Summary

This thesis consists of four parts in addition to the references and a summary in Arabic.

Part I: Introduction and Literature Review

This part includes three sections.

Section (A): **Introduction and Literature Review of Cetylpyridinium Chloride, Chlorocresol, and Lidocaine**

Section (B): **Introduction and Literature Review of Yohimbine Hydrochloride, Vitamin E Acetate, Vitamin B_3, and Caffeine**

Section (C): **Introduction and Literature Review of Sulfacetamide Sodium**

This part includes an introduction about the pharmacological action of Cetylpyridinium Chloride (CE), Chlorocresol (CH), Lidocaine (LI), **Section (A)**, Yohimbine Hydrochloride (YH), Vitamin E Acetate (VE), Vitamin B_3 (VE), Caffeine (CAF), **Section (B)**, and Sulfacetamide Sodium (SCA), **section (C)**, their chemical structures, physical properties and summary of the published methods developed for their analysis alone, with other drugs, or in their ternary mixtures.

Part II: Quantitative Determination of Cetylpyridinium Chloride, Chlorocresol, and Lidocaine in Their Ternary Mixtures

This part includes two sections.

Section (A): **Determination of Cetylpyridinium Chloride, Chlorocresol, and Lidocaine by Different Spectrophotometric Methods**

In this section, mean centering of ratio spectra (MCR) and ratio isoabsorptive point and ratio difference in subtracted spectra (RDSS) spectrophotometric

methods were developed for quantitative determination of Cetylpyridinium Chloride (CE), Chlorocresol (CH), and Lidocaine (LI). In MCR method, the second mean centered ratio spectra were obtained where peak amplitudes at maximum or minimum wavelengths were measured so, CE, CH, and LI were determined at peak to peak 231-232, 244-245, and 255-264 nm, respectively while in RDSS method, CH was determined by measuring the absorbance values of the ratio spectra at 290 nm, the plateau region, using 6 µg mL^{-1} of CH as a divisor then CE and LI absorption spectra were divided by the standard spectrum of 6 µg mL^{-1} of CH and the differences in absorbance values of the obtained ratio spectra at 242 and 256 nm for CE and 210 and 216 nm for LI were plotted against the corresponding concentrations of CE and LI to construct their respective calibration curves for their determination.

The suggested methods were applied for determination of CE, CH, and LI in different laboratory prepared mixtures. The results obtained upon applying the proposed methods on Canyon® oral gel were statistically compared to those obtained by applying the reported HPLC ones and no significant difference was found.

Section (B): Determination of Cetylpyridinium Chloride, Chlorocresol, and Lidocaine by Different Chromatographic Methods

In this section, simple and accurate TLC-Densitometric and RP-HPLC chromatographic methods have been suggested for simultaneous determination of CE, CH, and LI in their ternary mixtures. The best separation resulted upon using methanol: acetone: acetic acid (7: 3: 0.2, by volume) as a developing system and detecting at 215 nm for TLC-Densitometric method while for RP-HPLC method, a mobile phase of 0.05% phosphoric acid solution: acetonitrile: methanol (15: 24: 61, by volume), pH = 5 with a flow rate of 1 mL min^{-1} using C_{18} column and 220 nm as a detection wavelength were the optimum separation conditions. The suggested TLC-Densitometric and RP-HPLC methods were successfully applied for analysis of the cited drugs in Canyon® oral gel and the results showed good

agreement with the labeled amount and were compared to the results obtained from the reported methods where no statistical difference was found.

Part III: Quantitative Determination of Yohimbine Hydrochloride, Vitamin E Acetate, Vitamin B_3, and Caffeine in Their Quaternary Mixtures

This part includes two sections.

Section (A): Determination of Yohimbine Hydrochloride, Vitamin E Acetate, Vitamin B_3, and Caffeine by Different Spectrophotometric Methods

In this section, mean centering of ratio spectra (MCR) and triple divisor (TD) spectrophotometric methods were developed for quantitative determination of Yohimbine Hydrochloride (YH), Vitamin E Acetate (VE), Vitamin B_3 (VB), and Caffeine (CAF). In MCR method, the amplitudes of the mean entered third ratio spectra at 250 nm and 268 nm for YH and VE, respectively and at peak to peak 272-273 and 262-263 nm for VB and CAF, respectively were used for their respective determination. In TD method, YH was determined by measuring the amplitudes of the first derivative ratio spectra at 222 nm using a spectrum of a mixture containing equal concentrations of VE, VB, and CAF (5 µg mL^{-1} of each) as a divisor. VE, VB, and CAF were similarly determined measuring the amplitudes of their respective first derivative ratio spectra at 284, 265, and 287 nm, respectively using a spectrum of a mixture containing equal concentrations of the other three drugs (10 µg mL^{-1} of each) as a divisor. Moreover, the suggested methods have been applied for determination of the four drugs in their pharmaceutical preparation. Statistical comparison with the reported HPLC methods showed no significant difference.

Section (B): Determination of Yohimbine Hydrochloride, Vitamin E Acetate, Vitamin B_3, and Caffeine by Different Chromatographic Methods

In this section, selective and accurate TLC-Densitometric and RP-HPLC chromatographic methods were validated for simultaneous determination of YH, VE, VB, and CAF in their quaternary mixtures. In TLC-Densitometric method, well defined peaks were completely separated on upon using methanol: methylene chloride: ethyl acetate: acetic acid (pH 6.5 ± 0.2) (1: 8: 3: 0.5, by volume) as a developing system and detecting at 220 nm. In RP-HPLC method, a mobile phase of water: acetonitrile: methanol (30: 20: 50, by volume) with a flow rate of 0.8 mL min^{-1} and the effluent was monitored at 270 nm.

The utility of the suggested methods was verified by application to super act® capsules where no interference from additives were found. No significant difference was observed upon comparing the results of the proposed methods and those of the reported HPLC ones.

Part IV: Full Stability Study of Sulfacetamide Sodium and Development of Different Stability Indicating Methods of Analysis

This part includes two sections.

Section (A): Kinetic Study and Characterization of Sulfacetamide Sodium Hydrolytic Degradation Rate

In this section, a kinetic study of Sulfacetamide Sodium (SCA) acidic and alkaline degradation as a function of drug concentration, acid and alkaline concentration and temperature has been established utilizing first derivative of ratio spectra spectrophotometric method as a resolving method in analytical chemistry. Measuring the amplitudes at peak maximum λ = 221 nm of the first

derivative of ratio spectra of sulfacetamide using 10 µg mL^{-1} sulfanilamide, SCA degradation product, as a divisor allowed selective determination of SCA in presence of sulfanilamide.

The method was applied for determination of SCA in marketed formulation and laboratory prepared mixtures with Sulfanilamide. Moreover it was used for the kinetic study of the hydrolysis of SCA. The kinetic degradation of SCA obeyed Arrhenius equation and was found to follow pseudo-first order kinetics under the established experimental conditions and is pH and temperature dependent. Activation energy at different temperatures, kinetic rate constants, and $t_{1/2}$ at different pH values were calculated.

Section (B): Full Stability Study of Sulfacetamide Sodium and Stability Indicating Chromatographic Methods for Determination of Sulfacetamide Sodium in Presence of its Stress Degradation Products

In this section, SCA was subjected to full stability study. The drug was found to be sensitive to most of the studied conditions. Stability indicating TLC-Densitometric and RP-HPLC chromatographic methods have been optimized for determination of (SCA) in presence of its degradation products resulted from different stress conditions. In TLC-densitometric method good separation of (SCA) from its degradation products using ethyl acetate-chloroform-acetic acid (10: 90: 20, by volume) as a developing system with UV detection at 254 nm. While in RP-HPLC method, the drug was completely separated from all degradation products using trifluoroacetic acid solution (0.05%) (TFA)- Methanol (80:20, v/v) as a mobile phase. Quantification was achieved by ultraviolet (UV) detection at 270 nm.

The suggested chromatographic methods were successfully applied for analysis of the cited drug in pharmaceutical formulations and the results showed good agreement with the labeled amount and showed no significant difference with those of the reported HPLC one.