

Analytical Study on Some Amino Containing Drugs

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Abstract

This thesis includes six parts:

PART I: GENERAL INTRODUCTION

In this part, physical properties of amines, their structures, basicity, their synthesis and different methods of analysis were discussed.

PART II: ANALYSIS OF CARVEDILOL

This part is divided into four sections. The first **section [A]** reviewed different methods reported in the literature for the determination of carvedilol. **Section [B]** involves the simultaneous determination of carvedilol and hydrochlorothiazide in their binary mixture by using different methods. This section included seven methods.

The **first method** involves third derivative spectrophotometry that depends on measuring (D_3) values at 230.4 and 247.6 nm for HZ and CV, respectively.

The **second method** includes first derivative of ratio of spectra which depends on measuring DD_1 values at 239 and 246 nm for CV determination using the spectrum of $8.0\mu\text{g.ml}^{-1}$ HZ as a divisor. Also DD_1 values were measure at 260.4 and 291.8 nm for HZ determination using the spectrum of $10.0\mu\text{g.ml}^{-1}$ CV as a divisor.

The **third method** describes the use of bivariate calibration spectrophotometry which depends on quantitative evaluation of the absorbance values at 225.6 and 270.6 nm both CV and HZ.

The **fourth method** involves the use of isosbestic point which depends on measuring the absorbance values at 255.8 nm (isosbestic point) that correspond

to the total concentrations of both CV and HZ, while D_3 values at 247.6 nm for CV were measured. The concentration of HZ was calculated by subtraction.

The **fifth method** relies on the use of the absorbance ratio spectrophotometry which depends on measuring the absorbance values at 242.8 nm (λ_{max} for carvedilol), 270.8 nm (λ_{max} for hydrochlorothiazide) and 255.8 nm (isosbestic point) in the original spectra of the binary mixture in methanol. These values were set in the general formula of absorbance ratio technique to get the concentrations of either CV or HZ.

The **sixth method** includes TLC-densitometry which depends on quantitative densitometric evaluation of thin-layer chromatographs of both CV and HZ without any interference. Ethyl acetate: methanol: chloroform (8: 2: 2, v/ v/ v) was used as a mobile phase and the chromatograms were scanned at 243 and 270 nm for the determination of CV and HZ, respectively.

At **last**, an HPLC method was described. The mobile phase was consisted of acetonitrile: 0.01 M phosphate buffer (40: 60, v/ v), adjusted to pH 3.5 by orthophosphoric acid with UV detection at 243 nm for the determination of CV and HZ.

Section [C] involves spectrofluorimetric method that depends on measuring the fluorescence intensity of CV at 335 nm upon excitation at 277 nm, without interference from HZ.

Section [D] involves a colorimetric method for the determination of CV in its pharmaceutical formulations. The method depends on the reaction of CV with MBTH in presence of ceric sulfate as an oxidizing agent to give a highly colored condensation product that can be measured at 544 nm.

PART III: ANALYSIS OF MOEXIPRIL HCL

This part is divided into four sections. The first **section [A]** reviewed different methods reported in the literature for the determination of moexipril HCl. **Section [B]** describes three stability-indicating methods for the determination of MOX in presence of its alkaline-induced degradation product.

The **first method** involves the use of first derivative of ratio of spectra which depends on measuring DD_1 values at 218.2, 244, 263.6 and 298.3 nm with using the spectrum of $10.0 \mu\text{g}.\text{ml}^{-1}$ of degradation product as a divisor.

The **second method** includes TLC-densitometry method which depends on quantitative densitometric evaluation of thin-layer chromatographs of MOX without any interference from its degradation product. Chloroform: methanol: ammonia (8: 2: 0.1, v/ v/ v) was used as a mobile phase and the chromatograms were scanned at 283 nm for the determination of MOX.

The **third method** involves the application of new membrane selective electrodes for the determination of Moexipril hydrochloride either in pure form, dosage forms, biological fluids or in presence of its degradation product. In this section the construction and electrochemical response characteristics of polyvinyl chloride membrane sensors were described. The sensors are based on the use of the ion association complexes of drug cation with ammonium reineckate or tetraphenyl borate or phosphotungstic acid counter anions as ion exchange sites in the PVC matrix. The performance characteristics of these sensors were evaluated according to IUPAC recommendations.

Section [C] involves spectrophotometric determination of moexipril HCl through formation of ternary complexes with Cu (II) eosin or Fe (III) thiocyanate in presence of acetate buffer. The method depends on measuring the

absorbance values of the extracted color at 532 or 439 nm in the case of Cu (II) eosin or Fe (III) thiocyanate, respectively.

Section [D] includes spectrophotometric determination of Moexipril hydrochloride through reaction with α -naphthylamine and sodium nitrite to produce a stable diazo-amino colored product. The method depends on measuring the absorbance values of the produced color at 466.5 nm.

PART IV: ANALYSIS OF LAMIVUDINE

This part is divided into three sections. The first **section [A]** reviewed different methods reported in the literature for the determination of lamivudine. **Section [B]** involves five stability-indicating methods for the determination of LAM in presence of its oxidation product.

The **first method** involves the first derivative of ratio of spectra which depends on measuring DD_1 values at 264.4 and 290 nm with using the spectrum of $10.0 \mu\text{g}.\text{ml}^{-1}$ of oxidation product as a divisor.

The **second method** includes TLC-densitometry which depends on quantitative densitometric evaluation of thin-layer chromatographs of LAM without any interference from its oxidation product. Ethyl acetate: methanol (8: 2, v/ v) was used as a mobile phase and the chromatograms were scanned at 270 nm for the determination of LAM.

In the **third method** an HPLC method was described. The mobile phase consisted of methanol: water: acetonitrile (70: 20: 10 v/ v/ v) with UV detection at 270 for the determination of LAM without interference of its oxidation product.

Fourth method involves the spectrophotometric determination of LAM either in pure form or in presence of its oxidation product through charge transfer complex formation using p-chloranilic acid (p-CA) or dichloro- dicyano p-benzoquinone (DDQ) or 7, 7, 8, 8- tetracyanoquinodimethane (TCNQ). The method depends on measuring the absorbance values either at 522, 460.5 or 845.5 nm in the case of p-CA, DDQ or TCNQ methods, respectively.

Fifth method involves the application of new membrane selective electrode for the determination of lamivudine either in dosage forms or in biological fluids or in presence of its oxidation product. In this section the construction and electrochemical response characteristics of polyvinyl chloride membrane sensors were described. The sensors are based on the use of the ion association complexes of drug anion with iron-phenanthroline counter cations as ion exchange sites in the PVC matrix. The performance characteristics of these sensors were evaluated according to IUPAC recommendations.

Section[C] describes a spectrophotometric method for the determination of lamivudine in its dosage forms with comparative kinetic study. The method depends on the reaction of the drug with KMnO_4 in alkaline medium to produce manganate ion which was measured spectrophotometrically at 610 nm. Also a comparative kinetic study was carried out.

PART V: ANALYSIS OF ARIPIPRAZOLE

This part is divided into three sections. The first **section [A]** reviewed different methods reported in the literature for the determination of aripiprazole. **Section [B]** describes five stability-indicating methods for the determination of ARP in presence of its oxidation product.

The **first method** involves second derivative spectrophotometry that depends on measuring (D_2) values at 217.2 and 229.2 nm for aripiprazole without interference from its oxidation product.

The **second method** involves the first derivative of ratio of spectra which depends on measuring DD_1 values at 209.8, 222.0, 246.8 and 283.2 nm with using the spectrum of $5 \mu\text{g}.\text{ml}^{-1}$ oxidation product as a divisor.

The **third method** describes a bivariate calibration spectrophotometry which depends on quantitative evaluation of the absorbance values at 210.0 and 216.2 nm for ARP.

The **fourth method** includes TLC-densitometry which depends on quantitative densitometric evaluation of thin-layer chromatographs of ARP without any interference from its oxidation product. Ethyl acetate: methanol (11: 4, v/ v) was used as a mobile phase and the chromatograms were scanned at 255 nm for the determination of ARP.

The last method involves the spectrophotometric determination of ARP through charge transfer complex formation using p-chloranilic acid (p-CA) or dichloro- dicyano *p*-benzoquinone (DDQ) or 7, 7, 8, 8-tetracyanoquinodimethane (TCNQ) without interference from its oxidation product. The method depends on measuring the absorbance values either at 526, 467 or 845.5 nm in the case of p-CA, DDQ or TCNQ, respectively.

Section [C] involves a spectrophotometric method for the determination of ARP. The method depends on the reaction of ARP with MBTH in presence of ferric chloride as an oxidizing agent to give a highly colored condensation product that can be measured at 565 nm.

PART VI: REFERENCES

The thesis refers to (246) references, contains (163) tables, (145) figures and ends with an arabic summary.

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