5. COLUMN STUDIES WITH QUINIDINE AND CINCHONINE SULFATES.

5 COLUMN STUDIES WITH QUINIDINE AND CINCHONINE SULFATES :

Introduction :

This chapter includes the column study of quinidine and cinchonine sulfates. The variables studied were the solvent (water and N/100 sulfuric acid) of the alkaloid sulfate solution, ionic form of the resin, treatment of the exchanged resin with aqueous sodium hydroxide and then extraction of the alkaloid bases by distilled ethyl alcohol and the concentration of the ammonical alcohol as eluent.

Experimental :

Known weight of the airdry resin Amberlite IR-200 was taken, slurried with distilled water and transferred into columns fitted with zero porosity sintered glass discs. The columns were backwashed with distilled water, allowed to settle under gravity and then the column data were determined.

Nomenclature :

W_x = the amount in milliequivalents of the alkaloid exchanged per sample,

W_l = the amount in milliequivalents of the alkaloid eluted per sample,

TW_x = the total amount in milliequivalents of the alkaloid exchanged,

TW_l = the total amount in milliequivalents of the alkaloid eluted.

Results and discussion :

The study in this chapter was divided into two parts.

Part I

In this series, eight runs were carried out to study the exchange of quinidine sulfate and cinchonine sulfate from water and N/100 sulfuric acid on resin columns in hydrogen form and sodium form and the extent of the extraction of the exchanged alkaloids from the resin bed using aqueous sodium hydroxide and distilled ethyl alcohol. Each run consists of three parts a, b and c carried out in succession.

A column of resin IR-200 in hydrogen form was used. The column data were : bed length = 21 cms. ; bed volume = 9 cc. ; capacity of the resin in the column = 16.3 meq.

Run 1 :

1a. Four liters of aqueous quinidine sulfate solution (concentration = 2 meq. per liter) were passed through the column at the rate of 50 cc. per minute. The effluent was collected in eight samples, each of 500 cc. and the milliequivalents of quinidine sulfate exchanged (W_x) for each sample were calculated by measuring the ultraviolet absorption at the invarient wavelength(1).

1b. Then the column was washed with distilled water. N sodium hydroxide solution (30 cc.) was added, the column was inverted four to five times, allowed to stand for an hour with intermittent shaking and then drained. N sodium hydroxide solution (20 cc.) was again added, the column was shaken, allowed to stand for an hour and then drained. The resin bed was washed with two bed volumes of distilled water. Distilled ethyl alcohol (50 cc.) was then added and the column was allowed to stand for 30 minutes with intermittent shaking. The alcoholic solution was run into a 500 cc. volumetric flask. Distilled ethyl alcohol (50 cc.) was again added, the column was allowed to stand for 30 minutes with intermittent shaking and the alcoholic solution was run into the same flask. This operation was repeated till all the alkaloid was removed from the resin bed (determined by the ultraviolet absorption) and further treatment of the resin bed with N sodium hydroxide solution and subsequent extraction with distilled ethyl alcohol did not show the presence of alkaloid in the alcohol. The alcoholic solution was made upto the mark with distilled ethyl alcohol and the total amount of quinidine eluted (TW_1) was calculated by measuring ultraviolet absorption. This was checked gravimetrically by taking 200 cc. of the alcoholic solution from the same flask, concentrating by distillation, evaporating on a water bath, drying at $100 \pm 1^{o}C$ and finally weighing. The results obtained by both the methods agreed.

1c. Then the column was regenerated with excess of hydrochloric acid, washed free of acid, backwashed and

allowed to settle under gravity. This was then ready for the next run.

Runs 2 to 8 :

Run 2 was the repetition of run 1 except that the influent quinidine sulfate solution in part 2a was in N/100 sulfuric acid medium instead of in aqueous medium. Runs 3 and 4 were the repetition of runs 1 and 2 respectively except that cinchonine sulfate replaced quinidine sulfate. Runs 5, 6, 7 and 8 were the repetition of runs 1, 2, 3 and 4 respectively except that the column was converted into sodium form instead of in hydrogen form before the commencement of the runs.

Table (5.01) summarises the runs with quinidine and cinchonine sulfates in aqueous and N/100 sulfuric acid medium with columns of resin IR-200 in hydrogen and sodium forms. Table (5.02) gives the amounts of alkaloids exchanged and eluted in each case. It is observed that the amount exchanged with a column of resin IR-200 in hydrogen form decreases to some extent when solution medium is changed from aqueous to N/100 sulfuric acid. When the resin is in sodium form this change of solution medium has little effect on the amounts of both the alkaloids exchanged. The total amount exchanged with cinchonine sulfate is more than that exchanged with quinidine sulfate. This may be attributed to the smaller molecular size of cinchonine than that of quinidine and this is also consistent with the higher P_R

Table 5.01

Exchange of cinchona alkaloid sulfates with a column of resin IR-200.

Alkaloid =	quinidine sulfate			
ionic form =	H^+		Na^+	
	medium of solution		medium of solution	
	aqueous	N/100 H_2SO_4	aqueous	N/100 H_2SO_4
sample No.	100 W_x	100 W_x	100 W_x	100 W_x
1	96	74	60	59
2	76	42	32	32
3	55	27	27	27
4	42	22	19	20
5	28	20	17	18
6	24	16	16	16
7	21	14	14	15
8	18	13	13	13

Table 5.01 (Contd.)

Alkaloid =	cinchonine sulfate			
ionic form =	H^+		Na^+	
	medium of solution		medium of solution	
	aqueous	N/100 H_2SO_4	aqueous	N/100 H_2SO_4
Sample No.	100 W_x	100 W_x	100 W_x	100 W_x
1	97	84	77	77
2	86	55	48	47
3	67	38	34	34
4	50	30	28	28
5	38	24	23	23
6	28	20	20	21
7	23	18	18	18
8	20	16	17	17

Table 5.02

Total amount of cinchona alkaloids exchanged (TW_x) and eluted (TW_1) from a column of resin IR-200.

Alkaloid =		quinidine sulfate		cinchonine sulfate	
ionic form	medium of the solution	TW_x	TW_1	TW_x	TW_1
H^+	aqueous	3.60	3.60	4.09	4.09
H^+	N/100 H_2SO_4	2.28	2.28	2.85	2.85
Na^+	aqueous	1.98	1.98	2.65	2.65
Na^+	N/100 H_2SO_4	2.00	2.00	2.65	2.65

value for cinchonine (2). It is also seen that the exchanged alkaloids are completely eluted by treatment with sodium hydroxide followed by distilled ethyl alcohol.

When sodium hydroxide solution was added to the column of resin IR-200 after part (a) of a run, the liberated alkaloid base caused jamming of the resin bed and decreased considerably the flow of sodium hydroxide solution ; it was found that if the column was frequently inverted and thus the resin kept loose the jamming of the column could be avoided.

Part II

In this part, runs were carried out to study (a) the exchange with quinidine sulfate and cinchonine sulfate from aqueous and N/100 sulfuric acid medium on columns of resin IR-200 in hydrogen and ammonium forms and (b) the elution of the exchanged alkaloids with N/10 and N/25 ammonical ethyl alcohol.

The runs were divided into two series, each run consisting of three parts a, b and c carried out in succession.

Series one :

In this series eight runs were carried out to study the effect of (a) ionic form of the resin and solution medium on the exchange of the alkaloid sulfate and (b) elution with N/10 ammonical ethyl alcohol. The column used in this series of runs was the same as that used in Part I.

Run 1 :

1a. This was the repetition of run 1a of Part I.

1b. Then the column was washed with distilled water and eluted with N/10 ammonical ethyl alcohol at a flow rate of 20 cc. per minute. The effluent was collected in 100 cc. samples and the milliequivalents of alkaloid base eluted (W_1) per sample was calculated by measuring the ultraviolet absorption at the invariant wavelength. After the 16th sample the run was discontinued.

1c. Then the column was washed, regenerated with excess of hydrochloric acid, washed free of acid, backwashed and allowed to settle under gravity. It was then ready for the next run.

Run 2 :

This was the repetition of run 1 except that in part 2a. The quinidine sulfate passed was in N/100 sulfuric acid medium instead of in aqueous medium.

Runs 3 and 4 :

These were the repetition of the runs 1 and 2 respectively except that cinchonine sulfate replaced quinidine sulfate.

Runs 5 to 8 :

Runs 5, 6, 7 and 8 were the repetitions of runs 1, 2, 3 and 4 respectively except that the resin column was in ammonium form before the exchange runs.

Series two :

In this series eight runs were carried out to study the elution of quinidine and cinchonine with N/25 ammonical ethyl alcohol.

Runs 9 to 16 :

These were the repetitions of the runs 1 to 8 respectively of the series one of Part II except that in part b of each run the concentration of the eluent ammonical ethyl alcohol was N/25 instead of N/10.

Parts (a) of tables (5.03 to 5.10 ; the volume of each sample =500 cc.) give the exchange runs with quinidine sulfate and cinchonine sulfate in aqueous and N/100 sulfuric acid medium with columns of resin IR-200 in hydrogen and ammonium forms. Parts (b) of tables (5.03 to 5.18 ; volume of each sample = 100 cc.) give the elution runs with N/10 and N/25 ammonical ethyl alcohol. Table (5.19) gives the total amounts of the alkaloids exchanged from the sulfate solutions in aqueous and N/100 sulfuric acid medium and the total amounts of the alkaloids eluted from columns of resin IR-200 in hydrogen and ammonium forms. It is observed that the amount exchanged with resin in hydrogen form decreases to some extent when the medium of the solution was changed from aqueous to N/100 sulfuric acid. When the column is in ammonium form solution medium has little effect on the amount exchanged. The amount exchanged from cinchonine sulfate is greater than that exchanged from quinidine sulfate. This may be attributed

Table 5.03a

Data for the run 1a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	96	5	28
2	76	6	24
3	55	7	21
4	42	8	18

Table 5.03b

Data for the run 1b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	511	9	56
2	317	10	48
3	192	11	41
4	150	12	35
5	113	13	30
6	100	14	24
7	81	15	21
8	68	16	19

Table 5.04a

Data for the run 2a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	74	5	20
2	42	6	16
3	27	7	14
4	22	8	13

Table 5.04b

Data for the run 2b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	303	9	35
2	158	10	32
3	120	11	27
4	97	12	23
5	79	13	21
6	72	14	19
7	46	15	17
8	43	16	15

Table 5.05a

Data for the run 3a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	97	5	38
2	86	6	28
3	67	7	23
4	50	8	20

Table 5.05b

Data for the run 3b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	569	9	70
2	361	10	59
3	255	11	44
4	140	12	37
5	124	13	34
6	110	14	32
7	81	15	22
8	79	16	18

Table 5.06a

Data for the run 4a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	84	5	24
2	55	6	20
3	38	7	18
4	30	8	16

Table 5.06b

Data for the run 4b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	352	9	52
2	213	10	37
3	149	11	31
4	145	12	26
5	95	13	24
6	93	14	22
7	83	15	20
8	62	16	18

Table 5.07a

Data for the run 5a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	72	5	23
2	45	6	19
3	32	7	17
4	26	8	16

Table 5.07b

Data for the run 5b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	725	9	6.6
2	236	10	5.2
3	122	11	4.4
4	62	12	4.0
5	33	13	3.5
6	20	14	3.3
7	13	15	3.0
8	8.8	16	2.8

Table 5.08a

Data for the run 6a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	71	5	23
2	46	6	20
3	32	7	17
4	27	8	16

Table 5.08b

Date for the run 6b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	443	9	23
2	211	10	22
3	141	11	18
4	104	12	14
5	81	13	12
6	59	14	10
7	47	15	9
8	37	16	8

Table 5.09a

Data for the run 7a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	86	5	30
2	61	6	26
3	46	7	22
4	37	8	20

Table 5.09b

Data for the run 7b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	977	9	6.2
2	314	10	5.4
3	170	11	4.0
4	77	12	3.8
5	38	13	3.2
6	20	14	2.6
7	12	15	2.4
8	7.7	16	2.0

Table 5.10a

Data for the run 8a of the series one of Part II.

Sample No.	100 W_x	Sample No.	100 W_x
1	85	5	29
2	60	6	26
3	47	7	23
4	36	8	20

Table 5.10b

Data for the run 8b of the series one of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	503	9	44
2	267	10	32
3	194	11	31
4	140	12	20
5	133	13	16
6	96	14	14
7	75	15	13
8	57	16	11

Table 5.11a

Data for the run 9a of the series two of Part II.

These are the same as in Table 5.03a

Table 5.11b

Data for the run 9b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	269	9	62
2	362	10	55
3	237	11	48
4	185	12	39
5	156	13	34
6	125	14	30
7	100	15	25
8	80	16	23

Table 5.12a

Data for the run 10a of the series two of Part II.
These are the same as in Table 5.04a

Table 5.12b

Data for the run 10b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	159	9	30
2	257	10	24
3	159	11	21
4	149	12	15
5	87	13	14
6	78	14	8
7	65	15	5
8	54	16	4

Table 5.13a

Data for the run 11a of the series two of Part II.

These are the same as in Table 5.05a

Table 5.13b

Data for the run 11b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	334	9	70
2	419	10	58
3	289	11	34
4	220	12	22
5	159	13	20
6	112	14	19
7	102	15	18
8	87	16	17

Table 5.14a

Data for the run 12a of the series two of Part II.

These are the same as in Table 5.06a

Table 5.14b

Data for the run 12b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	238	9	45
2	329	10	36
3	217	11	31
4	134	12	26
5	116	13	19
6	76	14	15
7	68	15	11
8	55	16	10

Table 5.15a

Data for the run 13a of the series two of Part II.

These are the same as in Table 5.07a

Table 5.15b

Data for the run 13b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	486	9	11
2	307	10	8
3	181	11	7.3
4	117	12	4.3
5	71	13	3.7
6	51	14	3.2
7	26	15	2.7
8	16		

Table 5.16a

Data for the run 14a of the series two of Part II.

These are the same as in Table 5.08a

Table 5.16b

Data for the run 14b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	254	9	46
2	208	10	36
3	146	11	30
4	123	12	26
5	100	13	20
6	82	14	17
7	65	15	14
8	63	16	12

Table 5.17a

Data for the run 15a of the series two of Part II.

These are the same as in Table 5.09a

Table 5.17b

Data for the run 15b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	680	9	12
2	350	10	8
3	215	11	5.5
4	120	12	4.1
5	85	13	3.3
6	50	14	2.5
7	28	15	1.7
8	22	16	1.7

Table 5.18a

Data for the run 16a of the series two of Part II.

These are the same as in Table 5.10a

Table 5.18b

Data for the run 16b of the series two of Part II.

Sample No.	500 W_1	Sample No.	500 W_1
1	350	9	51
2	303	10	43
3	210	11	33
4	147	12	27
5	116	13	21
6	100	14	19
7	70	15	15
8	61	16	14

Table 5.19

Summary of the Tables (5.03 - 5.18)

Alkaloid =	quinidine sulfate					
	Medium of Solution					
	aqueous			N/100 H_2SO_4		
Ionic form	TW_x	TW_1 with [alcohol] = N/10	ammonical N/25	TW_x	TW_1 with [alcohol] N/10	ammonical N/25
H^+	3.60	3.61	3.66	2.28	2.21	2.26
NH_4^+	2.50	2.51	2.59	2.52	2.48	2.48

Table 5.19 (Contd.)

Alkaloid = cinchonine sulfate

Ionic form	Medium of solution: aqueous			Medium of solution: N/100 H_2SO_4		
	TW_x	TW_1 with [ammonical alcohol] =		TW_x	TW_1 with [ammonical alcohol] =	
		N/10	N/25		N/10	N/25
H^+	4.09	4.07	3.96	2.85	2.84	2.85
NH_4^+	3.28	3.29	3.17	3.26	3.29	3.16

to the smaller molecular size of cinchonine relative to that of quinidine.

The elution runs for both the alkaloids with the resin in hydrogen form are similar. The same is valid with resin in ammonium form. However, the elution of a alkaloid from the resin in hydrogen form is slower than that from the resin in ammonium form. This may be so because when the resin is in hydrogen form, initially ammonia will be used in converting it into ammonium form. The difficulties encountered in part (b) of the runs in Part I, when sodium hydroxide was used, were not encountered here. The flow of ammonical alcohol was satisfactory and hence there was no jamming of the column.

Conclusion :

It may be concluded that resin IR-200 may be used in the ammonium form, N/100 sulfuric acid may be used as the extraction solvent for the materials containing the cinchona alkaloids and N/10 ammonical alcohol may be used to elute the alkaloids from the resin column.

References :

1. Kanhere, S. S., Shah, R. S. and Bafna, S. L. Indian J. Chem. 3, 251 (1965).

2. Kanhere, S. S., Ph. D. Thesis (Baroda 1964).