CHAPTER III

EXPERIMENTAL

Equipments and Materials

Potentiograph E536 (Metrohm Herisau); Glass electrode AG9100 (Metrohm Herisau); Calomel electrode AG9100 (Metrohm Herisau); 655 Multi-dosimat Metrohm Herisau : Automatic titrator; Exchange units - model 3005(501); Magnetic stirrer E649 (Metrohm Herisau).

Potassium hydrogenphthalate AR (E-Merck, lot#1146670); Sodium hydroxide AR (E-Merck, lot#2514680); Potassium chloride AR (J.T.Baker Chemical, lot#1-3040); Absolute ethanol AR (E-Merck, lot#3247517); Glacial acetic acid AR (E-Merck, lot#R864163); Perchloric acid AR; Acetic anhydride AR (obtained from department of Pharmaceutical Chemistry,C.U.); Mercuric acetate AR (E-Merck, lot#CC400410); Distilled water; Cryscal violet; p-Naphthalbenzein (Bristish Drug House, lot#3030650).

Weak acidic drugs obtained from Medic Pharma Co.Ltd. are Triprolidine hydrochloride USP (RMA850215); Dextromethorphan hydrobromide USP (RMA850422); Quinine sulfate USP (RMA850611); Diphenhydramine hydrochloride USP (RMA850632); Phenylpropanolamine hydrochloride USP

(RMA850802); Chlorpheniramine maleate USP (RMA850814); Pseudoephedrine hydrochloride USP (RMA850213).

Preparation of Sodium Hydroxide Standard Solution

Ten grammes of sodium hydroxide were weighed and dissolved in 20 ml distilled deionized water. The supernatant was decanted after precipitated sodium carbonate had settled out. Eight milliliters of this liquid was pipetted into 1-liter volumetric flask and then diluted with distilled deionized water to the volume. The solution of 0.1 N sodium hydroxide was standardized with potassium hydrogenphthalate and end point volume was determined by potentiometry (parallel tangents method).

Preparation of Weak Acidic Drugs in 0.1 M Potassium Chloride

Potassium chloride was weighed and dissolved in the distilled deionized water, and diluted with the same solvent to give a final concentration 0.100 M.

All weak acidic drugs were accurately weighed with suitable quantities (according to their molecular weights) to produce 0.005 M. They were dissolved in the solution of 0.100 M potassium chloride in order to control ionic strength of solution, warmed if necessary to effect solution. Fifty milliliters of the resulting solution was pipetted and then transfered to a 100-ml beaker.

Preparation of Weak Acidic Drugs in 40%v/v Ethanol/Water

The weak acidic drugs were prepared in the similar way as the preparation in 0.100 M potassium chloride but used 40% volume by volume of ethanol and distilled deionized water as solvent.

Titration of Weak Acidic Drugs with 0.1 N Sodium Hydroxide

Fitty milliliters of the pipetted solutions were titrated with 0.1 N sodium hydroxide standard solution. The electrodes were submerged into titrated solution for 5 minutes prior to commencement of titration to assure that electrodes were in equillibrium with titrated solution. The sample solution was mixed with a magnetic bar and magnetic stirrer after each addition of titrant and the pH value was measured with the stirrer off.

Non-Aqueous Titrations

Weak acidic drugs were titrated in non-aqueous systems as described in the United State Pharmacopeia XXI; triprolidine HCl (33), dextromethorphan HBr (34), quinine sulfate (35), diphenhydramine HCl (36), phenylpropanolamine HCl (37), chlorpheniramine maleate (38), pseudoephedrine HCl (39).

Determination of End Point Volumes

End point volumes of the aqueous titration and titration in 40%v/v ethanol/water were obtained from extrapolation of linear plots according to equations 9, 21, 29, 31, 42, 51, 52, 53, 62, 63, 69. 72, 76. The variables to be calculated and ploted were showed in Table 1. Computer programs as shown in Appendix, were employed for the calculations and the extrapolations were obtained from linear regression method.

Percentage purity of weak acidic compounds were calculated as followed :

$$\% \text{ purity} = \frac{Ve \times N \times Eq.Wt.A \times 100}{Wt.A}$$

where Ve was end point volume (ml),

N was normality of titrant (meq/ml),

Eq.Wt.A was equivalence weight of sample A (mg/meq),

Wt.A was weight of sample A (mg).

Table 1 Expression of Variables in Gran PLot

Substance	Function Plotted			
	Before End Point		After End Point	
	Y-axis	X-axis	Y-axis	X-axis
1.Weak acid group I (a)				
1.1 in 0.1 M KCl	G[H+]	G (c)	V_t Kw/[H+]	V
	V[H+]	V	"	"
1.2 in mixed solvent (d)	V[H+]	V	"	"
2.Weak acid group II (b)				
2.1 in 0.1 M KCl	[H+](Vo+V)	G	"	"
	[H+](Vo+V)	V	"	"
2.2 in mixed solvent (d)	V[H+]	V	"	"

Note : (a) Weak acid group I are potassium hydrogenphthalate, phenylpropanolamine HCl and pseudoephedrine HCl.

(b) Weak acid group II are triprolidine HCl, quinine sulfate, dextromethorphan HBr, diphenhydramine HCl and chlorpheniramine maleate.

(c) $G = VN + (Vo+V)\{[H+]-[OH]\}$

(d) mixed solvent = 40%v/v ethanol/water

Table 2 Weak Acidic Compounds in this Investigation

Weak Acidic Compounds	pKa (40)
Potassium hydrogenphthalate	5.4
Chlorpheniramine maleate	9.2
Phenylpropanolamine HCl	9.4
Pseudoephedrine HCl	9.9
Triprolidine HCl	6.5
Quinine sulfate	8.8
Dextromethorphan HBr	8.3
Diphenhydramine HCl	9.0