create and solve a simultaneous equation in phosphate buffer at pH 7.4. The second method is Q value analysis, which uses 319 nm and 289 nm as an iso-absorptive point to quantify absorptivity.In a concentration range of 10–50 mcg/mL, metronidazole and amoxicillin exhibit linearity at their respective maxes of 319 nm and 272 nm as well as at the iso-absorptive point of 289 nm.. The results of analysis have been validated statistically, the standard deviation lies in the range of 0.012

- 0.071 for amoxicillin and 0.028 - 0.153 for amoxicillin in case of simultaneous equation methodand 0.020 - 0.098 for amoxicillin and 0.032 - 0.231for amoxicillin in case of Q - analysis method.Recovery studies range from 98.45 - 99.0% for amoxicillin and 101.10 – 102.06% for metronidazole in case of simultaneous equation method and 99.60 – 101.0% for amoxicillin and 100.20-100.90% for metronidazole in case of Q - analysis method confirming the accuracy of theproposed method.

Suddhasattya Dey and etal in their work entitled "Analytical method development & validation of carvedilol by HPLC in bulk and dosage form" / Journal of Pharmacy Research 2010, 3(12),3075-3077, showed that Carvedilol, a ß-blocker, could be estimated using a straightforward,accurate, and exact HPLC approach in both bulk and pharmaceutical dosage form. 1.77g of potassium dihydrogen phosphate, dissolved in distilled water, was used as the mobile phase, whichwas then diluted to 650 ml with the same solvent and had its pH raised to 2.0 with phosphoric acid.Acetonitrile (350 ml) was added and blended. After that, it was put through a 0.2-micronmembrane filter. The chromatographic system's specifications are as follows: wave length 240nm, flow rate 1ml/min, column 4.6mm*25cm*5micron (c8), and oven temperature 55°c. With a regression coefficient of 0.994, a linear response was seen within the concentration ranges of 806and 1202 g/ml. The procedure was subsequently validated for several parameters in accordance with the ICH (International Conference for Harmonisation) standards.

Nitin Mahajan & etal in "Analytical method development and validation for known andunknown impurities profiling for carvedilol pharmaceutical dosage form (tablets)", International Journal of Current Pharmaceutical Research ISSN- 0975-7066 Vol 13, Issue 6, 2021, For the quantitative determination of known and unknown impurity profile of Carvedilol pharmaceutical dosage forms (Tablets), a novel gradient stability indicating reverse phase HPLC approach that isstraightforward, sensitive, tough, robust, and specific has been developed. They tried to Chromatographic separation has been achieved on an Inertsil ODS 3V column (150 mm x 4.6 mm, 5µm) with mobile phase consisting Mobile phase-A (Water, Acetonitrile and Trifluroacetic acid in the ratio of 80:20:0.1 v/v/v respectively and pH adjusted to 2.0 with dilute potassium hydroxide solution) and Mobile phase-B (Water and acetonitrile in the ratio of 100:900 v/v respectively) delivered at flow rate of 1.0 ml min-1 and the detection wavelength 240 nm. The temperature within the column compartment was kept at 40 °C.

L. Nandhakumar and etal "An Overview of Pharmaceutical Validation: Quality Assurance View Point" International Journal of Research in Pharmacy and Chemistry, Ijrpc 2011, 1(4) Issn: 2231–2781, Any industry and the items it produces have quality as their primary goal. The pharmaceutical sector is currently interested in many different perspectives on how to acquire suchquality. On the dais of the pharmaceutical arena, familiarity with a practise that places us in common and routine convention ensured to offer a quality that sounds internationally in terms of a spoken quality. Validation is a method of providing huge advantages to even higher levels of acceptable quality than those found in the worldwide scale of standards. In recent years, giving validation importance has become more significant. Designing and practising the planned procedures while also documenting them is the art of validation. Together, validation and qualitycontrol will guarantee the items' overall quality. Hence, an emphasis made on to review that gives a detailed, overview of validation concept of designing, organizing and conducting validation trials. Additionally a view of validation against the quality assurance, drug development and manufacturing process has been discussed.

CHAPTER-III AIM & OBJECTIVES

4. AIM &OBJECTIVES OF RESEARCH WORK: -

- The aim of the present study is to establish a new analytical method that is more safe,fast ,accurate and precise with the following objectives.
- To check the appropriate solvent for studying the contents of formulation.
- To prepare different aloquits of the API , using solvents like petroleum ether, chloroform,ethyl acetate, acetone ,Water and methanol and establish a solvent system as alternative fororganic solvents.
- To develop an analytical method and validate for a specific formulation.

CHAPTER-IV PLAN OF WORK

4. PLAN OF WORK:-

Sr.No.	Particulars	Duration
1	Literature review	01 months
2	Procurement of Drug powder and solubility studies with different solvents	01 months
3	Analytical method development	01 months
4	Validation of proposed analytical method	01 months

CHAPTER-V DRUG PROFILE

5.0 Drug profile

Employed is a Shimadzu UV1900i double beam spectrophotometer with matched 1 cm quartz cells. We received a bulk medicine sample of carvedilol as a gift from Intas Ltd. in Ahemdabad, Gujarat, India. The formulation is made from commercially available Carvedilol (CARDIVAS -12.5 mg) coated tablet tablets. All other substances, including solvents, were of analytical grade.

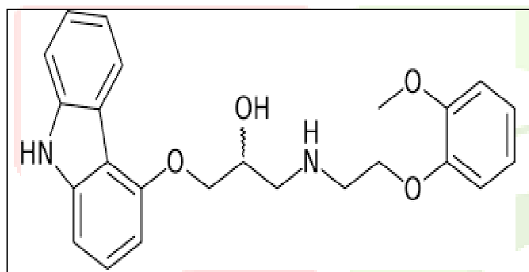


Fig:02- Carvedilol (CV)

As per the Ich guidelines following parameters will be tested for establishing the validity of the proposed analytical procedure.

2.1. SPECIFICITY

When validating identification tests, determining impurities, and performing the assay, specificity should be investigated. The methods used to prove specificity will vary depending on the analytical procedure's intended goal. It is not always possible to show that an analytical technique is completely discriminatory for a given analyte. In this situation, it is advised to combine two or more analytical techniques to reach the required level of discrimination.

2.2. LINEARITY

It is important to assess a linear relationship over the entire analytical procedure. It can be proven using the suggested approach directly on the drug substance (by diluting a standard stock solution) and/or separately weighing synthetic mixtures of the drug product's constituent parts. When examining the range, the latter feature might be investigated. By visually inspecting a plot of signals as a function of analyte concentration or content, linearity should be assessed. If a linear relationship exists, test findings should be examined using the proper statistical techniques, for as by computing a regression line using the least squares approach. In some circumstances, the test results may need to be treated to a mathematical transformation prior to the regression analysis in order to obtain linearity between tests and sample concentrations. It may be possible to calculate the degree of linearity using data from the regression line itself.

2.3. RANGE

The chosen range typically results from linearity tests and is based on how the process will be used. When applied to samples having levels of analyte within or at the extremes of the analytical methods defined range, it is confirmed that the analytical procedure offers an appropriate level of linearity, accuracy, andprecision. Consider the minimum specified ranges listed below:

- for content uniformity, a minimum of 70 to 130 percent of the test concentration, unless a wider more appropriate range, based on the nature of the dosage form (e.g., metered dose inhalers), is justified; - for the assay of a drugsubstance or a finished (drug) product: typically from 80 to 120 percent of the test concentration;
- for dissolution testing: +/-20 % over the specified range;

e.g., if the specifications for a controlled released product cover a region from 20%,after 1 hour

2.4. ACCURACY

Accuracy should be established across the specified range of the analyticalprocedure.

2.4.1. Assay

2.4.1.1 Drug Substance

Several methods of determining accuracy are available:

a) application of an analytical procedure to an analyte of known purity (e.g. reference material);

b) comparison of the results of the proposed analytical procedure with those of a second well-characterized procedure, the accuracy of which is stated and/or defined .

c) accuracy may be inferred once precision, linearity and specificity have been established.

2.4.1.2 Drug Product

Several methods for determining accuracy are available:

a) application of the analytical procedure to synthetic mixtures of the drug product components to which known quantities of the drug substance to be analysed have been added;

b) in cases where it is impossible to obtain samples of all drug product components ,it may be acceptable either to add known quantities of the analyte to the drug product or to compare the results obtained from a second, well characterized procedure, the accuracy of

which is stated and/or defined Once precision, linearity, and specificity have been verified, accuracy can bededuced.

2.4.2. Recommended Data

Accuracy should be assessed using a minimum of 9 determinations over aminimum of 3 concentration levels covering the specified range (e.g. 3 concentrations/3 replicates each of the total analytical procedure).

Accuracy should be reported as percent recovery by the assay of known added amount of analyte in the sample or as the difference between the mean and the accepted true value together with the confidence intervals.

2.5. PRECISION

Validation of tests for assay and for quantitative determination of impurities includes an investigation of precision.

5.1. Repeatability

Repeatability should be assessed using:

a) a minimum of 9 determinations covering the specified range for the procedure(e.g. 3 concentrations/3 replicates each)or

b) a minimum of 6 determinations at 100% of the test concentration.

5.2. Intermediate Precision

The extent to which intermediate precision should be established depends on the circumstances under which the procedure is intended to be used. The applicant should establish the effects of random events on the precision of the analytical procedure.

Typical variations to be studied include days, analysts, equipment, etc. It is not considered necessary to study these effects individually. The use of an experimental design (matrix) is encouraged.

5.3. Reproducibility

Reproducibility is assessed by means of an inter-laboratory trial. Reproducibility should be considered in case of the standardization of an analytical procedure, for instance, for inclusion of procedures in pharmacopoeias. These data are not part of the marketing authorization dossier.

5.4. Recommended Data

The standard deviation, relative standard deviation (coefficient of variation) and confidence interval should be reported for each type of precision investigated.

2.6. DETECTION LIMIT

Several approaches for determining the detection limit are possible, depending on whether the procedure is a non-instrumental or instrumental. Approaches other than those listed below may be acceptable.

6.1. Based on Visual Evaluation

Visual evaluation may be used for non-instrumental methods but may also be usedwith

instrumental methods.

The detection limit is determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably detected .

6.2. Based on Signal-to-Noise

This approach can only be applied to analytical procedures which exhibit baseline noise.Determination of the signal-to-noise ratio is performed by comparing measured signals from samples with known low concentrations of analyte with those of blank samples and establishing the minimum concentration at which the analyte can be reliably detected. A signal-to-noise ratio between 3 or 2:1 is generally considered

2.7. QUANTITATION LIMIT

Several approaches for determining the quantitation limit are possible, depending on whether the procedure is a non-instrumental or instrumental. Approaches other than those listed below may be acceptable.

Based on the Standard Deviation of the Response and the Slope

The quantitation limit (QL) may be expressed as:

$$QL = \frac{10\,\sigma}{S}$$

where σ = the standard deviation of the responseS = the slope of the calibration curve

The slope S may be estimated from the calibration curve of the analyte.

2.8. ROBUSTNESS

The evaluation of robustness should be considered during the development phase and depends on the type of procedure under study. It should show the reliability of an analysis with respect to deliberate variations in method parameters.If measurements are susceptible to variations in analytical conditions, the analytical conditions should be suitably controlled or aprecautionary statement should be included in the procedure. One consequence of the evaluation of robustness should be that a series of system suitability parameters (e.g., resolution test) is established to ensure that the validity of the analytical procedure is maintained whenever used.

Selection of solvent : Solvent used in spectrophotometry must meet followingrequirements to assure successful and accurate results:

1) Must dissolve the sample,
2) Should not react with cuvette material,
3) Must be relatively transparent in the spectral region of interest,
4) Should not interfere with the UV spectra of the analyte,
5) Should be available in high purity

All spectrophotometric methods for samples with many components are based on the fact that at all wavelengths:

The total absorbance of a solution is equal to the sum of the constituent components' absorbances,or The total absorbance of the solution in the sample cell minus the total absorbance of the solutionin the reference cell is the measured absorbance. There are many spectrophotometric techniques,such as:

3.1 QUANTITATIVE SPECTROPHOTOMETRIC ASSAY:-

Assay of single component samples

a) **Single standard or Direct Comparison Method:** In this method the absorbance of a standard solution of known concentration and a sample solution is measured .The concentration of unknown can be calculated using the formula.
C2 =C1xA2/A1
A1& A2 = Absorbance of standard and sample
C1 and C2 = Concentration of standard and sample

b) **Calibration curve method or multiple standard method:** A calibration curve is plotted using –concentration vs. absorbance value of five or more standard solution. A straight line is drawn either through maximum number of points or in such a way that there is equal magnitude of positive and negative errors that is line of best fit. From the absorbance of the sample solution and using the calibration curve, the concentration of the drug, amount and percentage purity can be calculated.

c) **Molar absorptivity and Percent molar absorptivity**
The molar absorptivity and percent molar absorptivity was calculated by using formula

€1%, 1cm = Absorbance / Concentration (g/100ml).
€max = Absorbance × mol. wt. × 100/ wt (in mg) of compound in 100ml ×pathlength

d) **Assay of substances in multi compound sample:** The basis of all the spectrophotometric techniques for multi compound samples is the property that all samples show the property of ----
1. Absorbance which is the sum of absorbance of the individual components.
2. The measured absorbance is the difference between the total absorbance of the solution in the sample cell and that of the solution in the reference (blank) cell.

Simultaneous equation method:- Two wavelengths selected for the method λ1 and λ2 that are absorption maximas of cardivilol and Carvedilol/Lisinopril dihydrate/Losartan potassium respectively in methanol: 1N NaOH (1:1) or methanol: 0.1N NaOH (1:1). The stock solutions of both the drugs were further diluted separately with methanol: 1N NaOH (1:1) or methanol: 0.1N NaOH (1:1) to get a series of standard solutions of 0-30μg/ml concentrations. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs at both wavelengths were determined as mean of three independent determinations. Concentrations in the sample were obtained by using following equations-

$$Cx = \frac{A1\ ay2 - A2\ a\ y1}{ax1ay2 - ax2ay1} \quad \text{.......... Eq. (i)}$$

$$Cy = \frac{A1\ a\ x2 - A2\ a\ x1}{a\ y1ax2 - ay2a\ x1} \quad \text{.......... Eq. (ii)}$$

Where, A1 and A2 are absorbances of mixture at λ1 and λ2 respectively, ax1 and ax2 are absorptivities of cardivilol at λ1 and λ2 respectively and ay1 and ay2 are absorptivities of Carvedilol at λ1 and λ2 respectively. Cx and Cy are concentrations of cardivilol and Carvedilol/Lisinopril dihydrate/Losartan potassium respectively.

At λ1: A1 = ax1Cx + ay1Cy ....(1)

$At\lambda 2: A2 = ax2Cx + ay2Cy$ ....(2)

CHAPTER-VI MATERIAL AND METHODS

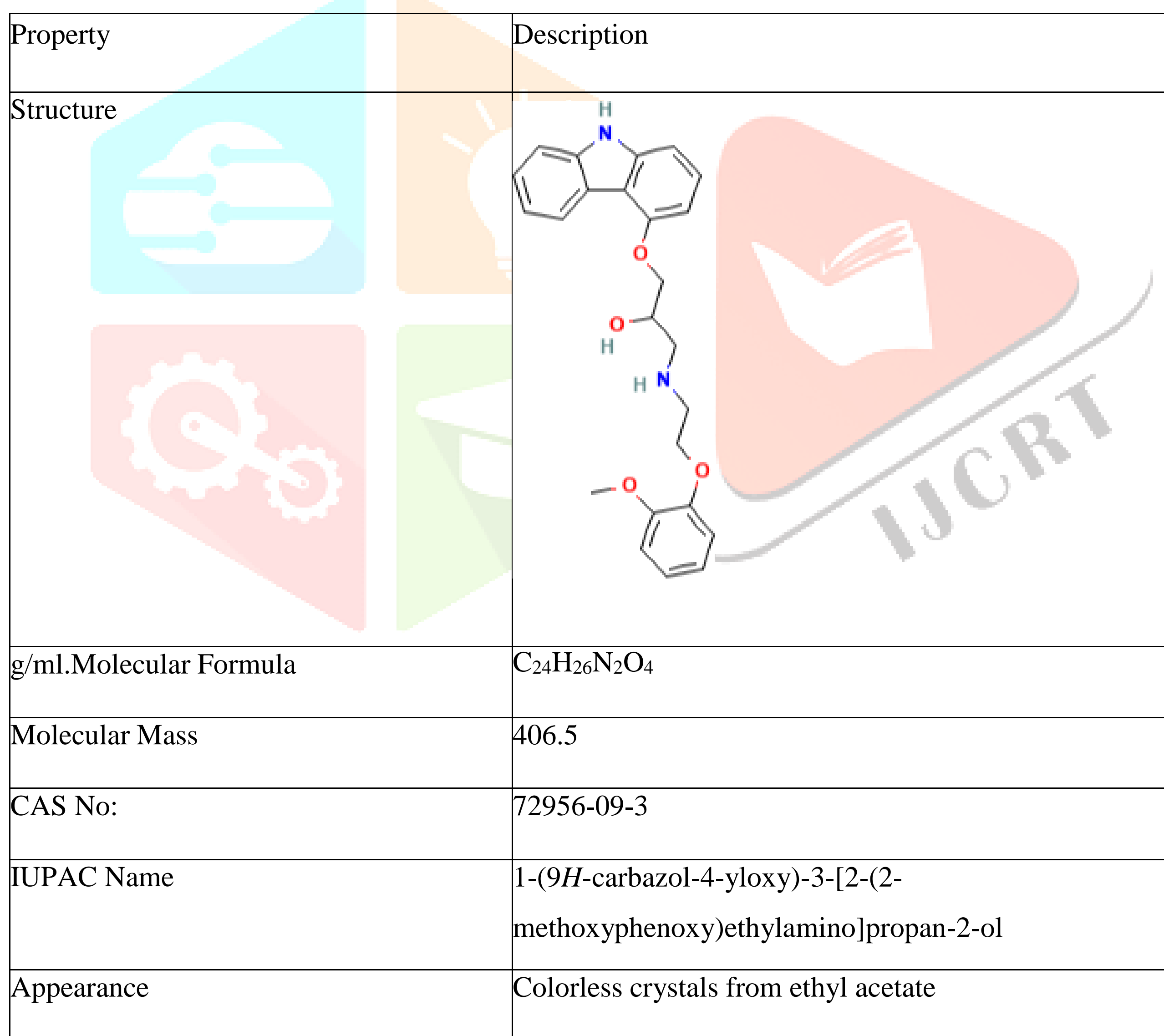
6.0 Material and Methods Preformulation

studies of carvedilol.

Melting Point :- The melting point of the crystalline drug was determined by using the digitalmelting point apparatus (Vego) and was found to ; $114^{0}C$.

DRUG PROFILE:

Table no. 1: Drug Profile of Carvedilol

Property	Description
Structure	
g/ml.Molecular Formula	$C_{24}H_{26}N_2O_4$
Molecular Mass	406.5
CAS No:	72956-09-3
IUPAC Name	1-(9*H*-carbazol-4-yloxy)-3-[2-(2-methoxyphenoxy)ethylamino]propan-2-ol
Appearance	Colorless crystals from ethyl acetate

Solubility	Carvedilol is an hydrophobic Compound Freelysoluble in dimethylsulfoxide; soluble in methylene chloride, methanol; sparingly soluble in ethanol, isopropanol; slightly soluble in ethyl ether
Bioavailability	25-35%.
Storage	Store at -20° C
Protein Binding	Carvedilol >99.7% plasma protein bound and pharmacologically active
Biological Half Life	Between 7-10 hours
Excretion	16% of carvedilol is excreted in the urine with <2% excreted as an unmetabolized drug
PKa	7.97
Melting Point	114.5 °C
Standard	Minimum purity: 98.0 %

UV spectra of Carvedilol:-

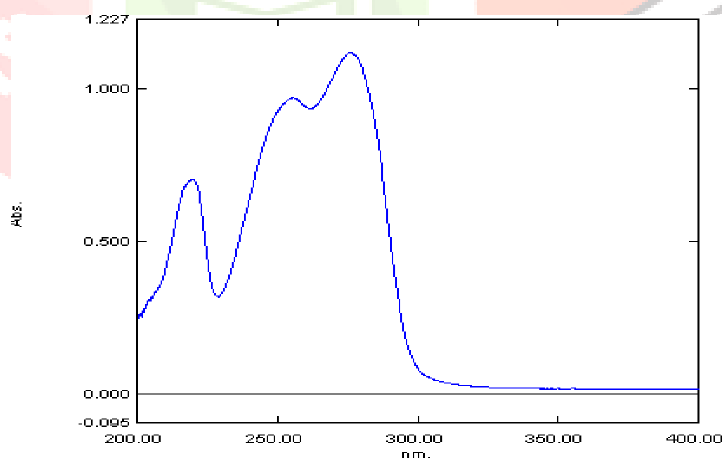


Fig. No. 1 Uv spectra of carvedilol

IR characterisation of drug is done but graphs awaited.

The FTIR spectra of given sample is as shown below and coincides with the standard valuesof

functional groups thereby confirming the authenticity of the drug.

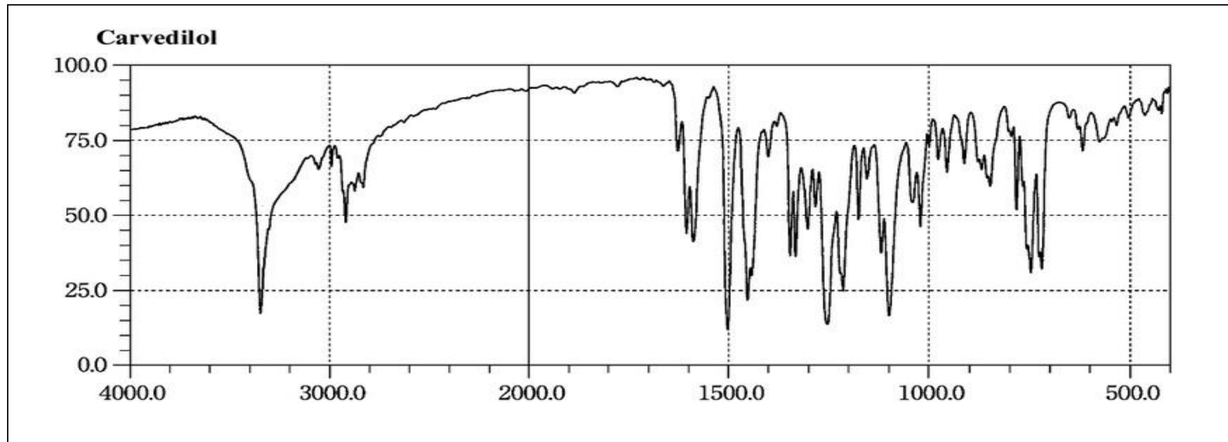


Fig 2:- Standard FTIR spectra of Carvedilol

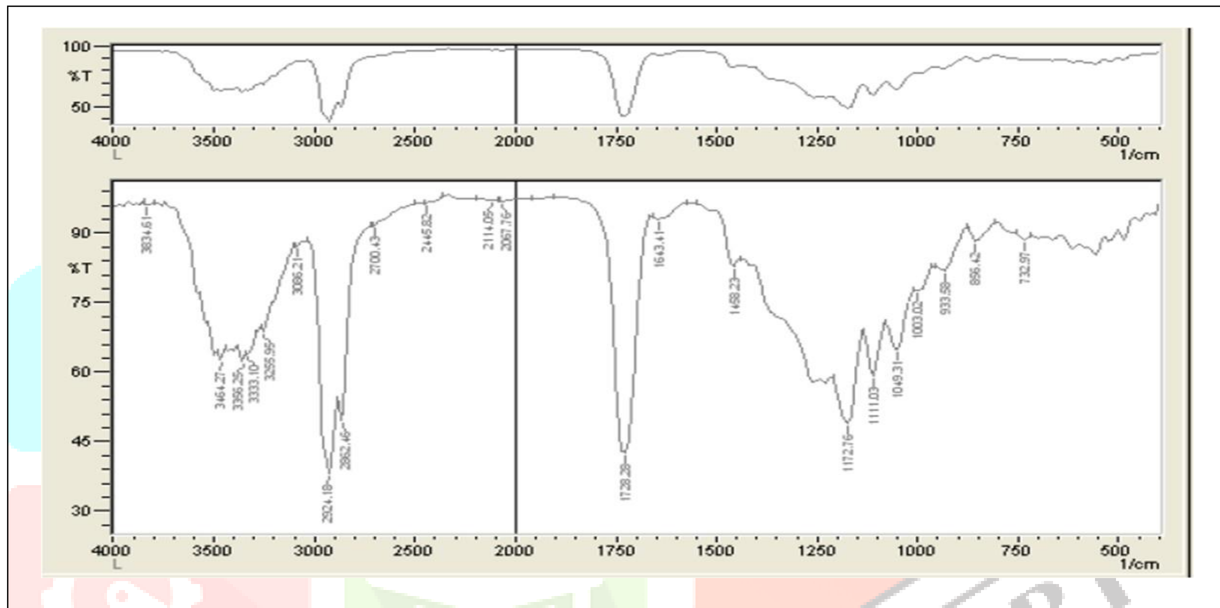


Fig 3:- FTIR spectra of Carvedilol procured drug

Sr.No.	Band (cm^{-1})	Characteristic	Functional Group
1	2924 2862 2700	strong	C-H stretch

2	1594	Medium	C=C
3	3060	Medium and strong	-C-H-Stretching
4	3345	Medium and strong	O-H Stretching
5	752	Medium and strong	=C-H Stretching
6	1111	Medium and strong	C-O stretch
7	1458	medium	N-H bending
8	933 856	Sttrong an medium	N-H rocking
9	1217 1728	strong	C-N stretch aromatic aldehyde
10	3464 3356 3333	strong	=C-H Stretching Aromatic
11	732	Medium	Disubstituted(meta)

6.1. Equipments used:-

Table no.1.A List of instruments used in study.

INSTRUMENT	**MAKE**
Weighing Balance	**Wensar ,high precision**
UV Spectrometer	**Schimadzu UV 1900i**

6.2. CHEMICALS REQUIRED:-

Table no.2. List of chemicals used with their specification.

Sr.No.	**CHEMICAL(GRADE)**	***MANUFACTURER***
1	Carvedilol	*Zeon Pharma Industries India Pvt ltd*
2	Valsartan	*Intas Pharma ,Ahmedbad,India*
3	Sodium hydroxide(AR)	*Merck ,India*

4	Double Distilled Water	*Merck ,India*
5	*Sodium lauryl Sulphate*	*Merck ,India*

6.3. Experimental

6.3.1 Instruments

Double beam UV–Vis spectrophotometer (Shimadzu, kyoto, Japan), model UV-1900i with1 cm quartz cells, the spectral band is 1 nm and scanning speed is 2800 nm/min with 0.1 nm interval.

6.3.2 Chemicals and reagents

1. Pharmaceutical grade CV was obtained as a gift by Zeon Pharma Industries India Pvt ltd. It was certified to contain 98.75% according to the company analysis certificates.
2. 5%Sodium Lauryl Sulphate solution, double distilled water and Sodium Lauryl Sulphate were purchased from (Merck ,India).

6.3.3 Marketed formulation

Cardivas (12.5 mg) tablets , is labeled to contain 12.5 mg CV, manufactured by Sun Pharmaceuticals Industries Ltd.purchased from the local market.

6.3.4 Solutions

Standard stock solutions each containing 1000 µg/mL of CV were prepared separately indistilled water,and 5%,10 % Sodium Lauryl Sulphate solution. Working standard solutions of these drugs (100 µg/mL) were obtained by dilution of the respective stock solutions in distilled water,and 5%,10 %Sodium Lauryl Sulphate solution.

6.3.5 Procedure

6.3.6 Calibration Curve in Presence and Absence of sodium lauryl sulphate

For preparation of calibration curve of Carvedilol, 10 mg Carvedilol is transferred to a 100 ml volumetric flask. To this flask, 20 ml of AR Methanol was added and the flask was sonicated to solubilize the drug. Rest of methanol was used to make up the volume up to the mark to give a stock solution (100 mcg/ml). This stock solution was diluted suitably with methanol to produce various standard solutions containing 5, 10, 15, and 20µg/ml of drug. Also similarly stock solution is prepared

with same quantity of drug and distilled water with 5% & 10% of Sodium lauryl sulphate with respect to drug, instead of methanol as solvent Absorbance's of these solutions were observed at 241 nm against corresponding reagent blanks. (Fig.no.1.1 &1. 2).

6.3.7 Preliminary Solubility Studies of Carvedilol

In the solubility studies, it was found that there was more than 3 fold enhancement in the solubility of Carvedilol in distilled water with 5% & 10% of Sodium lauryl sulphate with respect to drug ,at 28±1ºC (in comparison to solubility in distilled water).(Table no.1.3,1.4 &1. 5)

6.3.8 Analysis of Carvedilol in Tablets using United States Pharmacopoeial Method

For analysis of Carvedilol in tablets using United States Pharmacopoeial method, twenty tablets were weighed and powdered finely. A portion of this powder containing 10 mg Carvedilol was accurately weighed and transferred to a 100 ml volumetric flask. Methanol (30 ml) was added and sonicated for 5 minutes. After, it was diluted to 100 ml with methanol and filtered through a sintered glass funnel (G-3). The filtrate was diluted suitably with methanol to produce a solution containing 15µg/ml of Carvedilol. The absorbance of this solution was noted at 241 nm and the drug content was determined (Table 11.2).

6.3.9 Analysis of Carvedilol in Tablets by the Proposed Method

For the analysis of Carvedilol in tablets by the proposed method, 20 tablets were powdered and tablet powder equivalent to 10 mg Carvedilol (27.5 mg) was transferred to a 100 ml volumetric flask containing 20 ml of distilled water with 0.5mg and 1.00 mg of sodium lauryl sulphate solution separately. Flasks were sonicated for about 10 minutes to solubilize the drug present in tablet powder and volume was made up to the mark with distilled water. After filtration through sintered glass funnel (G-3), the filtrate (tablet extract) was appropriately diluted with distilled water containing 5% & 10% of SLS to produce a solution containing 15µg/ml of Carvedilol and absorbance was noted at 241 nm against reagent blank. Table no.1.7 & 1. 8.

6.4 Accuracy/Recovery Studies

To study the accuracy of the proposed methods in both Spectrophotometric and chromatographic methods, recovery study were carried out by addition of known amount of bulk drug to solution. To perform recovery studies, Carvedilol bulk drug sample was added (13.5 mg) to the pre- analyzed tablet powder (equivalent to 5 mg of Carvedilol) and drug content was determined by the proposed method. The results of recovery studies were presented in (Table no.1.10). which shows 100.97 & 100.29 % recovery respectively.

6.5 Effect of SLS Concentration:-

To elucidate the concentration dependent solubilising effect of SLS the three stock solutions with plain distilled water and with distilled water having 5% & 10% of SLS solution as solvent were prepared to get 100µg/ml stock solution .This was further diluted with respective solution to yield 15 ppm solution and absorbance at 241 nm was reported as shown in (table no.1.3, 1.4 & 1.5)

6.6 Limit of detection (LOD) and limit of quantitation (LOQ)

The detection limit and quantitation limit were computed to assess quantity of analyte which can be detected and minimum quantity of analyte which can be determined quantitatively by proposed UV-spectrophotometric and chromatographic methods. The LOD and LOQ of Carvedilol were estimated from the standard deviation of the response and the slope of the calibration curve by using following formula.

3.3 x σ

________________________________ S

10 x σ

________________________________ S

Where σ = the standard deviation of the responseS = the

slope of the calibration curve

LOD and LOQ were found to be 0.1980 µg / ml and 0.0287 µg / ml respectively with USP methodwhile, LOD and LOQ were found to be 0.0151 µg / ml and 0.0458 µg / ml respectively with the proposed method.

6.7 PRECISION:

Precision of the method reported as % RSD, was estimated by repeatability, reproducibility and intermediate precision by measuring absorbance of three replicates of 10 µg / ml of Carvedilol Trihydrate. % RSD values as in Table no.13.8 is less than 2% that illustrate the good precision of the analytical method.

Fig.no.1.1 Linearity of API in methanol

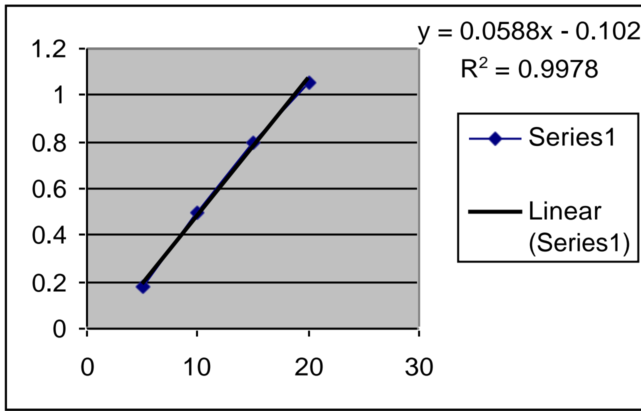


Fig.no.1. 2 Linearity of tablet in methanol

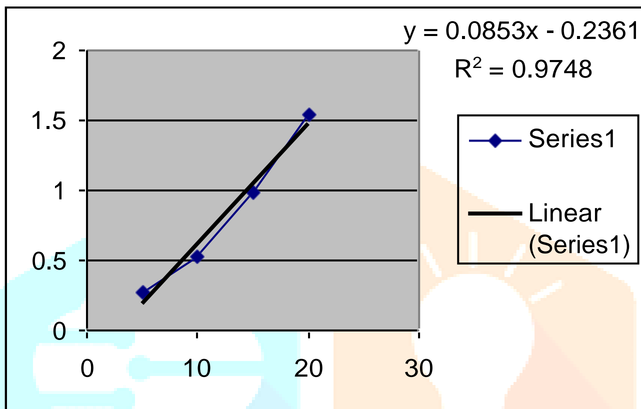


Table no.1. 1Absorbance of API dissolved in Methanol at 241 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.178	0.180	0.176	0.178	0.0888
2	10	0.4980	0.499	0.4973	0.4984	0.2490
3	15	0.7989	0.7899	0.7994	0.7980	0.3980
4	20	1.0580	1.0601	1.0589	1.0590	0.5295

N=3 SD=standard deviation

Table no.1.2 Concentration of API & Tablet in methanol at 241 nm

Sr no.	Conc.taken	Solvent	Abs.241 nm API	Con.obtained	Abs. 241 nm Tablet	Conc.obtained

1	5 ppm	Methanol	0.178	4.761-95.23%	0.173	4.676-93.52%
2	10 ppm	Methanol	0.4980	10.20-102.04%	0.4900	10.12-100.60%
3	15 ppm	Methanol	0.7989	15.32-102.14%	0.7880	15.75-100.90%
4	20 ppm	Methanol	1.0580	19.72-98.63%	1.05321	19.64-98.23%

N=3 SD=standard deviation

Table no.1.3 Absorbances of TABLET in Methanol at 241 nm.

Sr.no.	**Conc.taken**	**Abs. I**	**Abs. II**	**Abs. III**	**Abs. Mean**	**±S.D.**
1	5	0.172	0.175	0.172	0.173	0.0865
2	10	0.4910	0.4885	0.4905	0.4900	0.2450
3	15	0.7889	0.7870	0.7886	0.7881	0.3940
4	20	1.0580	1.0585	1.0576	1.05803	0.5290

N=3 SD=standard deviation

Table no.1.4 Absorbances of API in distilled water without SLS at 241 nm.

Sr.no.	**Conc.taken**	**Abs. I**	**Abs. II**	**Abs. III**	**Abs. Mean**	**±S.D.**
1	5	0.0588	0.0597	0.0568	0.0584	0.280
2	10	0.162	0.158	0.161	0.1603	0.0801
3	15	0.461	0.498	0.475	0.478	0.1994
4	20	0.501	0.506	0.494	0.500	0.250

N=3 SD=standard deviation

Table no.1.5 Absorbances of API in distilled water with 5% SLS at 241 nm.

Sr.no.	**Conc.taken**	**Abs. I**	**Abs. II**	**Abs. III**	**Abs. Mean**	**±S.D.**

1	5	0.0865	0.0868	0.0870	0.0869	0.407
2	10	0.3054	0.3046	0.3045	0.3048	0.1524
3	15	0.6364	0.6357	0.6362	0.6361	0.3180

N=3 SD=standard deviation

Table no.1.6 Absorbance's of API in distilled water with 10% SLS at 241 nm.

Sr.no.	**Conc.taken**	**Abs. I**	**Abs. II**	**Abs. III**	**Abs. Mean**	**±S.D.**
1	5	0.173	0.172	0.177	0.174	0.0780
2	10	0.4910	0.4900	0.4890	0.4900	0.2450
3	15	0.7828	0.7826	0.7836	0.7830	0.3915
4	20	1.0541	1.0540	1.0539	1.0540	0.5270

N=3 SD=standard deviation

Table no.1.7 Absorbances of tablet in distilled water at 241 nm.

Sr.no.	**Conc.taken**	**Abs. I**	**Abs. II**	**Abs. III**	**Abs. Mean**	**±S.D.**
1	10	0.4849	0.4856	0.4848	0.4851	0.242
2	15	0.7826	0.7830	0.7830	0.7828	0.3914

N=3 SD=standard deviation

Table no.1.8 Analysis of tablet by both methods

Sr.no.	**Tablet label claim**	**Method**	**Absorbance 241 nm**	**Conc.mean ±SD**	**SE**	**LOD**	**LOQ**
1	200 mg-10	USP Method	0.4905	100.76±0.2450	0.1416	0.1980	0.0287

2	200 mg-15	USP Method	0.7886	100.97±0.3940	0.2277	0.0152	0.0017
3	200 mg-10	Proposed Method	0.4851	99.63±0.242	0.1398	0.1598	0.0283
4	200 mg-15	Proposed Method	0.7828	100.31±0.3914	0.2262	0.0151	0.0458

N=3 SE=stand. Error LOD=limit of detection LOQ=limit of quantitation

Table no.1.9 Comparison of both methods of estimation of Carvedilol.

Tablet formulation	Label claim/ tablet (mg)	Method of analysis	% Label claim estimated*(Mean±S.D.)	% Coefficient of variation	Standard error
II	200	USP	100.86±1.119	1.1094	0.6468
II	200	PM	99.97±1.414	1.4144	0.8173

Table no.1.10 Recovery study.

SR NO.	Stock.sol.+spiking	Method	Abs.at 288	Conc.	%Recovery
1	10+5 ppm	USP	0.7880	15.22	100.97
2	10+5 ppm	PM	0.7826	15.04	100.296

7.1 CHEMICALS REQUIRED:-

Table no.. List of chemicals used with their specification.

Sr.No.	CHEMICAL(GRADE)	*MANUFACTURER*
1	Carvedilol (CAR)	*Zeon Pharma Industries India Pvt ltd*
2	Valsartan(VAL)	*Intas, Ahemdabad, Gujarat, India*
3	Sodium hydroxide(AR)	*Merck ,India*
4	*Double Distilled Water*	*Merck ,India*

Chemicals and reagents:-

Pharmaceutical grade CAR was obtained as a gift by Zeon Pharma Industries India Pvt ltd. It wascertified to contain 98.75% according to the company analysis certificates.

Pharmaceutical grade VAL was obtained as gift by Intas, Ahemdabad, Gujarat, India It was certified to contain 98.5% according to the manufacturer's method.

0.1 N NaOH solution ,double distilled water and NaOH were purchased from (Merck ,India).

Marketed formulation:-

Solutions:-

Standard stock solutions each containing 1000 lg/mL of CAR and VAL were prepared separatelyin 0.1 N NaOH solution. Working standard solutions of these drugs (100 lg/mL) were obtained bydilution of the respective stock solutions in 0.1 N NaOH solution.

PROCEDURE:-

Spectral characteristics and wavelength selection

The absorption spectra of 8 lg/mL each of CAR, VAL and their 1:1 mixture (containing 4 µg/mL of each) in 0.1N NaOH were recorded over the range 200–350 nm using 0.1N NaOH as blank. The overlain spectra were observed for selection of the suitable wavelengths for each of the developed methods.

7.2.1 : Simultaneous determination of Valsartan and Carvedilol in tablet dosage form using methanol: 1N NaOH (1:1) as solvent.

7.2.2 : Preparation of stock solution

The standard stock solutions (1mg ml-1) of Valsartan and Carvedilol were prepared by transferring 100mg (approximately but accurately weighed) of Valsartan and Carvedilol in 100 ml of calibrated volumetric flask separately and volume was made up to the mark with solvent. From this stock solution different dilutions were prepared ranging from 2 µg ml-1 to 30 µg ml-1.

7.2.3 : Determination of absorption maxima

1ml of stock solution (1000µg/ml) of Valsartan solution and Carvedilol was pipette out into 100ml calibrated volumetric flask separately and volume was made up to mark with methanol : 1N NaOH(1:1). The final concentration of drugs was 10µg/ml. The solution was then scanned in the UV region 200–400 nm to get absorption maxima using methanol: 1N NaOH (1:1) solution as blank.

7.2.4 : Preparation of standard curve :- The standard curve was prepared by measuring absorbance of various concentration of drug against blank solvent. The graph was plotted for studying the linear

relationship between absorbance and concentration.

Procedure: In different 10 ml volumetric flasks 2,4,6 ……30µg/ml (1000µg/ml) solution of Valsartan solution and Carvedilol was placed and volume was made up to the mark with solvent. The absorbance of solution was measured at 241 nm and 250 nm respectively.

7.2.5 : Preparation of sample solution

Twenty tablets of marketed formulation containing Valsartan 5 mg and Carvedilol 5 mg were weighed, and finely powdered. For analysis of drug, a standard addition method was used. Quantity of powder equivalent to 5 mg of Carvedilol and 5 mg of Valsartan was weighed and dissolved in 40 ml of methanol: 1N NaOH (1:1) and sonicated for 10 minutes. Then the solution was filtered through Whatman filter paper and then final volume of the solution was made up to 100 ml with methanol: 1N NaOH (1:1) to get a stock solution containing 1000µg/ ml of Valsartanand 1000µg/ ml of Carvedilol. In 100ml volumetric flask 2 ml of the sample solution was placed and volume was made up to the mark with solvent and absorbance was measured at 241 nm and 250 nm. The absorbance values were recorded and with the help of standard curve of both drugs, the concentration of Valsartan and Carvedilol in sample solution was calculated.

8. Results

8.1 Characterization and Identification

a) Melting Point : Table 3 :

Melting point

Drug	Melting point	
	Reported	Found (Avg ± SD)
Valsartan	178-179	178 ± 1
Carvedilol	114-1160C	114.3 ± 0.5

It was observed that showed melting point of Valsartan, and Carvedilol are nearby to their reportedvalue.

b) Solubility:

Solubility of Valsartan, and Carvedilol were observed by dissolving them in different solvents andthe observed results are given in the table 4.

Table 4 : Solubility

Drug	Solubility

Valsartan	Slightly soluble in water, freely soluble in methanol & 1N NaOH methanol & 0.1N NaOH sparingly soluble in ethanol, slightly soluble in 2-propanol.
Carvedilol	Insoluble in water, freely soluble in methanol& 1N NaOH methanol & 0.1N NaOH slightly soluble in acetonitrile, soluble in isopropyl alcohol

8.2 **: Method development and validation by UV spectrophotometry**.

8.2.1 **:** Simultaneous determination of Valsartan and Carvedilol in tablet dosage form using methanol : 1N NaOH (1:1) as solvent.

8.2.1.1 : Determination of absorption maxima :

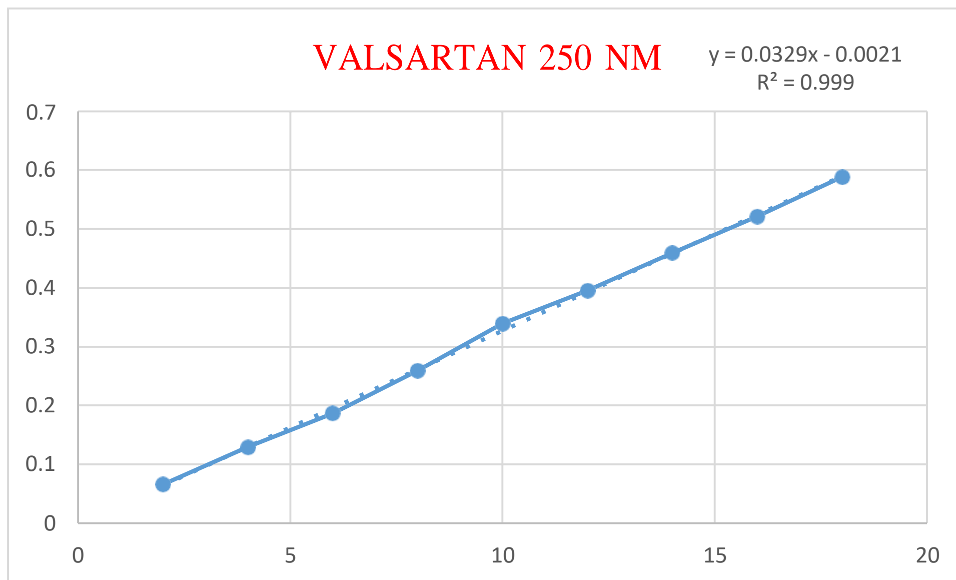
The absorbance maximum of Valsartan was found to be 250 nm. The

absorbance maximum of Carvedilol was found to be 241 nm.

Graph 6.1 : Standard curve of Valsartan and Carvedilol

Table 5: Dilutions for standard curve of Valsartan

Sr. No.	Concentration (µg/ml)	Absorbance at 250 nm
1	2	0.0655
2	4	0.129
3	6	0.1865
4	8	0.2591
5	10	0.3391
6	12	0.3951
7	14	0.4592
8	16	0.521
9	18	0.5883



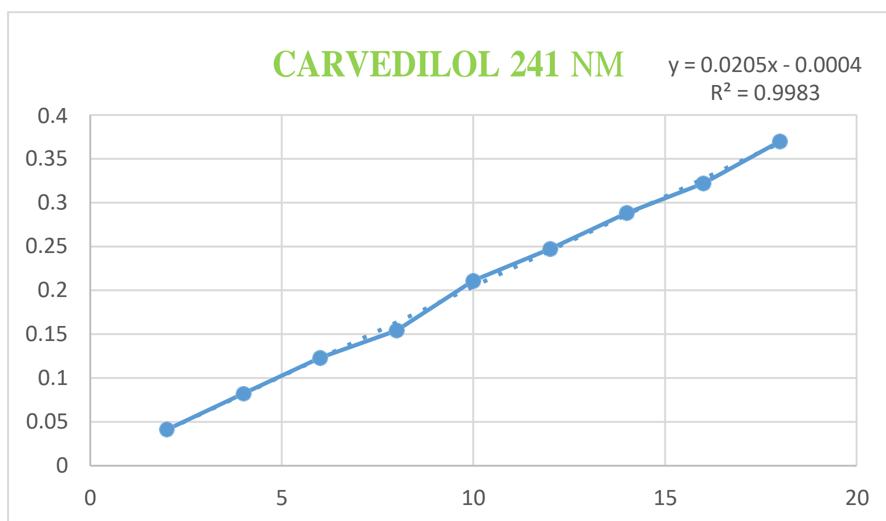
Graph 6 : Calibration curve of valsartan

The calibration curve shows that Beer's Law is obeyed in the concentration range 2 - 18 µg/ml,with regression coefficient value 0.999 and straight line equation y= 0.0329x-0.0021.

Table 6 : Dilutions for standard curve of Carvedilol

Sr. No.	Concentration (µg/ml)	Absorbance at 241 nm
1	2	0.0412
2	4	0.0822
3	6	0.1231
4	8	0.1542
5	10	0.211
6	12	0.2471
7	14	0.2882
8	16	0.3219
9	18	0.3699

Graph 7 – Calibration curve of Carvedilol



The calibration curve shows that Beer's Law is obeyed in the concentration range 2- 18 µg/ml,with regression coefficient value 0.9983 and straight line equation y= 0.0205x-0.0004.

8.2.1.2 : Simultaneous equation method

1. The absorptivities of VAL at λ1 and λ2, ax1 and ax2 respectively.
2. The absorptivities of CAR at λ1 and λ2, ay1 and ay2 respectively.
3. The absorbances of diluted sample at λ1 and λ2, A1 and A2 respectively.
4. Let Cx and Cy be the concentrations of VAL and CAR respectively in diluted sample.The two equations were constructed based upon the fact that at λ1 and λ2 the absorbance of the mixture isthe sum of individual absorbances of VAL and CAR.

At λ1, A1=ax1bcx + ay1bcy…… (1)At λ2,

A2=ax2bcx + ay2bcy…… (2)

Where, A1 and A2 are absorbances of mixture at 241 nm and 250 nm respectively.

Rearrange and substitute the above equations,

$$Cx = \frac{A_2\, a_{y1} - A_2\, a_{y2}}{A_{x2}\, a_{y1} - a_{x1}\, a_{y2}}$$

$$Cy = \frac{A_1\, a_{x2} - A_2\, a_{x1}}{A_{x2}\, a_{y1} - a_{x1}\, a_{y2}}$$

OBSERVATION TABLE:-8

Sr.No.	Absorbance of Valsartan	Absorbance of Carvedilol	λmax(ηm)
1	0.00165	0.0032	250
2	0.001662	0.0032	250
3	0.00160	0.0033	250
4	0.00166	0.00312	250
T=0.00164		K=0.00321	

Sr.No.	Absorbance of Carvedilol	Absorbance of Valsartan	λmax(ηm)
1	0.0032	0.00372	241
2	0.00321	0.00370	241
3	0.00319	.00372	241
4	0.0032	0.00368	241
N=0.0032		H=0.00371	

Sr.No.	Compound	λ1	λ2
1	VALSARTAN	T=0.0016	H=0.00371
2	CARVEDILOL	K=0.0032	N=0.0032
3	UNKNOWN	A1=4.78	A2=5.79

At λ248nm : 7.54 = 0.37Cx + 0.32Cy................. (1)

Atλ224nm : 6.40 = 0.16Cx + 0.41Cy.................. (2)

8.2.1.3 : Preparation of sample solution Table 9:

Weight of tablet taken for analysis

Particulars	Weight
Total wt. of 20 tablets	41.8557 g
Average weight	2.0925 g

Table 10 : Result of tablet analysis

Particulars		Result	
Absorbance of 20µg/ml (Valsartan) solution of tablet at	250 nm	0.003361	
	241 nm	0.00744	
Drug found/claim label(mg)		10.11/10	10.02/10
%found/%limit		101.2/90-110	100.23/90-110

8.2.1.4 : Validation of developed method

The developed method for simultaneous estimation of Valsartan and Carvedilol was validated asper ICH guidelines.

Linearity :- From table 6.3 & 6.4 linearity of the method is established from 2 to 18 ppm.(r2) for

Valsartan = 0.999

(r2) for Carvedilol = 0.9983

Accuracy

Recovery study of Valsartan

Table 11 : Recovery study of Valsartan

Sr.No.	Conc. of stock (Tab) µg/ml	Conc. Spiked µg/ml	Total conc./ml	Conc. found	Abs at 250 nm	Abs at 241 nm	% Recovery	Avg
01	50	0	50	50.02	0.5068	0.6077	100.04	99.43
02	50	2	52	51.89	0.5191	0.6740	99.78	
03	50	2	52	51.85	0.5198	0.6739	99.71	
04	50	2	52	51.95	0.5195	0.6729	99.90	
05	50	2.5	52.5	52.31	0.5290	0.6976	99.63	
06	50	2.5	52.5	52.29	0.5284	0.6974	99.6	
07	50	2.5	52.5	52.37	0.5290	0.6978	99.75	
08	50	3	53	52.81	0.5372	0.7190	99.64	
09	50	3	53	52.9	0.5371	0.7181	96.66	
10	50	3	53	52.79	0.5372	0.7179	99.60	

The recovery was found between 99.6% to 99.95%, with an average of 99.43%. Standard deviation was found to be 1.639. Percent relative standard deviation was found to be 1.75. This obeys the acceptance criterion.

Recovery study of Carvedilol

Table 12: Recovery study of Carvedilol

Sr.No.	Conc. of stock (Tab) µg/ml	Conc. Spiked µg/ml	Total conc./ml	Conc. found	Abs at 250 nm	Abs at 241 nm	% Recovery	Avg
02	50	2	52	51.97	0.8508	0.9707	98.5	
03	50	2	52	51.89	0.8504	0.9708	94.5	
04	50	2	52	51.78	0.8508	0.9706	99	
05	50	2.5	52.5	52.38	0.9384	1.0689	95.2	
06	50	2.5	52.5	52.49	0.9385	1.0686	99.6	
07	50	2.5	52.5	52.46	0.9387	1.0686	98.4	97.23
08	50	3	53	52.86	1.0232	1.1581	95.3	
09	50	3	53	52.89	1.0235	1.1584	96.3	
10	50	3	53	52.95	1.0233	1.1586	98.3	
02	50	2	52	51.97	0.8508	0.9707	98.5	

The recovery was found between 94.5% to 99.6%, with an average of 97.23%. Standard deviation was found to be 1.639. Percent relative standard deviation was found to be 1.96. This obeys the acceptance criterion.

Precision Table 13 : Precision Intraday

Sr. No.	Sample conc. (µg/ml)	Absorbance at		Label claim mg/tab		Label claim estimated		%Label claim estimated	
		224 nm	248 nm	Valsartan	Carvedilol	Valsartan	Carvedilol	Valsartan	Carvedilol
01	10	0.5080	0.6124	5	5	5.25	5.18	105	103.65

2	10	0.508 2	0.612 2	5	5	5.21	5.23	104.02	104.6
3	10	0.508 4	0.612 2	5	5	5.16	5.21	103.2	104.2
4	15	0.762 8	0.916 4	5	5	5.13	5.15	102.6	103
5	15	0.762 6	0.916 8	5	5	5.18	5.23	103.6	104.6
6	15	0.762 8	0.916 2	5	5	5.14	5.21	102.8	104.2
7	20	1.015 8	1.224 4	5	5	5.26	5.19	105.2	103.8
8	20	1.015 6	1.224 2	5	5	5.23	5.17	104.6	103.4
9	20	1.015 6	1.224 6	5	5	5.22	5.22	103.6	104.4

Table 14 : Relative Standard Deviation (RSD) of Precision Interday

Drugs	Average ± Standard deviation	Percent relative standard deviation	Error
Valsartan	103.867 ± 0.938	0.90	0.3127
Carvedilol	103.978 ± 0.5607	0.54	0.1869

CHAPTER-VII RESULTS AND DISCUSSION

7 RESULTS AND DISCUSSION

The characterization and identification of Carvedilol was found in respect of melting point, solubility and stability of drug. As per the above characterization, all the samples were found within the range and the best suited solubility and stability in a binary mixture i.e methanol: 1 N NaOH (1:1).

The wavelength of Valsartan (VAL) and Carvedilol (CAR)in methanol: 1N NaOH(1:1) was found to be 250 nm and 241 nm [Graph 6.1], respectively. Standard calibration curves for VAL and CAR were linear with correlation coefficients (r) values in the range of 0.9987 and 0.999 at all the selected wavelengths. The accuracy of the method was confirmed by recovery studies fromtablet at three different levels of standard additions; recovery in the range of 95 – 110% justifies the accuracy of method. The % RSD of intraday precision was less than 1 [Table 14], which showsthat the method is precise, reproducible, and repeatable. [Parimoo et al. as per the ICH guidelineshas proved the validation procedures]

CHAPTER-VIII CONCLUSION

8.0 CONCLUSION

The proposed method is simple, sensitive and reproducible and hence can be used in routine for simultaneous determination of Valsartan (VAL) and Carvedilol (CAR) in bulk as well as in pharmaceutical preparations. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The % RSD for all parameters was found to be less than one, which indicates the validity of method and assay results obtained by this method are in fair agreement. [Chaudhary J et al. has also concluded that % RSD value for all parameters of method validation was less than 1.

Future Aspects:-

Further method can be evaluated by changing ratio of solvent system.

The method can also be developed by changing concentration of Sodium Hydroxide

The combination of other antihypertensive drugs can also be developed and validated by using the same solvent system.

CHAPTER-IX REFERENCES

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