Summary

This present thesis comprises four chapters:

1- Chapter 1 includes an introduction and a literature survey on the method of determination of amikacin sulphate, neomycin sulphate, tobramycin sulphate and vancomycin hydrochloride.

2- Chapte 2 includes the experimental part, the materials, preparations of the solid ion-pair complexes, solutions, instruments, determination of the optimum experimental conditions for ion-pair precipitation from aqueous solutions and the quantitative determination of the drug used. Also, this chapter includes the optimum experimental conditions for conductimetric determination, atomic absorption study and spectral measurement of the investigated drugs.

3- Chapter 3 includes the results and discussion:

i- The solid ion-pair complexes of the drugs under investigation with ammonium reineckate, potassium ferrocyanide, cobalt thiocyanate, nickal thiocyanate and sodium nitroprusside are confirm by elemental analysis and determination of metal content.

ii- Conductimetric titration of the drugs with ammonium reineckate, potassium ferrocyanide, cobalt thiocyanate, nickal thiocyanate and sodium nitroprusside carried out to give further insight to the stoichiometric composition of the ion-pair formed in solutions. The results indicated that, ammonium reineckate reacts

with Amik.SO_4, Neom.SO_4, Tobr.SO_4 and Vanc.Cl to form 1: 4, 1: 2, 1: 10 and 1: 1 [drug] : [X^{n-}] ion-pairs, whereas potassium ferrocyanide form 1: 1, 2: 1, 2: 5 and 4: 1 ion-pairs with the investigated drugs. Cobalt thiocyanate, nickal thiocyanate and sodium nitroprusside forms 1: 2, 1: 1, 1: 5 and 2: 1 ion-pairs with the same drugs respectively.

iii- The effect of solvent, dilution of titrand and titrant and temperature on the end point of conductimetric titration of the investigated drugs was studied to evaluate the optimum conditions for determination of the cited drugs conductimetrically.

iv- Conductimetric determination of the investigared drugs was carried out in pure solutions, in pharmaceutical preparations (tables,eye drops, vials and lotion) and in urine at the optimum conditions using the standard addition techniques.

v- Studies on the influence of the pH and temperature on the solubility of ion-pairs are carried out to establish the optimum experimental conditions for ion-pairs precipitation from aqueous solutions. The optimum pH value for formation of solid ion-pairs with each drug is determined.

vi- The ion-pairs are used for analytical determination of the drugs under investigation in pure solution, using atomic absorption spectrometry (AAS). An excess of the reagents (reineckate, ferrocyanide, Co, Ni thiocyanate and nitroprusside) were added to

definite amount of the drug, at the optimum conditions of pH, to form solid ion-pair and the unreacted reagents were determined by AAS. The results obtained were treated statistically for estimation of their precision and accuracy.

Vii- In order to investigate the optimum reaction conditions for the reaction of the studied drugs with potassium ferrocyanide, as the effect of different experimental variables, the following studies should be taken into consideration. At the optimum conditions of pH, time, temperature, solvents and sequence of additions. The aminoglycoside drugs oxidize the ferrous ions present in potassium ferrocyanide to ferric ion forming ferri ferrocyanide (Prussian blue) and under the action of the drug, it form an ion pair complex which absorb maximally at 523, 523, 504 and 507 nm for Amik.SO_4, Neom.SO_4, Tobr.SO_4 and Vanc.Cl, respectively.

$$K_4[Fe(CN)_6] \xrightarrow[\text{Heat}]{\text{Acid}} Fe_4[Fe(CN)_6]_3$$

The stoichiometry of the ion-pair that formed with potassium ferrocyanide are also evaluated from spectrophotometric methods namely the molar ratio and continuous variation methods. The optimum conditions for the complex formation are investigated.

viii- The effect of acid, effect of time and temperature as well as the sequence of addition and effect of solvent were also studied. The results indicated that the molecular ratio of the reagent to

Amik.SO_4 is 2:3, to Neom.SO_4 is 1:3, to Tobr.SO_4 is 5:3 and to Vanc.Cl is 1:3.

ix- Beer's law was applied to determine of the drugs under investigation. For more accurate determination, Ringbom method was used. Good results are obtained by calculating Sandell sensitivity, molar absorptivity, detection and quantification limits, and the relative standard deviation.

x- The results of different analyses were compared with the pharmacopoeial or the official methods for determination of the cited drugs, to test significance difference between them. Statistical analyses for such comparison includes F-test and t-test was tested. The F- and t-values were determined and were found to be less than the tabulated values at 95% confidence level. This indicated that, the present methods are suitable methods for the drug's determination, as they are accurate, precise and have a very low detection limits.

4- Chapter 4 includes the microbiological activity for vancomycin and its complexes.

i- Introduction about the control of microbial growth by antibiotics and vancomycin resistance in microorganisms.

ii- Five vancomycin complexes were prepared by the reaction between Vanc.Cl and the reagent mentioned before forming the ion-pairs. The Vanc.Cl used as control and the ion-pairs are tested on

seven microorganisms, which are *Esccherichia coli, Bacillus subtlus, Bacillus cereus, Candida albicance, Pseudomonas fluorescens, Aspergillus flvus* and *Aspergillus niger*. The method based on the measured the diameter of the clear zones at the optimum concentration, pH and temperature.

iii- The results indicated that Vanc.Cl complexes were found to be more effective than the control preparation that is Vanc.Cl itself.