Abstract

"Analysis of some amide group and/or ester group containing pharmaceutical drugs"

This thesis consists of three parts, each part includes an introduction, literature review and descriptive experimental work for the studied drugs; in addition to refernces and a summary in Arabic.

Part I: STABILITY INDICATING METHODS FOR DETERMINATION OF BUMADIZONE IN PRESENCE OF ITS DEGRADATION PRODUCT

This part includes:

Introduction and Literature Review

This introduction describes the pharmacological action of Bumadizone, its chemical structure, physical properties and review of the published methods developed for its analysis.

Section (A): Stability Indicating First Derivative and First Derivative of Ratio Spectra Spectrophotometric Methods for Determination of Bumadizone

In this section, a first derivative and first derivative of ratio spectra spectrophotometric methods were applied to determine intact Bumadizone in presence of its degradation product in methanol at 245.5 nm for ^{1}D method and at 242.6, 260 and 274 nm for ^{1}DD method. A linear correlation was obtained in the range of 6-26 μg mL^{-1} of Bumadizone with mean percentage recovery of 100.43 ± 0.88 for ^{1}D method while ^{1}DD method showed good linearity at 242.6, 260 and 274 nm in the range of 6-20 μg mL^{-1} with the mean percentage recoveries 100.13±1.21 , 100.18±1.29 and 99.62±0.63 at 242,6, 260 and 274 nm respectively. The proposed methods retained their accuracy in the presence of up

to 70 % of the degradation product at 245.5 nm, while up to 60% of the degradation product at 242.6 and 274 nm, and up to 40% of the degradation product at 260 nm.

The proposed methods were applied for the determination of Bumadizone in its pharmaceutical formulation where the validity was further assessed by applying the standard addition technique.

Section (B): Stability Indicating Isoabsorptive Spectrophotometric Method for Determination of Bumadizone

In this section Isoabsorptive spectrophotometric method was proposed for determination of Bumadizone in presence of its degradation product, while the degradation product can be measured at its λ max 320 nm and Bumadizone can be measured at λ 242.2 nm (Aiso) using 0.1 M HCl as a solvent. The suggested method was applied for determination of Bumadizone in its pharmaceutical formulation and the validity of the method was further assessed by applying the standard addition technique.

Section (C): Stability Indicating Ratio-Subtraction Spectrophotometric Method for Determination of Bumadizone

In this section the suggested Ratio-Subtraction spectrophotometric method was applied for determination of Bumadizone in presence of its degradation product, while the abosorbance was measured at 236.6 nm using 10 μg mL^{-1} of the degradation product as a divisor and methanol as a solvent. The suggested method was applied for determination of Bumadizone in its pharmaceutical formulation and the validity of the method was further assessed by applying the standard addition technique.

Section (D): Stability Indicating Multivariate Calibration Method for Determination of Bumadizone

Two chemometric techniques; principal component regression (PCR) and partial least squares (PLS) were used for the determination of Bumadizone in presence of its degradation product Training set consisted of fifteen mixtures containing different ratios of Bumadizone and its degradation product was used for construction of the models. The

selectivity of the proposed method was checked using laboratory prepared mixtures (validation set consisted of nine mixtures). Satisfactory results were obtained upon applying the proposed methods for the analysis of Bumadizone in its pharmaceutical formulation. Applying standard addition technique assessed the validity of the suggested methods.

Section (E): Stability Indicating HPTLC and RP-HPLC Methods for Determination of Bumadizone

In this section two chromatographic methods were used for separation of the drug from its degradation product. HPTLC-densitometric method was applied by using hexane :ethylacetate :glacial acetic acid (8:2:0.2, by volume) as a developing system. The bands measured quantitatively at 240 nm, while RP-HPLC was achieved by using methanol :water : acetonitrile (20:30:50, by volume) as a mobile phase, adjusted pH of the solution to 3.5 using phosphoric acid at a flow rate 2 mL min^{-1}.and UV detection at 235 nm. The suitability of the proposed chromatographic methods was ascertained by the determination of system suitability parameters of the separated components.The suggested methods could be considered as a stability-indicating method as they could determine the drug in presence of upto 70% of its degradation product for HPTLC method and upto 90% of its degradation product for RP-HPLC method. The suggested methods were successfully applied for the determination of Bumadizone in its pharmaceutical formulation.

Part II: DETERMINATION OF PARACETAMOL AND DIPHENHYDRAMINE HYDROCHLORIDE IN BINARY MIXTURE AND IN PRESENCE OF PARACETAMOL DEGRADATION PRODUCT

This part includes:

Introduction and Literature Review

This introduction comprises a brief idea about the structure, properties, stability and different methods for the analysis of Paracetamol and Diphenhydramine Hydrochloride either alone or in their binary mixture.

Section (A): First Derivative and First Derivative of Ratio Spectra Spectrophotometric Methods for Determination of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product

In this section, ^{1}D and ^{1}DD spectrophotometric methods were applied to determine Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product, where Paracetamol was determined at 264.5 nm using ^{1}D method and methanol as solvent, while ^{1}DD method used for determination of Diphenhydramine Hydrochloride using 10 μg mL^{-1} of Paracetamol degradation product as a divisor and methanol as a solvent. The linearity range of Paracetamol and Diphenhydramine Hydrochloride were 2-12 μg mL^{-1} and 5-18 μg mL^{-1} respectively. Paracetamol and Diphenhydramine Hydrochloride were determined successfully in laboratory prepared mixtures using the proposed method. The validity of the suggested methods was checked by the analysis of Paracetamol and Diphenhydramine Hydrochloride in their pharmaceutical formulation and the standard addition technique assessed this validity.

Section (B): Multivariate Calibration Technique for Determination of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product

Two chemometric techniques; principal component regression (PCR) and partial least squares (PLS) were used for simultaneous determination of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product. Training set consisted of thirteen mixtures of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product containing different ratios, was used for construction of the models in the spectral region 220-340 nm. Eeight mixtures were used as validation set; the proposed method was successfully applied for

determination of the binary mixture in their pharmaceutical formulation. Results obtained by the proposed method were statistically compared with that obtained by the official method indicating no significant difference between them.

Section (C): HPTLC Method for Determination of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product

In this section, a simple and accurate TLC-densitometric method was suggested for simultaneous determination of Paracetamol and Diphenhydramine Hydrochloride in presence of Paracetamol degradation product in bulk powder and in pharmaceutical formulation. The method is based on the difference in Rf values of the cited drugs. Satisfactory separation was obtained by using chloroform : ethyl acetate : ammonia solution (4:6:0.2 by volume) as a developing system. The Rf values are 0.13, 0.5 and 0.3 for Paracetamol, Diphenhydramine Hydrochloride and P-aminophenol respectively. The bands were scanned at 220 nm giving maximum sensitivity for the drugs. The proposed method was successfully applied for determination of the binary mixture in their pharmaceutical formulation and validity was assessed by applying standard addition technique.

Part III: SPECTROFLUORIMETRIC AND SPECTROPHOTOMETRIC DETERMINATION OF GLIQUIDONE

This part includes:

Introduction and Literature Review

This introduction describes the pharmacological action of Gliquidone, its chemical structure, physical properties and review of the published methods developed for its analysis.

Section (A): Spectrofluorimetric Determination of Gliquidone

In this section the native fluorescence of Gliquidone was measured at 404 nm upon excitation at 311 nm. The linearity range was 0.05-0.45 μg mL^{-1} with mean percentage recovery 100.00±0.92. The high sensitivity attained by the proposed method allows the determination of Gliquidone in spiked human plasma. The suggested method was used for determination of Gliquidone in its pharmaceutical formulation, where satisfactory results were obtained. The validity of the proposed method was further assessed by applying standard addition technique. Statistical analysis of the results proved no siginifican difference compared with the reported method.

Section (B): Spectrophotometric Determination of Gliquidone Using 7,7,8,8,-Tetracyanoquinodimethane (TCNQ)

This method based on formation of charge transfer complex between the Gliquidone and the reagent, where the drug acted as an electron-donor and TCNQ acted as electron-acceptor. The obtained complex has an absorption maximum at 745.5 nm and the pure drug was determined in the linearity range 0.2-2 mg mL^{-1}. Factors affecting the reaction condition and drug sensitivity were investigated. The suggested method was successfully applied for determination of Gliquidone in pure form and in pharmaceutical formulation and the results obtained were statistically compared with the reported one.

This thesis refers 239 refernces, contains 83 figures and 68 tables and ends with a summary in Arabic