Abstract

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

Part I: Determination of Paracetamol and Pamabrom in their binary mixture and in presence of their potential impurities

This part includes:

Section A: Introduction and literature review

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

Section B: Determination of Paracetamol and Pamabrom by dual wavelength spectrophotometric method.

In this section, dual wavelength spectrophotometric method was applied for simultaneous determination of Paracetamol and Pamabrom in their binary mixture using their zero order absorption spectra. The difference in absorbance values at 252.4 and 295.8 nm was used for determination of Paracetamol, and the difference in absorbance values at 211 and 225.6 nm was used for determination of Pamabrom. The developed method was successfully applied for determination of Paracetamol and Pamabrom in their pharmaceutical formulation.

Section C: Determination of Paracetamol and Pamabrom by ratio difference spectrophotometric method.

In this section, ratio difference spectrophotometric method was applied for determination of Paracetamol and Pamabrom in their binary mixture. The zero order spectra of the prepared solutions of Paracetamol were divided by the spectrum of 10 μg mL^{-1} of Pamabrom and calibration curve was constructed relating the ratio difference between 244 and 222 nm to the corresponding Paracetamol concentrations. The zero order spectra of the prepared solutions of Pamabrom were divided by the spectrum of 20 μg mL^{-1} of Paracetamol, and the ratio difference between 287 and 248 nm to the

corresponding Pamabrom concentrations. The developed method was successfully applied for determination of Paracetamol and Pamabrom in their pharmaceutical formulation.

Section D: Determination of Paracetamol and Pamabrom by mean centering of ratio spectra spectrophotometric method (MCR).

In this section, mean centering of ratio spectra spectrophotometric method was applied for simultaneous determination of Paracetamol and Pamabrom in their binary mixture. The recorded absorption spectra of Paracetamol from 210-260 nm were divided by the absorption spectrum of Pamabrom (10 µg mL^{-1}) and the absorption spectra of Pamabrom from 210-260 were divided by the absorption spectrum of PCM (20 µg mL^{-1}) to obtain the ratio spectra which were then mean centered. These mean centered values of the ratio spectra at 245nm and 215 nm for Paracetamol and Pamabrom, respectively were recorded and plotted versus the corresponding concentrations. Calibration curve for each drug was constructed and regression equation was computed. The developed method was successfully applied for determination of Paracetamol and Pamabrom in their pharmaceutical formulation.

Section E: High performance liquid chromatographic method for simultaneous determination of Paracetamol and Pamabrom in presence of their potential impurities (HPLC).

In this section, HPLC method was applied for simultaneous determination of Paracetamol and Pamabrom in presence of their potential impurities. Chromatographic separation was carried out by gradient elution using a developing system consisting of 0.05M sodium dihydrogen phosphate buffer as solvent A and a mixture of methanol and acetonitrile in the ratio of (2: 1) as solvent B. The gradient program (T (min)/ % B/ flow rate (mL min^{-1})) was set as 0/15/1, 7.5/15/1 and 8/30/1.5, respectively. Scanning was carried out at 277 nm at room temperature. The developed method was successfully applied for determination of Paracetamol and Pamabrom in their pharmaceutical formulation.

Section F: High performance thin layer chromatographic method for simultaneous determination of Paracetamol and Pamabrom in presence of their potential impurities (HPTLC).

In this section, highly selective and sensitive HPTLC method was applied for simultaneous determination of Paracetamol and Pamabrom in presence of their potential impurities. Chromatographic separation was carried out using chloroform: methanol: ethyl acetate: glacial acetic acid (8: 0.8: 0.6: 0.2, by volume) as a developing system and scanning was carried out at 254 nm. The developed method was successfully applied for determination of Paracetamol and Pamabrom in their pharmaceutical formulation.

Part II: Determination of Norfloxacin and Tinidazole in presence of Tinidazole potential impurity.

This part includes:

Section A: Introduction and literature review

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

Section B: Determination of Norfloxacin and Tinidazole in presence of Tinidazole potential impurity by double divisor ratio derivative spectrophotometric method (DDRD).

In this section, DDRD method was applied for determination of Norfloxacin (NF), Tinidazole (TZ) and 2-Methyl-5-nitro-imidazole (MNZ). The absorption spectra of the solutions prepared of different concentrations of pure Norfloxacin and the ternary mixture were recorded and divided by the absorption spectra of the mixed solution of TZ and MNZ (10µg mL^{-1} of each as a double divisor). The peak amplitudes of first derivative of these ratio spectra at 287.2 nm were used for determination of Norfloxacin. For determination of Tinidazole, mixed solution of NF and MNZ (8µg mL^{-1} of each) was used as a double divisor. The peak amplitudes of second derivative of these ratio spectra at 326 nm were used for determination of Tinidazole. For determination of 2-Methyl-5-nitro-imidazole, mixed solution of NF and

TZ (8μg mL^{-1} of each) was used as a double divisor. The peak amplitudes of first derivative of these ratio spectra at 226.4 nm were used for determination of 2-Methyl-5-nitro-imidazole. The developed method was successfully applied for determination of Norfloxacin and Tinidazole in their pharmaceutical formulation.

Section C: Determination of Norfloxacin and Tinidazole in presence of Tinidazole potential impurity by mean centering of ratio spectra spectrophotometric method (MCR).

In this section, MCR was applied for determination of Norfloxacin (NF), Tinidazole (TZ) and 2-Methyl-5-nitro-imidazole (MNZ). The absorption spectra from 250-350 nm were recorded and the second mean centered values of the ratio spectra at 304nm, 292 nm and 342nm were used for determination of Norfloxacin, Tinidazole and 2-Methyl-5-nitro-imidazole, respectively. The developed method was successfully applied for determination of Norfloxacin and Tinidazole in their pharmaceutical formulation.

Section D: Determination of Norfloxacin and Tinidazole in presence of Tinidazole potential impurity by different chemometric methods.

In this section, three multivariate chemometric models namely; classical least square (CLS), partial least squares regression (PLSR) and support vector regression (SVR) were developed for determination of Norfloxacin and Tinidazole in presence of 2-Methyl-5-nitro-imidazole. A comparison between the three different chemometric methods was established indicating their advantages and disadvantages. RMSEP values of independent test set show that the prediction ability of future samples and the generalization ability for linear SVR model are relatively better than PLSR model, yet both are statistically equal and comparable.CLS gives the worst results and should be avoided for such cases. PLSR and linear SVR methods were successfully applied for determination of Norfloxacin and Tinidazole in their pharmaceutical formulation.

Section E: High performance thin layer chromatographic method for simultaneous determination of Norfloxacin and Tinidazole in presence of potential impurity of Tinidazole (HPTLC).

In this section, highly selective and sensitive HPTLC method was applied for simultaneous determination of Norfloxacin and Tinidazole in presence of 2-Methyl-5-nitro-imidazole. Chromatographic separation was carried out using chloroform: methanol: formic acid (7.5: 1.5: 0.3, by volume) as a developing system and scanning was carried out at 298 nm. The developed method was successfully applied for determination of Norfloxacin and Tinidazole in their pharmaceutical formulation.

Part III: Stability indicating assay methods for determination of Meclofenoxate Hydrochloride.

This part includes:

Section A: Introduction and literature review

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

SectionB: Stability indicating derivative ratio spectrophotometric method for determination of Meclofenoxate Hydrochloride (^{1}DD).

In this section, ^{1}DD method was applied for determination of Meclofenoxate Hydrochloride (MFH) in presence of its potential degradation product; P-chlorophenoxyacetic acid (PCPA). The absorption spectra of the prepared solutions of MFH were divided by the absorption spectrum of 10 µg mL^{-1} of PCPA. ^{1}DD curves of the obtained ratio spectra were recorded at $\Delta\lambda$= 16 nm and scaling factor = 10. The peak amplitudes at 227.2 nm were recorded then calibration graph was constructed relating the peak amplitudes of (^{1}DD) to the corresponding concentrations. The developed method was successfully applied for determination of Meclofenoxate Hydrochloride in its pharmaceutical formulation.

SectionC: Stability indicating ratio difference spectrophotometric method for determination of Meclofenoxate Hydrochloride.

In this section, ratio difference spectrophotometric method was applied for determination of Meclofenoxate Hydrochloride (MFH) in presence of its potential degradation product; P-chlorophenoxyacetic acid (PCPA). The zero order spectra of the prepared solutions of MFH was divided by the spectrum of 10 μg mL^{-1} of PCPA, the peak amplitudes of the ratio spectra were measured at 223 and 237.4 nm. Calibration curve was constructed relating the difference in absorbance of the resultant ratio spectra at 223 and 237.4 nm (ΔA 223 – 237.4 nm) to the corresponding MFH concentrations. The developed method was successfully applied for determination of Meclofenoxate Hydrochloride in its pharmaceutical formulation.

SectionD: Stability indicating high performance thin layer chromatographic method for determination of Meclofenoxate Hydrochloride (HPTLC).

In this section, highly selective and sensitive HPTLC method was applied for simultaneous determination of Meclofenoxate Hydrochloride and its potential degradation product; P-chlorophenoxyacetic acid (PCPA). Chromatographic separation was carried out using chloroform: methanol: glacial acetic acid: triethylamine (6: 4: 0.2: 0.1, by volume) as a developing system and scanning was carried out at 226 nm. The developed method was successfully applied for determination of Meclofenoxate Hydrochloride in its pharmaceutical formulation.

This thesis contains 307 references, 70 figures, 64 tables and ends with a summary in arabic.