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RESEARCH ARTICLE OPEN ACCESS

A Simple Non-aqueous Titrimetric Method for Estimation of Carvedilol in Bulk Form

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Abstract

Carvedilol is commonly referred to as a 'third-generation beta blocker' that has a complex pharmacological profile, including non-selective beta-adrenergic and alpha-1 adrenergic receptor blocking actions, anti-oxidant activity, and other properties. For the assay of carvedilol, we are using the nonaqueous titration method. In this method perchloric acid is used for the titration and the indicator used is the crystal violet indicator which changes the color from violet to bluish green. In the present work, 0.01M perchloric acid and violet crystal as the indicator proved to be a useful approach for quantifying CAR in tablets and in compounded capsules containing this drug.

Keywords:

Nonaqueous Titration, Carvedilol, beta-blocker, Perchloric acid, Crystal violet

Introduction

Carvedilol is commonly referred to as a 'third-generation beta blocker' that has a complex pharmacological profile, including non-selective beta-adrenergic and alpha-1 adrenergic receptor blocking actions, anti-oxidant activity, and other properties. Carvedilol is the first beta-blocker approved for the treatment of all forms of congestive heart failure (mild, moderate, severe). Since its introduction, carvedilol has rapidly become the standard of care for the management of heart[1]

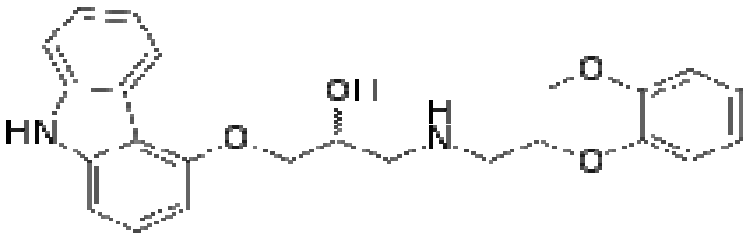

Fig-1- structure of carvedilol

Molecular formula:$C_{24}H_{26}N_2O_4$

IUPAC NAME: (2S)-1- (9H-Carbazol-4-yloxy)-3- { [2- (2-methoxyphenoxy)ethyl]amino}-2-praponal

Category: Beta-adrenergic blocker

Solubility: practically insoluble in water, freely soluble in dimethyl sulfoxide, and soluble in methylenechloride, and methanol.

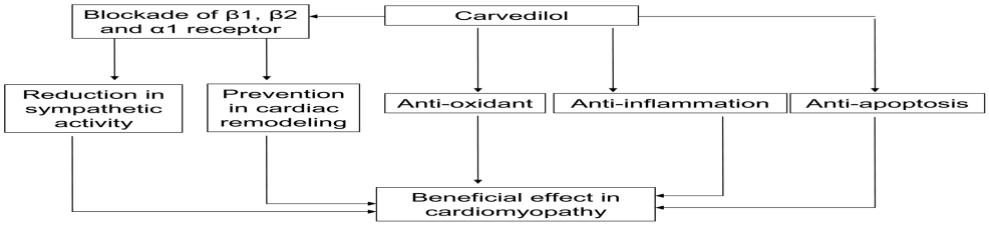

Fig-2-Mechanism of carvedilol

Carvedilol inhibits exercise and induces tachycardia through its inhibition of beta-adrenoceptors.Carvedilol's action on alpha-1 adrenergic receptors relaxes the smooth muscle in the vasculature, leading to reduced peripheral vascular resistance and an overall reduction in blood pressure. At higher doses, calcium channel blocking and antioxidant activity can also be seen. The antioxidant activity of carvedilol prevents oxidation of low-density lipoprotein and its uptake into coronary circulation[2]

Nonaqueous titration is the most important titrimetricprocedure used in pharmacopeial assays and serves a double purpose as it is suitable for titration of weak acids and bases and providesa solvent in which organic compounds are soluble the most commonly used procedure is the titration of organic bases with perchloric acid[3]. Water behaves as both a weak acid and weak base thus in the aqueous environment it can compete with very weak acids and bases with regard to proton donation and acceptance.

Materials and methods

Chemicals :

Carvedilol,perchloric acid,acetonitrile,ethanol,glacial acetic acid,Crystal violet indicator.

Sample preparation:

Preparation of 0.1M perchloric acid

Take about 08.50 ml of perchloric acid using a pipette in a volumetric flask, mix with 500 ml anhydrous glacial acetic acid and 25.00 ml of acetic anhydride. Allow it to cool at room temperature and make up the volume to 1000 ml with anhydrous glacial acetic acid.
Let allows the mixture stand for one day and determine the water content. If it exceeds 0.5 percent, add extra acetic anhydride and let it stand again. The amount of water in the solution must be between 0.2 and 0.5 %.

Nonaqueous titration method

An accurately weighed quantity of the powdered tablets equivalent to 40 mg CAR was placed in a 125 mL flask, and add 5 mL of acetonitrile and 25 mL of ethanol. The solution was stirred mechanically for 10 min and filtered through a quantitative paper filter (Schleicher & Schuell); this filtrate was evaporated to dryness on a water bath. The residue was dissolved in 30 mL anhydrous acetic acid, 0.5ml crystal violet indicator was added, and the solution was titrated with 0.01M perchloric acid until the violet color of the solution turned to bluish-green. The same procedure was used for the compounded capsules. A blank determination was also performed by taking without the sample.

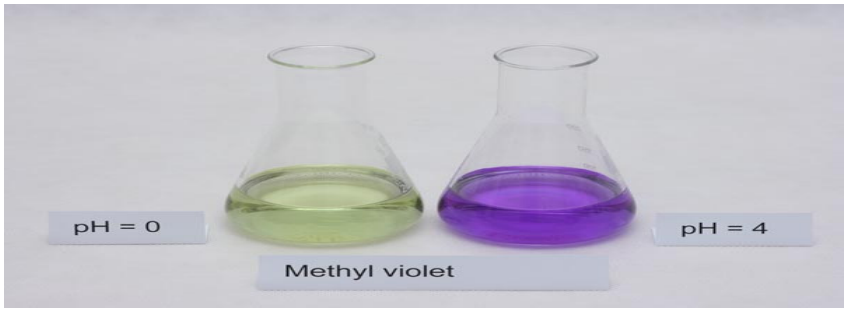

Fig-3-Titration of carvedilol before and after the titration with perchloric acid

Results and Discussion:

In the present work, 0.01M perchloric acid and violet crystal as the indicator proved to be a useful approach for quantifying CAR in tablets and in compounded capsules containing this drug. First, samples of tablets and compounded capsules were dissolved in anhydrous acetic acid and titrated. However, the results revealed interference from excipients, probably due to the magnesium stearate present in the formulations. Therefore, a filtration step was needed to remove this interference.

Table1:standardization of perchloric acid

SNO	The volume of content in a conical flask	Burette reading		Titre value
		Initial	final	
1	CAR+5mlACN+25MLethanol+30mlaceticacid+0.5mlindicator	0	9.5	9.5
2	CAR+5MLACN25MLEthanol+30mlaceticacid+0.5mlindicator	0	9	9
3	CAR+5MLACN25MLEthanol+30mlaceticacid+0.5mlindicator	0	9.5	9.5

Percentage purity=volume of perchloric acid×equivalent factor×actual normality×100

Weight of carvedilol in mg× estimated normality

%purity =9.5×40.65×0.1 x100

400

%purity=96.5%

CONCLUSION

The non-aqueous titration method which is proposed in the above study was simple and economic. The carvedilol was estimated using the nonaqueous titration method by titrating it against 0.1M perchloric acid solution usingcrystal violet as an indicator. The titration is done until the colorchangesfrom blue to green color. The percentage purity of carvedilol was found to be 96.5%.In the assay of carvedilol, the percentage purity was found to be within the limits.

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