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ORIGINAL ARTICLE

Spectrophotometric methods for simultaneous determination of Carvedilol and Hydrochlorothiazide in combined dosage form

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KEYWORDS

Carvedilol;
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Absorbance ratio method;
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Abstract Two simple, precise, rapid and economic spectrophotometric methods have been developed for simultaneous determination of Carvedilol (CV) and Hydrochlorothiazide (HCT) in bulk powder and combined dosage form. Method (I) is based on dual wavelength analysis while Method (II) depends on UV-spectrophotometric determination using Q-analysis (graphical absorbance ratio) method.

In Method (I), two wavelengths were selected for each drug in such a way that the difference in absorbance is zero for the second drug. At wavelengths 238 and 248.8 nm HCT has equal absorbance values, therefore, these two wavelengths have been used to determine CV, on similar basis 266 and 289.4 nm were selected to determine HCT in the combined formulation. Method (II) involves the formation of Q-absorbance equation using the respective absorptivity values at 229.2 nm (isoabsorptive point) and 241 nm (λ_{max} of CV). The drugs obey Beer's Lambert's law in the concentration range of 1–10 μg/mL for both CV and HCT (for Method I) and in the range of 1–10 and 2–10 μg/mL for CV and HCT, respectively (for Method II). The accuracy and precision were determined and recovery studies confirmed the accuracy of the developed methods that were carried out following the International Conference on Harmonization (ICH) guidelines. Statistical

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comparison of the suggested methods with the reported spectrophotometric one using *F* and *t* tests showed no significant difference regarding both accuracy and precision.

1. Introduction

Hydrochlorothiazide (HCT), Fig. 1, is an official drug in both British and United States Pharmacopoeias (BP, 2007; USP, 2007), it is a thiazide diuretic used to treat mild to moderate hypertension, usually in combination with other antihypertensive agents with different mechanisms of action (Wellington and Faulds, 1998). HCT is chemically designated as (6-chloro-3,4-di hydro-2H-1,2,4-benzothiadiazine-7-sulfonamide1,1-dioxide) (Budavari, 2002). Carvedilol (CV), Fig. 2, is an official drug in British and European Pharmacopoeias (BP, 2007; European Pharmacopoeia, 2001), it is an antagonist of α^1 and β^1, β^2 membrane adrenoceptors and also a modulator of cardiac electrophysiological properties via interaction with K^+ and Ca^{2+} ion channels (Karle et al., 2001; Chen and Shih, 2003; Franciosa et al., 2004). It is chemically designated as 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy) ethyl] amino]-2-propanol (Budavari, 2002). CV is administered alone or together with antihypertensive, diuretic HCT. Combined therapy of CV and HCT had a significantly greater blood pressure reduction than with the same dosage of the drug alone (Radevski et al., 1999).

Literature survey revealed that two RP-HPLC methods were reported for determination of the binary mixture in tablet dosage form (Sultan, 2008; Haggag et al., 2010). Only one method has been reported for estimation of the studied drugs in combined formulation by first derivative spectrophotometric method (Sultan, 2008). But so far no spectrophotometric method has been reported for simultaneous determination of CV and HCT in combination; hence an attempt has been made to develop simple, sensitive, rapid, precise, accurate and economic methods to analyze the studied drugs simultaneously by two spectrophotometric methods, dual wavelength and Q-analysis methods. The proposed methods have been optimized and validated as per the International Conference on Harmonization (ICH) guidelines ICH, 2005 and were found to comply with the acceptance criteria.

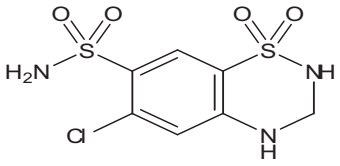

Figure 1 Chemical structure of HCT.

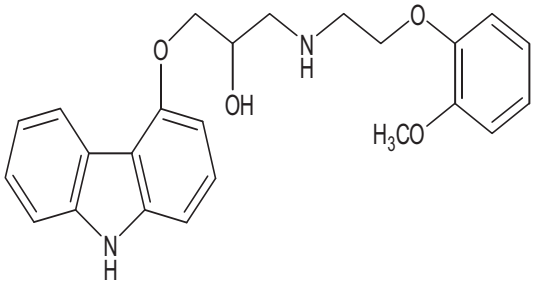

Figure 2 Chemical structure of CV.

2. Experimental

2.1. Instruments

Double beam UV–Vis spectrophotometer (Shimadzu, kyoto, Japan), model UV-1601 PC with 1 cm quartz cells, connected IBM compatible computer. The bundled software, UV-PC personal spectroscopy software version 3.7 was used, the spectral band is 2 nm and scanning speed is 2800 nm/min with 0.1 nm interval.

2.2. Chemicals and reagents

1. Pharmaceutical grade CV was obtained as a gift by Deltapharma S.A.E., Tenth of Ramadan city, A.R.E. It was certified to contain 98.75% according to the company analysis certificates.
2. Pharmaceutical grade HCT was obtained as gift by Amriya Pharmaceutical Industries, Alexandria, Egypt. It was certified to contain 98.5% according to the manufacturer's method.
3. Methanol and HCl were purchased from (El-NASR Pharmaceutical Chemicals Co., Abu-Zabaal, Cairo, Egypt). HCl (0.1N) aqueous solution was laboratory prepared.

2.3. Marketed formulation

Codilatrol® tablets (Batch No. 070140A), is labeled to contain 25 mg CV and 12.5 mg of HCT, manufactured by Chemipharm Pharmaceutical industries S.A.E. 6th October-Egypt, and purchased from the local market.

2.4. Solutions

Standard stock solutions each containing 1000 μg/mL of CV and HCT were prepared separately in methanol. Working standard solutions of these drugs (100 μg/mL) were obtained by dilution of the respective stock solutions in methanol.

3. Procedure

3.1. Spectral characteristics and wavelength selection

The absorption spectra of 8 μg/mL each of CV, HCT and their 1:1 mixture (containing 4 μg/mL of each) in 0.1N HCl were recorded over the range 200–350 nm using 0.1N HCl as blank.

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