3.

ESTIMATION OF CINCHONA ALKALOID SULPHATES :

3.1 Estimation of the alkaloid sulphate gravimetrically :

Water of crystallisation in the crystallised sulphates of quinine , cinchonine and cinchonidine may not be constant (1.4.a) . However the data given under 3.1.a to 3.1.d. (for two typical alkaloid sulphates) show that calculation of molecular weight of the crystallised alkaloid sulphate based on (a) gravimetric sulphate estimation and (b) moisture content determination , are in good agreement. As such gravimetric sulphate estimation can be used for the accurate determination of the concentration of the aqueous alkaloid sulphate solution irrespective of the water of crystallisation of the sample.

Hence , the gravimetric sulphate estimation has been used , all through this work , for rechecking the concentration of the aqueous alkaloid sulphate solution.

3.1.a. Moisture content determination of crystallised quinine sulphate :

Moisture content was determined by heating known weights of the sample of crystallised quinine sulphate in an oven (100 - 104 ^{o}C) to a constant weight. Knowing the molecular weight of anhydrous quinine sulphate molecule (746), the molecular weight of the crystallised quinine sulphate was calculated.

		I	II	III
Weight of crystallised salt taken (in grams .)	:	0.1722	0.2084	0.1949
Weight of moisture obtained (in grams .)	:	0.0072	0.0087	0.0079
% moisture content	:	4.181	4.199	4.080

Average moisture content = 4.153 %

Hence, molecular weight of the crystallised salt :

$$\frac{746 \times 100}{(100 - 4.153)} = 778.2$$

3.1.b. Gravimetric sulphate estimation of crystallised quinine sulphate :

A known weight of crystallised quinine sulphate (from the same sample as taken in 3.1.a.) was dissolved in about 500 cc. of distilled water, five drops of hydrochloric acid (1 N) were added and precipitation done in the usual way with 1 % aqueous barium chloride solution using G 4 sintered glass crucible . From the weight of barium sulphate obtained and knowing the molecular weight of barium sulphate (233) , the molecular weight of the crystallised quinine sulphate was calculated.

Weight of crystallised quinine -
sulphate taken = 0.4916 gms. / 500 cc.

Weight of barium sulphate
obtained = 0.1468 gms. / 500 cc.

Hence, molecular weight of crystallised quinine sulphate :

$$\frac{233 \times 0.4916}{0.1468} = 780.3$$

3.1.c. Mositure content determination of crystallised cinchonidine sulphate :

Moisture content was determined by heating known weights of the sample of crystallised cinchonidine sulphate in an oven (100 - 104 ^{o}C) to a constant weight. Knowing the molecular weight of anhydrous cinchonidine sulphate molecule (686), the molecular weight of the crystallised cinchonidine sulphate was calculated.

		I	II	III
Weight of the crystallised salt taken (in grams.)	:	0.1282	0.1866	0.2360
Weight of moisture obtained (in grams.)	:	0.0106	0.0156	0.0198
% moisture content	:	8.307	8.360	8.412

Average moisture content : 8.359 %

Hence , molecular weight of the crystallised cinchonidine sulphate :

$$\frac{686 \times 100}{(100 - 8.359)} = 748.5$$

3.1.d. Gravimetric sulphate estimation of crystallised cinchonidine sulphate :

A known weight of crystallised cinchonidine sulphate (from the same sample as taken in 3.1.c.) was dissolved in about 500 cc. of distilled water , five drops of hydrochloric acid (1 N) were added and precipitation was done in the usual way with 1 % aqueous barium chloride solution using G 4 sintered glass crucible . From the weight of barium sulphate obtained and knowing the molecular weight of barium sulphate (233), the molecular weight of the crystallised cinchonidine sulphate was calculated.

Weight of the crystallised cinchonidine sulphate taken = 0.3668 gms. / 500 cc.

Weight of barium sulphate obtained = 0.1139 gms. / 500 cc.

Hence molecular weight of crystallised cinchonidine sulphate:

$$\frac{233 \times 0.3668}{0.1139} = 750.6$$

3.2 Gravimetric total sulphate estimation of a mixture of sulphuric acid and alkaloid sulphate :

A known volume of standard sulphuric acid was added to an aqueous solution of quinine sulphate taken from the same sample as taken under 3.1.a. (mol.wt. = 779.2) and the total sulphate in the resulting mixture was estimated gravimetrically . Data given below show that the total sulphate in such a mixture can be estimated accurately.

Weight of crystallised quinine sulphate taken = 0.6023 gms. / 500 cc.

Volume of sulphuric acid added = 30.0 cc.

Strength of sulphuric acid added = 0.0408 N

Weight of barium sulphate obtained = 0.3217 gms.

Weight of barium sulphate required :

$$\frac{0.6023 \times 233}{779.2} + \frac{30 \times 0.0408 \times 49 \times 233}{1000 \times 98} = 0.3228 \text{ gms.}$$

3.3 Estimation of alkaloid sulphate or sulphuric acid in a mixture of the two :

When a cation exchanger is contacted with an aqueous solution of an alkaloid sulphate, exchange occurs

and an equivalent ammunt of sulphuric acid is liberated. To estimate the extent to which exchange has occured , estimation of sulphuric acid or alkaloid sulphate in presence of each other, becomes necessary.

The following sections describe the methods adopted for this purpose.

3.3.a. Usual titration method for the estimation of sulphuric acid in the mixture of sulphuric acid and an alkaloid sulphate with a standard alkali , using phenolphthalein or methyl orange indicators did not give a sharp end point and a good result.

3.3.b. Estimation of the free alkaloid base liberated by the addition of excess of ammonia to neutralise the sulphuric acid present in such a mixture (after boiling off the free ammonium hydroxide) with a standard acid did not give a sharp end point and a good result.

3.3.c. Polarimetric method :

The chief alkaloid sulphates of cinchona are optically active (1.4.a.). Hence this property could be utilised for the estimation of the alkaloid sulphate in the mixture. However aqueous solution of quinine sulphate (0.1 gm. / 100 cc. i.e. of the order of 2 meq./litre) gave only 0.25° as the angle of rotation with the polarimeter (Hilger model) using a two decimeter polarimeter tube. This angle of rotation was too small

to give an accurate determination of the alkaloid sulphate at low concentrations. Moreover the value of rotation varies with the amount of sulphuric acid present (1.4.a.)

3.3.d. Conductometric method :

Standard sodium hydroxide or ammonium hydroxide was run in a mixture of known weight of the alkaloid sulphate and a known concentration of sulphuric acid in a fixed total volume of 250 cc. The conductances of the solution were measured on a wheatstone bridge with amplifier. Estimations were made of known mixtures with varying amounts of sulphuric acid and the salt. The total volume of the solution (250 cc.) was always about 10 times the total titre value so as to minimise the effect of volume changes on the conductances measured.

Tables (3.01 and 3.02) give two such typical data for conductometric titrations with standard caustic soda and ammonium hydroxide solution. Plot ; figures (3.1 and 3.2),of conductances against the volumes of base added, give two points of intersection corresponding to the titre values for the sulphuric acid and the alkaloid sulphate.

The data given in tables (3.01 and 3.02) show that the values obtained differ from the expected values and hence this method was not found satisfactory.

Figure 3·1

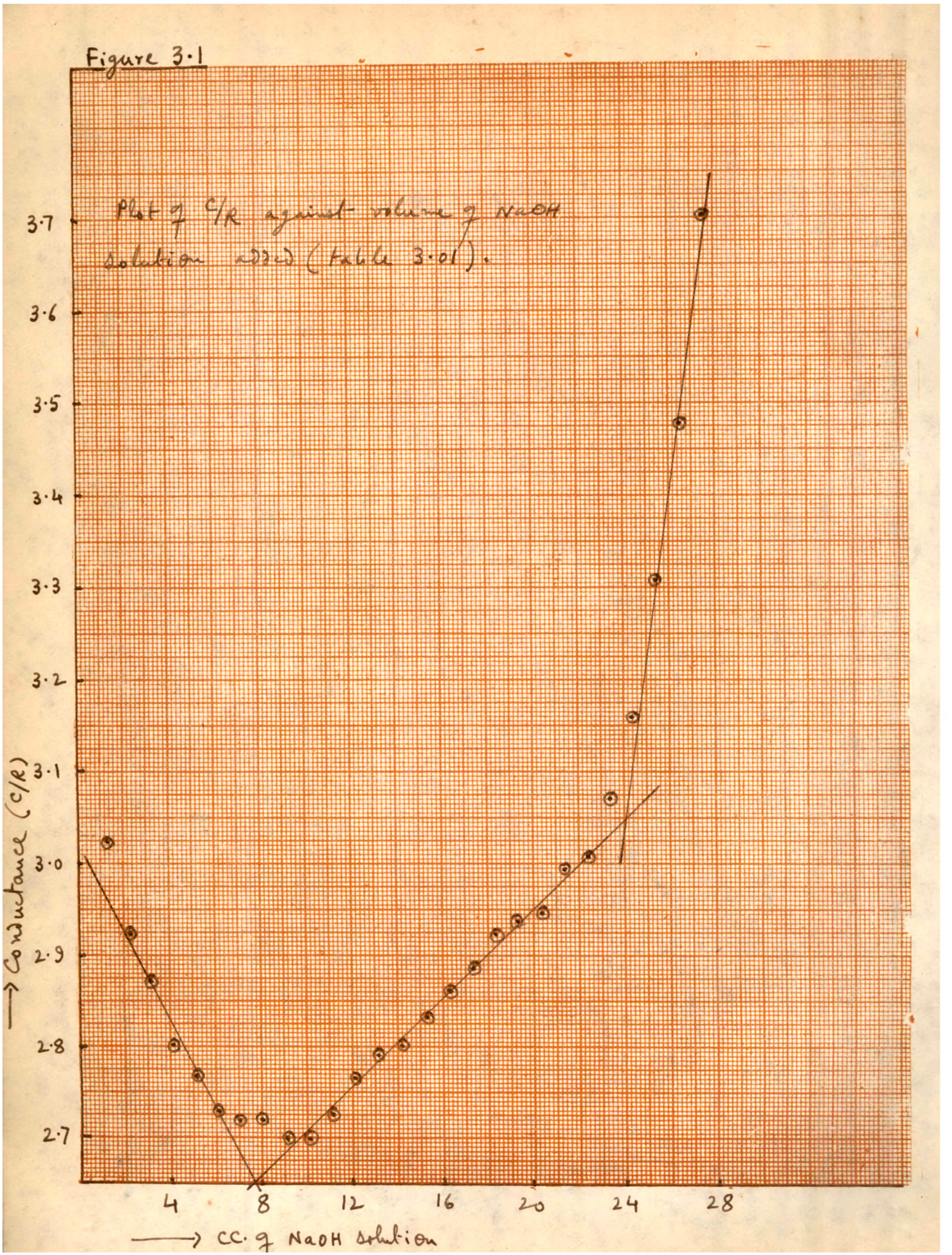
Plot of C/R against volume of NaOH solution added (Table 3·01).
3·7
3·6
3·5
3·4
3·3
3·2
3·1
3·0
2·9
2·8
2·7
→ Conductance (C/R)
4
8
12
16
20
24
28
→ CC. of NaOH Solution

Table 3.01

Conductometric titration with caustic soda solution.

Weight of quinine sulphate taken = 0.1856 grams.
Volume of sulphuric acid added = 12.0 cc.
Strength of sulphuric acid = 0.0408 N
Strength of caustic soda solution = 0.0408 N

Vol. of NaOH added in cc.	Conductance (C/R where C =const.)	Vol. of NaOH added in cc.	Conductance (C/R where C = const.)
1.0	3.019	15.0	2.829
2.0	2.919	16.0	2.860
3.0	2.869	17.0	2.886
4.0	2.803	18.0	2.918
5.0	2.767	19.0	2.937
6.0	2.731	20.0	2.944
7.0	2.720	21.0	2.988
8.0	2.720	22.0	3.004
9.0	2.700	23.0	3.067
10.0	2.700	24.0	3.156
11.0	2.725	25.0	3.305
12.0	2.764	26.0	3.476
13.0	2.789	27.0	3.702
14.0	2.803	28.0	3.863

From figure (3.1)

Result 1 : titre value obtained for acid = 7.6 cc.
required titre value = 12.0 cc.

Result 2 : titre value for salt = 16.2 cc.

Hence, molecular weight of quinine sulphate =

$$\frac{0.1856 \times 10^3 \times 2}{16.2 \times 0.0408} = 561.5$$

Required molecular weight = 782

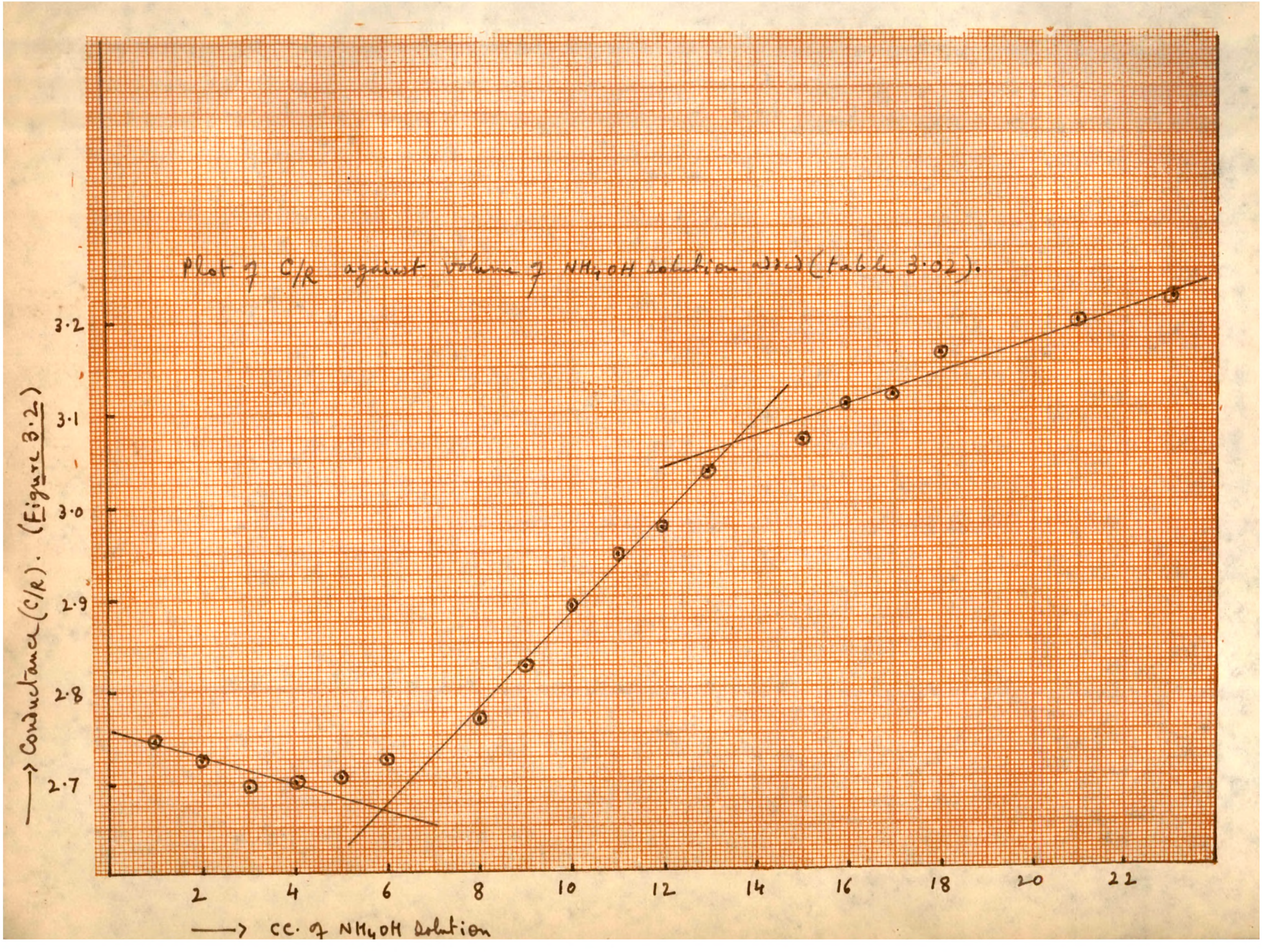
Plot of C/R against volume of NH4OH solution used (table 3·02).
Conductance (C/R). (Figure 3·2)
3·2
3·1
3·0
2·9
2·8
2·7
2
4
6
8
10
12
14
16
18
20
22
cc. of NH4OH solution

Table 3.02

Conductometric titration with ammonium hydroxide solution.

Weight of quinine sulphate taken = 0.1832 gms.
Volume of sulphuric acid added = 10.0 cc.
Strength of sulphuric acid = 0.0408 N
Strength of ammonium hydroxide solution = 0.0425 N

Vol. of NH_4OH added in cc.	Conductance (C/R where C=const.)	Vol. of NH_4OH added in cc.	Conductance (C/R where C=const.)
1.0	2.747	11.0	2.944
2.0	2.725	12.0	2.974
3.0	2.696	13.0	3.034
4.0	2.699	14.0	3.034
5.0	2.705	15.0	3.067
6.0	2.725	16.0	3.104
7.0	2.725	17.0	3.115
8.0	2.768	19.0	3.158
9.0	2.824	21.0	3.192
10.0	2.892	23.0	3.222

From figure (3.2)

Result 1 : titre value for acid = 5.9 cc.
required titre value = 9.6 cc.

Result 2 : titre value for salt = 7.7 cc.

Hence, molecular weight of quinine sulphate =

$$\frac{0.1832 \times 10^3 \times 2}{7.7 \times 0.0425} = 1119$$

required molecular weight = 782

3.3.e. pH titration method :

Caustic soda solution was run in a known volume of standard oxalic acid solution (10 cc. of the standard oxalic acid solution diluted to a fixed volume of 250 cc. with distilled water) and the resulting pH of the solution was measured by a pH meter (Beckmann model H - 2). Table (3.03) gives the volumes of caustic soda solution added , the pH of the solution and the change in pH with change in volume of alkali added i.e. Δ pH / Δ V. The volume of the alkali at which Δ pH /ΔV shows a maximum value represented the titre value.

Table (3.04) gives the data for standardisation of sulphuric acid in the same way.

Next a mixture of a known weight of the alkaloid sulphate and a known volume of sulphuric acid (standardised as above) were diluted to the same fixed volume of 250 cc. with distilled water. Standard caustic soda solution (standardised as above) was run in and the resulting pH of the solution was measured . Two maxima for the values of Δ pH / Δ V , table (3.05),represented the titre values for the added acid and the alkaloid sulphate.

A number of such estimations were made of known mixture with varying amounts of the acid and the salt . It can be seen from the results , table (3.05), which represents a typical titration, that the titre value of

Table 3.03

Standardisation of NaOH solution by pH titration.

Strength of oxalic acid solution = 0.0514 N

Volume of oxalic acid solution taken = 10.0 cc.

Volume of NaOH solution added in cc.	pH	$\frac{\Delta pH}{\Delta V}$	Volume of NaOH solution added in cc.	pH	$\frac{\Delta pH}{\Delta V}$
10.0	5.2	-	10.8	7.15	0.47
10.2	5.4	0.10	10.9	7.70	0.55
10.4	5.7	0.15	11.0	8.50	0.80
10.6	6.2	0.25	11.1	9.0	0.25

Result : titre value obtained = 11.0 cc.

Hence, strength of NaOH solution $\frac{10.0 \times 0.0514 \text{ N}}{11.0}$ = 0.0467 N

Table 3.04

Standardisation of H_2SO_4 by pH titration.

Volume of sulphuric acid solution taken = 10.0 cc.

9.0	3.9	-	10.0	6.3	0.80
9.5	4.2	0.06	10.1	7.2	0.90
9.6	4.35	0.15	10.2	8.9	1.70
9.7	4.5	0.15	10.3	9.2	0.30
9.8	4.7	0.20	10.4	9.4	0.20

Result : titre value obtained = 10.2 cc.

Hence, strength of H_2SO_4

$$\frac{10.2 \times 0.0467 \text{ N}}{10.0} = 0.0477 \text{ N}$$

Table 3.05

Estimation of quinine sulphate and sulphuric acid in a mixture of the two by pH titration.

Weight of quinine sulphate taken = 0.1999 gms.
Volume of sulphuric acid added = 10.0 cc.
Strength of caustic soda solution = 0.0467 N

Vol. of NaOH added in cc.	pH	$\frac{\Delta pH}{\Delta V}$	Vol. of NaOH added in cc.	pH	$\frac{\Delta pH}{\Delta V}$
10.0	6.0	-	15.0	8.3	0.02
10.1	6.15	0.15	17.0	8.6	0.01
10.2	6.3	0.15	19.0	8.9	0.01
10.3	6.5	0.20	21.0	9.4	0.02
10.4	6.65	0.15	22.0	9.7	0.03
11.0	7.2	0.09	23.0	10.1	0.04
13.0	7.85	0.03	24.0	10.4	0.03

Result : (1) titre value obtained for H_2SO_4 = 10.3 cc.
titre value required = 10.2 cc.

(2) titre value for quinine sulphate = (23.0 cc. - 10.3 cc.)
= 12.7 cc.

Hence, molecular weight of quinine sulphate

$$\frac{0.1999 \times 10^3 \times 2}{12.7 \times 0.0467} = 674.1$$

Required molecular weight = 782

the free acid can be obtained fairly accurately (± 1 %) ; however the value of the concentration of the salt calculated from it's titre value was unsatisfactory.

Hence this method was not considered to be suitable for the estimation of the alkaloid sulphate in a mixture of the two .

3.4 Estimation of alkaloid sulphate in presence of sulphuric acid by ultra-violet absorption spectra :

3.4.a. Introduction :

Dobbie and Fox (1) studied the absorption spectra of quinine and reported three maxima at 1 /λ 3050, 1 /λ 3500 and 1 / λ 3750 . The hydrochlorides of quinine and 6-methoxy quinoline exhibited identical bands and those given by 0.01 N solution of the sulphate of these two differed only in the greater absorption of the former.

Manta (2) obtained the extinction curves of the following alkaloids in 0.001 N and 0.005 N alcoholic solutions : quinoline and p-methoxy lepidine, quinidine and quinine ; cinchonine and cinchonidine ; ethyl iodo-quinine and diiodo ethyl quinine. The pair of compounds showed nearly the same form of curve.

Heidt and Forbes (3) studied the absorption spectra from 20,000 to 45000 $cm.^{-1}$ and the fluorescence spectra of the bisulphates of cinchonine, cinchonidine, quinine,

quinidine etc. in 0.09 M sulphuric acid solution. The curves were shifted about 200 $cm.^{-1}$ to the ultra-violet when water was used as a solvent.

Fuchs and Kampitsch (4) determined the ultra-violet absorption spectra of pure quinine, cinchonine, quinidine and cinchonidine under different conditions and noted two absorption types. The aqueous and alcoholic solutions of the neutral salts corresponded to the type of the absorption spectra of their bases. The influence of the pH only appeared in the solutions of acid salts or in excess acid. The latter formed the second type of absorption spectra . In between were found the aqueous solutions of acid salts, which in alcoholic solution , corresponding to the lower pH concentration, showed a very similar spectrum to the base . In all the solvents examined, a distinct difference between the quinine and cinchonine spectra was noted.

Carol (6) studied the ultra-violet absorption curve of quinine in dilute hydrochloric acid. The location and magnitude of the 3 regions of maximum absorption were found to be : 250.5 mμ $\epsilon^{1\%}_{1cm.}$ 901 ; 318.0 mμ $\epsilon^{1\%}_{1cm.}$ 142 ; 347.5 mμ $\epsilon^{1\%}_{1cm.}$ 168 . The Beer-Lambert law was followed at each maxima. It was suggested that quinine could be determined directly at 347.5 mμ without separation since practically all alkaloids and synthetics exhibit negligible absorption in this region.

Beguiristain (7) found maximum absorption in the ultra-violet for solutions of quinine hydrochloride and progressively weaker absorptions for strychnine sulphate morphine hydrochloride, aconitine nitrate and atropine sulphate.

Stimson and Reuter (8) measured the ultra-violet spectra of the 4 common naturally occuring alkaloids in alcoholic solutions or alcoholic / hydrochloric acid solutions and some related compounds over a pH range 1 - 10 to facilitate the estimation of methoxy cinchona alkaloids. The melting points and crystal habits are also given for quinine, quinidine, cinchonidine, cinchonine and their dihydro derivatives. Other compounds studied were epiquinine, epiquinidine and totaquine.

The above indicates that the ultra-violet absorption spectra of cinchona alkaloids are significantly affected by the pH of the solution ; however, detailed data, of interest in the estimation of cinchona alkaloid sulphates in dilute aqueous or aqueous sulphuric acid solutions of different pH , are not available .

This section gives the study of the ultra-violet absorption spectra of the sulphates of four cinchona alkaloids (as $Q_2H_2SO_4 . nH_2O$, where Q denotes the alkaloid) quinine, quinidine, cinchonine and cinchonidine , in aqueous solution of pH about 1 to 7 , adjusted by the addition of sulphuric acid or sodium hydroxide at room temperature ($\sim 30^{\circ}C$):

3.4.b. Experimental :

Chemicals :

Quinine sulphate (Government Quinine Factory, Madras) was crystallised eight times from hot water. Quinidine sulphate (P.B. ; Howard, London) was crystallised three times from hot water. Cinchonine sulphate was prepared by dissolving cinchonine (pure crystals ; Riedel, Germany) in aqueous sulphuric acid and crystallising out the sulphate ; this was then crystallised twice from hot water. Cinchonidine sulphate (Fluka, A.G.Switzerland) was crystallised four times from hot water . Sulphuric acid and sodium hydroxide used were A.R.quality. Distilled water was used.

Solutions and procedure :

The stock solution of alkaloid sulphate was first prepared in distilled water and the concentration in gram equivalents per litre was evaluated by sulphate estimation (as barium sulphate). Measured portion of the stock solution was then suitably diluted with distilled water or aqueous sulphuric acid or aqueous sodium hydroxide and the pH of the solution measured with Beckmann Model H 2 pH meter. The ultra-violet absorption was studied with Beckmann Model DU spectrophotometer using 10 mm. matched quartz cells in the range 250 - 350 mμ. The values of the extinction coefficients, ϵ , were calculated by dividing the observed optical density by the concentration of the alkaloid sulphate in gram-equivalents per litre.

3.4.c. R E S U L T S :

Tables (3.06 to 3.15) give the ultra-violet absorption (values of ϵ and wave-length in $m\mu$) for quinine sulphate in aqueous solution of pH about 1 to 7, adjusted by the addition of sulphuric acid or sodium hydroxide.

Figure (3.3) gives the plot of ϵ against wave-length in $m\mu$ for quinine sulphate in aqueous solution of pH about 1 to 7 .

Tables (3.16 to 3.23) give the ultra-violet absorption (values of ϵ and wave-lengths in $m\mu$) for cinchonidine sulphate in aqueous solution of pH about 1 to 7, adjusted by the addition of sulphuric acid or sodium hydroxide.

Figure (3.4) gives the plot of ϵ against wave-length in $m\mu$ for cinchonidine sulphate in aqueous solution of pH about 1 to 7.

Tables (3.24 and 3.25) give the values of λ (in $m\mu$) and for the minima and maxima of ultra-violet absorption spectra (figures 3.3 and 3.4) of quinine sulphate and cinchonidine sulphate in aqueous solution of pH about 1 to 7 , adjusted by the addition of sulphuric acid or sodium hydroxide.

Tables (3.26 to 3.29) give the calculated optical density at the invarient wave-lengths and % variation in optical density at the invarient wave-lengths , for quinine sulphate and cinconidine sulphate.

Table (3.30) gives a summary of the values of λ and ϵ for the invarient points of ultra-violet absorption spectra (figures 3.3 and 3.4) of cinchona alkaloid sulphates in aqueous solutions of pH about 1 to 7, adjusted by addition of sulphuric acid or sodium hydroxide.

Table 3.06

Ultra-violet absorption of quinine sulphate solution.

pH = 7.1 Concentration = 0.1255 meq./litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	4343	276	3052	305	2288
252	3060	278	3099	310	2654
254	2494	280	3148	315	3307
256	2271	282	3139	320	3889
258	2247	284	3091	325	4207
260	2303	286	3036	330	4383
262	2374	288	2964	335	4136
264	2471	290	2893	340	3028
266	2581	292	2773	345	1753
268	2694	294	2637	350	916.4
270	2805	296	2486	355	462.2
272	2885	298	2351	-	-
274	2956	300	2255	-	-

Table 3.07

Ultra-violet absorption of quinine sulphate solution.

pH = 6.3 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	4446	276	3004	305	2303
252	3163	278	3084	310	2645
254	2550	280	3109	315	3323
256	2335	282	3099	320	3889
258	2263	284	3052	325	4207
260	2295	286	2988	330	4383
262	2343	288	2932	335	4160
264	2431	290	2845	340	3109
266	2550	292	2742	345	1817
268	2654	294	2629	350	948.2
270	2773	296	2486	355	494.1
272	2853	298	2351	-	-
274	2925	300	2255	-	-

Table 3.08

Ultra-violet absorption of quinine sulphate solution.

pH = 6.0 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	4742	274	2893	298	2327
252	3394	276	2964	300	2231
254	2789	278	3028	305	2279
256	2519	280	3052	310	2629
258	2383	282	3068	315	3292
260	2319	284	3004	320	3865
262	2335	286	2956	325	4168
264	2399	288	2893	330	4367
266	2510	290	2829	335	4128
268	2614	292	2733	340	3068
270	2726	294	2605	345	1817
272	2805	296	2455	350	964.2

Table 3.09

Ultra-violet absorption of quinine sulphate solution

pH = 5.2 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	5649	274	2829	298	2359
252	4081	276	2893	300	2279
254	3674	278	2973	305	2351
256	3211	280	3012	310	2710
258	2829	282	3004	315	3347
260	2590	284	2964	320	3889
262	2455	286	2925	325	4184
264	2414	288	2869	330	4351
266	2486	290	2805	335	4152
268	2581	292	2717	340	3163
270	2645	294	2605	345	1968
272	2733	296	2486	350	1148

Table 3.10

Ultra-violet absorption of quinine sulphate solution.

pH = 4.6 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
250	8925	276	2614	305	2526
252	7747	278	2694	310	2885
254	6710	280	2742	315	3474
256	5539	282	2742	320	3928
258	4367	284	2726	325	4160
260	3402	286	2710	330	4343
262	2742	288	2669	335	4207
264	2406	290	2654	340	3427
266	2327	292	2614	345	2446
268	2335	294	2550	350	1745
270	2391	296	2471	355	1307
272	2471	298	2406	-	-
274	2534	300	2374	-	-

Table 3.11

Ultra-violet absorption of quinine sulphate solution.

pH = 4.0 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
256	9324	280	2255	310	3180
258	6789	282	2295	315	3674
260	4654	284	2335	320	3945
262	3163	286	2367	325	4049
264	2343	288	2391	330	4224
266	1953	290	2423	335	4264
268	1880	292	2431	340	3824
270	1888	294	2446	345	3259
272	1960	296	2455	350	2742
274	2032	298	2478	360	1968
276	2119	300	2526	370	1203
278	2176	305	2773	-	-

Table 3.12

Ultra-violet absorption of quinine sulphate solution.

pH = 3.7 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
258	9005	284	1865	325	3928
260	5737	286	1929	330	4104
262	3419	288	2016	335	4287
264	2168	290	2112	340	4224
266	1578	292	2200	345	3977
268	1378	294	2295	350	3698
270	1362	296	2406	355	3355
272	1394	298	2519	360	2869
274	1458	300	2645	365	2364
276	1546	305	3012	370	1713
278	1617	310	3443	375	1212
280	1697	315	3849	-	-
282	1777	320	3968	-	-

Table 3.13

Ultra-violet absorption of quinine sulphate solution.

pH = 3.1 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
262	3793	286	1697	325	3913
264	2192	288	1817	330	4049
266	1427	290	1953	335	4327
268	1155	292	2087	340	4478
270	1068	294	2231	345	4471
272	1083	296	2399	350	4327
274	1140	298	2574	355	3985
276	1212	300	2749	360	3482
278	1299	305	3196	365	2805
280	1387	310	3651	370	2096
282	1482	315	3992	375	1490
284	1593	320	4033	380	996.1

Table 3.14

Ultra-violet absorption of quinine sulphate solution.

pH = 1.9 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
260	7188	284	1427	320	4064
262	3985	286	1553	325	3904
264	2192	288	1690	330	4009
266	1291	290	1857	335	4367
268	964.2	292	2024	340	4702
270	860.6	294	2208	345	4838
272	876.6	296	2431	350	4765
274	940.4	298	2629	355	4471
276	1004	300	2845	360	3873
278	1083	305	3362	365	3132
280	1177	310	3809	370	2343
282	1299	315	4120	-	-

Table 3.15

Ultra-violet absorption of quinine sulphate solution.

pH = 0.8 Concentration = 0.1255 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
258	11550	284	1394	325	3881
260	7314	286	1538	330	4009
262	4009	288	1673	335	4367
264	2192	290	1841	340	4686
266	1275	292	2016	345	4853
268	932.4	294	2208	350	4797
270	844.7	296	2406	355	4486
272	860.6	298	2622	360	3889
274	900.5	300	2836	365	3124
276	972.3	305	3362	370	2335
278	1060	310	3809	375	1617
280	1163	315	4120	380	1091
282	1275	320	4049	-	-

Table 3.16

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 6.6 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
250	1587	282	4409	307	3174
252	1681	284	4460	308	3027
254	1813	286	4482	309	2830
256	1996	288	4496	310	2639
258	2194	290	4504	311	2523
260	2398	292	4357	312	2545
262	2610	294	4175	313	2749
264	2647	296	3956	314	3078
266	3070	298	3707	315	3312
268	3291	300	3721	316	3218
270	3510	301	3817	317	2815
272	3721	302	3853	318	2311
274	3926	303	3578	319	1740
276	4095	304	3641	320	1316
278	4240	305	3473	325	380.2
280	4336	306	3327	330	256.0
-	-	-	-	335	219.4

Table 3.17

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 5.7 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	1608	284	4424	309	2902
252	1696	286	4445	310	2683
254	1828	288	4489	311	2581
256	1989	290	4467	312	2581
258	2186	292	4336	313	2807
260	2383	294	4190	314	3085
262	2595	296	3970	315	3334
264	2822	298	3715	316	3269
266	3063	300	3736	317	2866
268	3276	301	3846	318	2361
270	3487	302	3880	319	1821
272	3670	303	3823	320	1396
274	3890	304	3700	325	424.0
276	4072	305	3510	330	292.5
278	4219	306	3363	335	248.6
280	4314	307	3203	340	197.4
282	4387	308	3070	-	-

Table 3.18

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 4.7 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	1660	284	4130	309	3524
252	1711	286	4190	310	3363
254	1799	288	4278	311	3283
256	1901	290	4336	312	3327
258	2018	292	4278	313	3538
260	2149	294	4182	314	3853
262	2318	296	4065	315	4072
264	2500	298	3963	316	3979
266	2690	300	4058	317	3597
268	2888	301	4116	318	3070
270	3092	302	4255	319	2581
272	3290	303	4226	320	2157
274	3473	304	4130	325	1039
276	3656	305	4022	330	738.4
278	3809	306	3926	335	563.0
280	3941	307	3817	340	416.8
282	4035	308	3670	345	270.5

Table 3.19

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 4.3 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	1784	284	3619	309	4291
252	1776	286	3744	310	4190
254	1784	288	3904	311	4130
256	1769	290	4042	312	4190
258	1784	292	4102	313	4365
260	1813	294	4116	314	4620
262	1887	296	4153	315	4810
264	2025	298	4175	316	4760
266	2172	300	4343	317	4482
268	2325	301	4489	318	4087
270	2494	302	4584	319	3568
272	2690	303	4620	320	3166
274	2852	304	4592	325	1799
276	3042	305	4569	330	1279
278	3203	306	4519	335	950.4
280	3327	307	4460	340	665.3
282	3473	308	4379	345	460.6

Table 3.20

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 4.0 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ϵ	Wave-length in mμ	ϵ	Wave-length in mμ	ϵ
250	1806	284	3502	309	4569
252	1784	286	3619	310	4495
254	1769	288	3802	311	4401
256	1733	290	3963	312	4452
258	1679	292	4065	313	4635
260	1755	294	4168	314	4920
262	1799	296	4219	315	5059
264	1915	298	4278	316	5037
266	2047	300	4460	317	4774
268	2208	301	4635	318	4416
270	2369	302	4760	319	3933
272	2545	303	4825	320	3487
274	2719	304	4804	325	2047
276	2874	305	4782	330	1470
278	3056	306	4752	335	1082
280	3196	307	4717	340	745.7
282	3356	308	4657	345	431.4

Table 3.21

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 3.5 Concentration= 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave_length in mμ	ε	Wave-length in mμ	ε
250	1872	284	2866	309	5469
252	1740	286	3085	310	5448
254	1630	288	3334	311	5441
256	1491	290	3590	312	5491
258	1368	292	3831	313	5637
260	1279	294	4065	314	5828
262	1250	296	4291	315	5981
264	1279	298	4533	316	6046
266	1375	300	4841	317	5856
268	1477	301	5001	318	5578
270	1608	302	5154	319	5169
272	1755	303	5278	320	4788
274	1915	304	5411	325	3070
276	2091	305	5454	330	2186
278	2267	306	5441	335	1580
280	2442	307	5491	340	1111
282	2646	308	5491	345	702.0

Table 3.22

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 2.0 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	1931	284	2194	309	6682
252	1718	286	2486	310	6711
254	1506	288	2830	311	6756
256	1265	290	3188	312	6858
258	1009	292	3597	313	6974
260	804.2	294	3992	314	7150
262	687.3	296	4401	315	7224
264	606.8	298	4804	316	7290
266	665.3	300	5285	317	7209
268	716.4	301	5484	318	6974
270	818.9	302	5754	319	6616
272	935.8	303	5929	320	6207
274	1075	304	6112	325	4226
276	1257	305	6266	330	3012
278	1447	306	6397	335	2157
280	1660	307	6515	340	1499
282	1915	308	6616	345	950.4

Table 3.23

Ultra-violet absorption of cinchonidine sulphate solution.

pH = 1.3 Concentration = 0.1368 meq. / litre.

Wave-length in mμ	ε	Wave-length in mμ	ε	Wave-length in mμ	ε
250	1959	284	2194	309	6713
252	1733	286	2486	310	6763
254	1514	288	2830	311	6814
256	1279	290	3218	312	6916
258	1023	292	3597	313	7034
260	818.9	294	4006	314	7150
262	680.0	296	4416	315	7290
264	643.4	298	4841	316	7384
266	665.3	300	5300	317	7268
268	738.4	301	5520	318	7026
270	826.2	302	5761	319	6705
272	943.2	303	5967	320	6302
274	1075	304	6179	325	4255
276	1257	305	6317	330	3034
278	1447	306	6471	335	2186
280	1660	307	6588	340	1521
282	1915	308	6668	345	965.1

T A B L E - 3.25

Values of λ (in mμ) and ϵ for the minima and maxima of ultra-violet absorption spectra (figure 3.4) of cinchonidine sulphate in aqueous solution of pH about 1 to 7 , adjusted by the addition of sulphuric acid or sodium hydroxide , at room temperature ($\sim 30^{\circ}C$).
(λN and λX stand for the wave-lengths in mμ for minima and maxima respectively)

pH	λN	$\epsilon/10$	λX	$\epsilon/10$	λN	$\epsilon/10$	λX	$\epsilon/10$	λN	$\epsilon/10$	λX	$\epsilon/10$
6.6	-	-	289	452	299	360	301.5	387	311.5	250	315.5	332
5.7	-	-	289	452	299	365	301.5	390	311.5	253	315.5	335
4.7	-	-	290	433	299	392	302.5	428	311.5	323	315.5	410
4.3	-	-	-	-	-	-	303	462	311.5	410	315.5	485
4.0	258	168	-	-	-	-	303	483	311.5	438	315.5	510
3.5	262	125	-	-	-	-	-	-	-	-	316	605
2.0	264	62	-	-	-	-	-	-	-	-	316.5	730
1.3	264	60	-	-	-	-	-	-	-	-	316.5	740

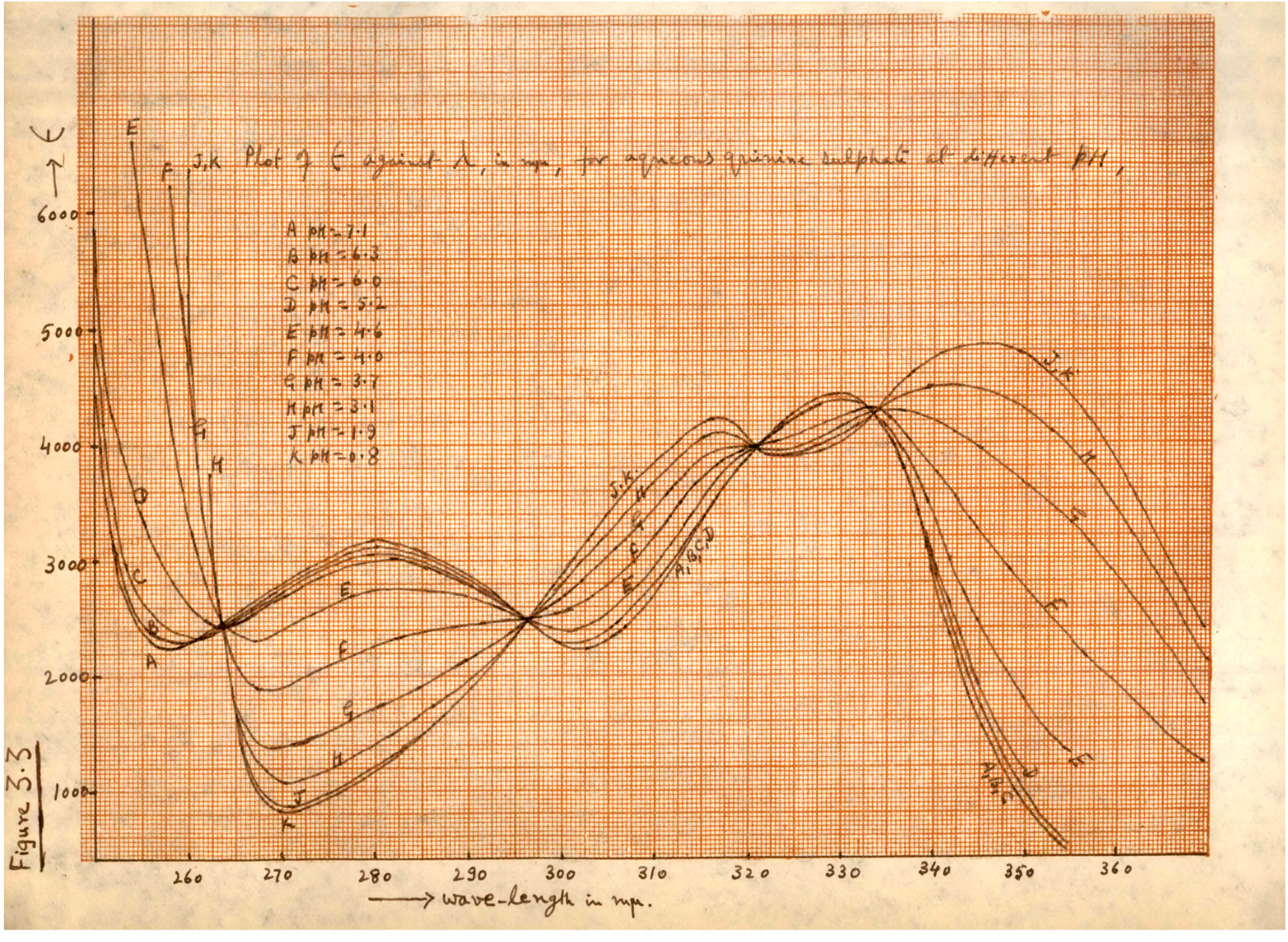
Plot of ε against λ, in mμ, for aqueous quinine sulphate at different pH,
A pH = 7·1
B pH = 6·3
C pH = 6·0
D pH = 5·2
E pH = 4·6
F pH = 4·0
G pH = 3·7
H pH = 3·1
J pH = 1·9
K pH = 0·8
ε
6000
5000
4000
3000
2000
1000
260
270
280
290
300
310
320
330
340
350
360
wave-length in mμ.

Figure 3.3

T A B L E - 3.24

Value of λ (in mμ) and ϵ for the minima and maxima of ultra-violet absorption spectra (figure 3.3) of quinine sulphate in aqueous solution of pH about 1 to 7, adjusted by the addition of sulphuric acid or sodium hydroxide, at room temperature ($\sim 30^{\circ}C$).
(λ_N and λ_X stand for the wave-lengths in mμ for minima and maxima respectively).

pH	λ_N	$\epsilon/10$	λ_X	$\epsilon/10$	λ_N	$\epsilon/10$	λ_X	$\epsilon/10$	λ_N	$\epsilon/10$	λ_X	$\epsilon/10$
7.1	257	224	281	316	301	220	-	-	--	-	330	438
6.3	257	226	281	312	301	220	-	-	-	-	330	438
6.0	261	232	281	306	301	220	-	-	-	-	330	435
5.2	263	238	281	300	301	224	-	-	-	-	330	435
4.6	267	230	282	274	301	236	-	-	-	-	331	440
4.0	269	186	-	-	-	-	-	-	-	-	334	432
3.7	269	134	-	-	-	-	318	396	325	392	336	430
3.1	270	106	-	-	-	-	318	410	324	388	343	450
1.9	271	84	-	-	-	-	318	422	324	388	346	486
0.8	271	82	-	-	-	-	318	422	324	388	346	488

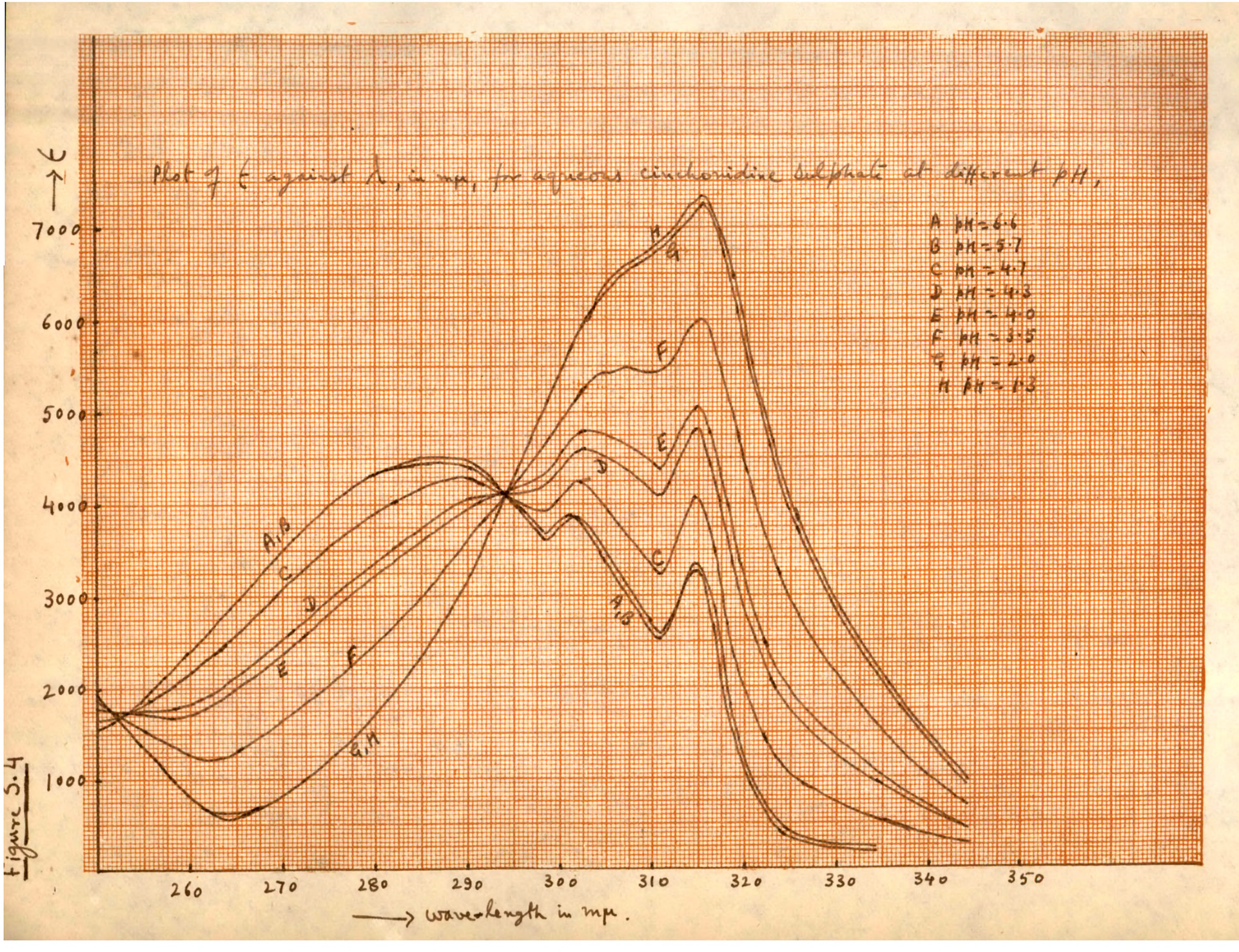
Plot of ε against λ, in mμ, for aqueous cinchoridine sulphate at different pH,
A pH = 6·6
B pH = 5·7
C pH = 4·7
D pH = 4·3
E pH = 4·0
F pH = 3·5
G pH = 2·0
H pH = 1·3
ε
7000
6000
5000
4000
3000
2000
1000
260
270
280
290
300
310
320
330
340
350
wavelength in mμ.
A,B
C
D
E
F
G,H
A,B
C
D
E
F
G,H

Figure 5.4

Table 3.26

Alkaloid salt : Quinine sulphate

Evaluation of invarient point :

Table No.	pH	Optical Density at (1) λ 296 mμ	Optical Density at (2) λ 298 mμ	Difference of (1) and (2)	Calculated Optical Density at λ 296.5 mμ
3.06	7.1	0.312	0.295	0.017	0.308
3.07	6.3	0.312	0.295	0.017	0.308
3.08	6.0	0.308	0.292	0.016	0.304
3.09	5.2	0.312	0.296	0.016	0.308
3.10	4.6	0.310	0.302	0.008	0.308
3.11	4.0	0.308	0.311	0.003	0.309
3.12	3.7	0.302	0.316	0.014	0.306
3.13	3.1	0.301	0.323	0.022	0.307
3.14	1.9	0.305	0.330	0.025	0.311
3.15	0.8	0.302	0.329	0.027	0.309

Average optical density at λ 296.5 mμ = 0.308

Value of ε at λ 296.5 mμ = 2452

Variation in optical density at λ 296.5 mμ = 0.007

% Variation in optical density at λ 296.5 mμ = ± 1.1 %

Table 3.27

Alkaloid salt : Quinine sulphate

Evaluation of the invarient point :

Table No.	pH	Optical Density at (1) λ 320 mμ	(2) λ 325 mμ	Difference of (1) and (2)	Calculated Optical Density at λ 321.5 mμ
3.06	7.1	0.488	0.528	0.040	0.496
3.07	6.3	0.488	0.528	0.040	0.496
3.08	6.0	0.485	0.523	0.038	0.493
3.09	5.2	0.488	0.525	0.037	0.495
3.10	4.6	0.493	0.522	0.029	0.499
3.11	4.0	0.495	0.508	0.013	0.498
3.12	3.7	0.498	0.493	0.005	0.497
3.13	3.1	0.506	0.491	0.015	0.503
3.14	1.9	0.510	0.490	0.020	0.506
3.15	0.8	0.508	0.487	0.021	0.504

Average optical density at λ 321 mμ = 0.499

Value of ε at λ 321 mμ = 3974

Variation in optical density at λ 321 mμ = 0.013

% Variation in opitcal density at λ321 mμ = ± 1.3 %

Table 3.28

Alkaloid salt : Quinine sulphate

Evaluation of the invarient point :

Table No.	pH	Optical Density at (1) λ330 mμ	(2) λ335 mμ	Difference of (1) and (2)	Calculated Optical Density at λ334 mμ
3.06	7.1	0.550	0.519	0.031	0.525
3.07	6.3	0.550	0.522	0.028	0.527
3.08	6.0	0.548	0.518	0.030	0.524
3.09	5.2	0.546	0.521	0.025	0.526
3.10	4.6	0.545	0.528	0.017	0.531
3.11	4.0	0.530	0.535	0.005	0.534
3.12	3.7	0.515	0.538	0.023	0.533
3.13	3.1	0.508	0.543	0.035	0.536
3.14	1.9	0.503	0.548	0.045	0.539
3.15	0.8	0.503	0.548	0.045	0.539

Average optical density at λ334 mμ = 0.531

Value of ϵ at λ334 mμ = 4235

Variation in optical density at λ334 mμ = 0.015

% Variation in optical density at λ334 mμ = ± 1.4 %

Table 3.29

Alkaloid salt : Cinchonidine sulphate

Evaluation of the invarient point :

Table No.	pH	Optical Density at (1) λ294 mμ	(a) λ296 mμ	Difference of (1) and (2)	Calculated Optical Density at λ 294.5 mμ
3.16	6.6	0.571	0.541	0.030	0.5635
3.17	5.7	0.573	0.543	0.030	0.5655
3.18	4.7	0.572	0.556	0.016	0.568
3.19	4.3	0.563	0.568	0.005	0.564
3.20	4.0	0.566	0.577	0.011	0.569
3.21	3.5	0.556	0.587	0.031	0.564
3.22	2.0	0.546	0.602	0.056	0.560
3.23	1.3	0.548	0.604	0.056	0.562

Average optical density at λ 294.5 mμ = 0.564

Value of ε at λ 294.5 mμ = 4128

Variation in optical density at λ 294.5 mμ = 0.009

% Variation in optical density at λ 294.5 mμ = ± 0.8 %

Table 3.30

Values of λ and ϵ for the invarient points of ultra-violet absorption spectra (figures 3.3 and 3.4) of cinchona alkaloid sulphates in aqueous solutions of pH about 1 to 7 , adjusted by the addition of sulphuric acid or sodium hydroxide, at room temperature ($\sim 30^{0}$C).

Alkaloid Salt	Wave-length in mμ	ϵ	
Quinine sulphate	296.5	2452	± 1.1 %
	321.0	3974	± 1.3 %
	334.0	4235	± 1.4 %
Quinidine sulphate*	296.5	2698	± 1.0 %
	320.5	4434	± 0.5 %
	334.0	4733	± 1.4 %
Cinchonine sulphate*	294.5	4289	± 1.0 %
Cinchonidine sulphate	294.5	4128	± 0.8 %

* Data for quinidine sulphate and cinchonine sulphate are from unpublished work of Shri. R. S. Shah of this laboratory.

3.4.d. Discussion :

The data (tables 3.24 and 3.25) together with the data of unpublished work of Shri R.S.Shah of this laboratory, indicate that the ultra-violet absorption spectra of each of the alkaloid sulphates can be, broadly divided into three groups : (a) pH 7 - 4.5 , (b) pH 4.5 - 3.5 and (c) pH 3.5 - 1.0 . The spectra of quinine and quinidine sulphates are similar but not the same ; the same applies to those of cinchonine and cinchonidine sulphates. The spectra of quinine and quinidine sulphates are distinctly different from those of cinchonine and cinchonidine sulphates.

For quinine and quinidine sulphates there are three invaient points, (tables 3.26 to 3.28 and 3.30) and for cinchonine and cinchonidine sulphates, there is one invarient point, (tables 3.29 and 3.30) where the extinction coefficient , ϵ , is independent of pH within $\pm$ 1.0 to 1.5 %.

These data (tables 3.24, 3.25 and 3.30) can permit the estimation of one alkaloid sulphate in dilute aqueous solution, in presence of sulphuric acid or in the absbsence of presence of other alkaloid sulphates studied, by suitable choice of experimental conditions.

REFERENCES :

1. Dobbi, J.J. and Fox, J.J., Chem.Abst., 6, 1284 (1912) .

2. Manta, I.Z. Physik.Chem., B 22 , 465 (1933).

3. Heidt, L.J. and Forbes, G.S., J.Am. Chem.Soc., 55, 2701 (1933).

4. Fuchs, L and Kampitsch, A., Chem.Abst., 30, 570 (1936) .

5. Arkel, C.G. and Wielen, P., Chem.Abst., 32, 1862 (1938).

6. Carol, J., J.Assoc. off.Agr. Chem., 26, 238 (1943) .

7. Beguiristain, J.M.B., Chem.Abst., 37, 3560 (1943) .

8. Stimson, M.M., and Reuter, M.A., J.Am. Chem.Soc., 68, 1192 (1946).