Summary

This thesis consists of five parts, in addition to references, an Arabic and an English summary.

Part I: General Introduction

In this part, a brief idea about the drugs affecting the respiratory system, their classification and mechanisms of action have been presented. Also this part includes the chemical structures, uses and general properties of the studied drugs.

Part II: Determination of Ambroxol HCl and Guaifenesin in presence of the oxidative degradation product of Ambroxol HCL and Guaicol, the main impurity of Guaifenesin by RP-HPLC, TLC-spectrodensitometry and multivariate calibration methods

This part is divided into four sections:

Section II A: Literature Review of Ambroxol HCl and Guaifenesin

This part includes the different reported methods for the quantitative determination of ambroxol HCl and guaifenesin.

Section II B: Simultaneous determination of Ambroxol HCl and Guaifenesin in presence of the oxidative degradation product of Ambroxol HCl and Guaicol, the main impurity of Guaifenesin by RP-HPLC

In this section, HPLC method was used for the determination of ambroxol HCl and guaifenesin in presence of the oxidative degradation product of ambroxol HCl and guaicol, the main impurity of guaifenesin. C-18 column was used as a stationary phase and methanol: water (15: 85,

v/v containing 1% triethylamine, pH 3 adjusted by phosphoric acid) as a mobile phase. The detection was carried out at 220 nm.

The proposed method was applied for the analysis of drugs in pure form, in laboratory prepared mixtures and in different pharmaceutical dosage forms. The obtained results were statistically compared with those obtained by the reported methods.

Section II C: Simultaneous determination of Ambroxol HCl and Guaifenesin in presence of the oxidative degradation product of Ambroxol HCl and Guaicol, the main impurity of Guaifenesin by TLC-Spectrodensitometric method

In this section, thin layer chromatographic separation followed by spectrodensitometric determination of ambroxol HCl and guaifenesin in presence of oxidative degradation product of ambroxl HCl and guaicol, the main impurity of guaifenesin was carried out. The mobile phase used for separation consisted of chloroform – methanol - ethyl acetate - acetic acid (70: 8: 12: 10, by volume). The plates were measured spectrodensitometrically at 270 nm.

The proposed method was applied for the analysis of drugs in pure form, in laboratory prepared mixtures and in different pharmaceutical dosage forms. The obtained results were statistically compared with those obtained by the reported methods.

Section II D: Simultaneous determination of a quaternary mixture of Ambroxol HCl, its oxidative degradation product, Guaifenesin and its main impurity (Guaicol) by Multivariate Calibration Methods

In this section, two multivariate calibration methods were applied; partial least squares (PLS) and principle component regression (PCR).

Twenty five mixtures were prepared; using five -level four -factor experimental design containing different ratios of the four components. The calibration set was constructed using seventeen mixtures, while the validation set was constructed of the rest eight mixtures to assist the validity of the constructed models.

The proposed method was applied for the analysis of drugs in pure form and in different pharmaceutical dosage forms. However for determination of Ambroxol HCl and Guaifenesin in Mucosin® syrup, model updating was required due to interfering excipients. The obtained results were statistically compared with those obtained by the reported methods.

Part III: Simultaneous determination of quaternary mixture of Oxomemazine, Sodium benzoate, Guaifenesin and Paracetamol by RP-HPLC, TLC-spectrodensitometry and multivariate calibration methods

Section III A: Literature Review for Oxomemazine, Sodium Benzoate and Paracetamol

This part includes the different reported methods for the quantitative determination of paracetamol, sodium benzoate and oxomemazine.

Section III B: Simultaneous Determination of a quaternary mixture of Oxomemazine, Sodium Benzoate, Guaifenesin and Paracetamol by HPLC method

In this section, an HPLC method was used for the simultaneous determination of oxomemazine, sodium benzoate, guaifenesin and paracetamol. The stationary phase was a C-18 column and the mobile phase consisted of methanol-acetonitrile-35 mM KH_2PO_4 (5:20:75, by volume, pH 2.9 ± 0.1 adjusted with phosphoric acid). All determinations were performed at ambient temperature and detection at 220 nm.

The proposed method was applied for the analysis of drugs in pure form, in laboratory prepared mixtures and in syrups and suppositories. The obtained results were statistically compared to those obtained by the reported methods.

Section III C: <u>Simultaneous determination of a quaternary mixture of Oxomemazine, Paracetamol, Guaifenesin and Sodium benzoate by TLC-spectrodensitometric method</u>

In this section, thin layer chromatographic separation followed by spectrodensitometric determination of oxomemazine, paracetamol, guaifenesin and sodium benzoate was carried out. The mobile phase used for separation consisted of methylene chloride – methanol – ammonia - acetic acid (89: 8.4: 0.6: 2, by volume). All determinations were done at 270 nm.

The proposed method was applied for the analysis of drugs in pure form, in laboratory prepared mixtures and in pharmaceutical dosage forms. The obtained results were statistically compared with those obtained by the reported methods.

Section III D: <u>Simultaneous determination of a quaternary mixture of Oxomemazine, Sodium benzoate, Guaifenesin and Paracetamol by multivariate Calibration Methods</u>

In this section two multivariate calibration methods were applied; partial least squares (PLS) and principle component regression (PCR).

Twenty five mixtures were prepared; using five -level four -factor experimental design containing different ratios of the four drugs. The calibration set was constructed using seventeen mixtures, while the rest eight mixtures were used as an external validation set to assist the validity of the constructed models.

The proposed method was applied for the analysis of drugs in pure form and in different pharmaceutical dosage forms.

The obtained results were statistically compared with those obtained by the reported methods.

Part IV: Spectrophotometric determination of Oxomemazine HCl, Guaifenesin and Carbocisteine in pure form and in Ultrasolv tablets

Section IV A: Literature Review of Carbocisteine

This part includes the different reported methods for the quantitative and determination of carbocisteine.

Section IV B: Spectrophotometric Determination of Oxomemazine HCl and Guaifenesin in presence of Carbocisteine

In this section, oxomemazine HCl was determined by measuring the absorbance of its zero order (D^0) absorption spectra at 338.2 and 294.4 nm, where there is no interference from either guaifenesin or carbocisteine. On the other hand guaifenesin was determined using the first derivative spectrophotometry, where the peak amplitude was measured at 280.6 and 266.6 nm corresponding to zero crossing with oxomemazine HCl and there was no interference from carbocisteine.

The proposed method was applied for the analysis of oxomemazine HCl and guaifenesin in pure form, in laboratory prepared mixtures with carbocisteine and in Ultrasov® tablets. The obtained results were statistically compared with those obtained by the reported methods.

Section IV C: Colorimetric determination of Carbocisteine using p-benzoquinone

In this section, a reported colorimetric method for the determination of carbocisteine was applied for its determination in presence of oxomemazine HCl and guaifenesin, where it was found that carbocisteine in pH (7 – 8) reacted with p-benzoquinone and the color formed was measured at 490 nm. On the other hand no color was formed with the other two drugs; therefore they do not interfere in the analysis of carbocisteine.

The method was applied for the analysis of carbocisteine in pure forms and in ultrasov tablets. The obtained results were statistically compared with those obtained by the reported HPLC method.

Part V: **Simultaneous determination of a ternary mixture of Terbutaline sulfate, Guaifenesin and Bromhexine HCl by RP-HPLC, TLC-spectrodensitometry and multivariate calibration methods**

Section V A: Literature Review of Terbutaline sulfate and Bromhexine HCl

This part includes the different reported methods for the quantitative determination of terbutaline sulfate and bromhexine HCl.

Section V B: Simultaneous determination of a ternary mixture of Terbutaline sulfate, Guaifenesin and Bromhexine HCl by RP-HPLC

In this section, HPLC method was used for the determination of terbutaline sulfate, guaifenesin and bromhexine HCl using C-18 column and a mobile phase of methanol – acetonitrile - 35m M KH_2PO_4 (27.5: 12.5: 60, by volume, pH 3.5 ± 0.1 adjusted with phosphoric acid). The pump was set at constant flow rate of 1.4 mL min^{-1}. All determinations were performed at ambient temperature with detection at 220 nm.

The proposed method was applied for the analysis of these drugs in pure form, in laboratory prepared mixtures and in All Vent® syrup. The obtained results were statistically compared with those obtained by the reported methods.

Section V C: <u>Simultaneous determination of a ternary mixture of Terbutaline sulfate, Guaifenesin and Bromhexine HCl by TLC-spectrodensitometric method</u>

In this section, a thin layer chromatographic separation followed by spectrodensitometric determination of terbutaline sulfate, guaifenesin and bromhexine HCl was carried out. The mobile phase used for separation consisted of chloroform – methanol – butanol - acetic acid (56: 4: 30: 10, by volume). Determination was done at 278 nm for terbutaline sulfate, 275 nm for guaifenesin and 250 nm for bromhexine HCl.

The proposed method was applied for the analysis of these drugs in pure form, in laboratory prepared mixtures and in All Vent® syrup. The obtained results were statistically compared with those obtained by the reported methods.

Section V D: Simultaneous determination of a quaternary mixture of Terbutaline sulfate, Bromhexine HCl, Guaifenesin and Sodium benzoate by multivariate Calibration Methods

In this section two multivariate calibration methods were applied; partial least squares (PLS) and principle component regression (PCR).

Twenty five mixtures were prepared; using five -level four -factor experimental design containing different ratios of the three drugs together with sodium benzoate (an additive in syrup dosage form). The calibration set was constructed using seventeen mixtures, while the validation set was constructed of the rest eight mixtures to assist the validity of the constructed models.

The proposed method was applied for the analysis of drugs in pure form and in All Vent® syrup. However for determination in syrup dosage forms, model updating was required. The obtained results were statistically compared with those obtained by the reported methods.

The thesis ends with the list of references (415) references.