STUDIES OF THE EFFECT OF ZETA POTENTIAL VARIATION ON SEDIMENTATION OF FLOCCULATED SUSPENSIONS IN INTERMEDIATE CONCENTRATION RANGE

by

PAKDEE POTHISIRI

A thesis submitted in partial fulfillment of the
requirements for the degree of

MASTER OF SCIENCE

Pharmacy
(Pharmaceutics)

at the

UNIVERSITY OF WISCONSIN

1972

ACKNOWLEDGEMENTS

I wish to take the liberty of expressing my deepest gratitude to Dr. Jens T. Carstensen, for his help, guidance and tolerance throughout the course of this study. The interest shown by him in even the most trivial of the problems encountered by me has provided a key source of motivation. His encouragement and his genuine interest have been crucial from the very inception of my graduate career.

I also gratefully acknowledge the financial support rendered by the Civil Service Commission of Thailand.

TABLE OF CONTENTS

Page

INTRODUCTION AND LITERATURE SURVEY

EXPERIMENTAL

RESULTS AND DISCUSSION

INTRODUCTION

For very dilute deflocculated suspensions the sedimentation rate of dispersed particles can be described by using Stokes' law (1).

$$V = \frac{2}{9}\,\frac{a^2(\Delta\rho)g}{\eta} \qquad (1)$$

where (V) is the steady state velocity of the settling particles, and the other symbols have their usual meaning. As proceeding to the more concentrated system or even dilute flocculated suspension, there appears to be some deviation from the above equation. Kynch (2) pointed out that a satisfactory theory of sedimentation of multiparticle coarse suspension has never been put forth. Although the settling rate constant may be varied by the reciprocal of viscosity and gravitational forces, nevertheless, Higuchi (3) and Hiestand (4) have shown that both in peptized and flocculated systems such a simple point of view is in agreement with neither theory nor fact.

In the last two decades, sedimentation of flocculated suspensions had been carefully studied (2-14), unfortunately, most of the cited references (2,5-8) attempt to modify Stokes' law to explain experimental data. In fact the more dilute a suspension is, the more closely should the fall of each particle adhere to Stokes' law.

Pharmaceutical suspensions are, however, rarely very dilute, and their behavior would not be expected to fall into this category.

In the works of Benedict, et al. (8), Michael and Bolger (10) and Carstensen and Su (14,15), the following pattern for the sedimentation of intermediate concentration suspensions was observed: as one lets the suspension stand undisturbed, the interface or sedimentation boundary moves downwards with greater and greater velocity until a certain critical height, H_o, is reached at which time (t_o) the rate decreases abruptly. The huge difference in the ratio between the first and second period suggests different settling mechanisms.

Robinson (7) considered the sediment to be uniform at all times and of increasing concentration during the descent of the boundary. However, Gaudin and Fuerstenau (13), by the aid of X-ray density data, have demonstrated that the density of the sediment remains constant at and for some (time dependent) distance below the initial boundary, with a compact body of higher density building up at the bottom of the container, and that therefore the system is uniform at time zero only.

During the first stage, sedimentation is primarily governed by the gravitational and frictional forces rather than electrical forces, as had been described by some references (3,7,10). Nonetheless, the electrical forces have been shown to be responsible for the stability of the floc-aggregate body (16) which will become obvious later.

Michael and Bolger (10) have shown that the basic flow units of flocculated suspensions are not the primary particles but are small clusters of particles (plus enclosed water), herein called flocs. The most probable flocs shape is a sphere because the flocs are originally formed under the severe agitation of a Waring blender. Formation of flocs seems to be very similar to that of agglomeration process in colloidal systems. Particles, dispersed in aqueous medium, with a high net charge density exhibit electrostatic forces of repulsion. When the forces of repulsion are greater than those of attraction, the particles remain apart. Overbeek (17) observed that the addition of electrolytes decreased the density of the ionic atmosphere surrounding the particles and causes the forces of repulsion to be effective only a shorter distance from the particle. Thus, when the magnitude of London-van der Waals attraction forces exceeds that of the electrostatic repulsion forces, the particles come together, this type of particle interaction produces flocculation. On the other hand, the floc-aggregate body grows by collision, break down by shear forces, and are able to form the extended networks which give the suspensions their structural properties.

With regard to the mathematical treatment of the sedimentation, Egolf and Mc Cabe (18) suggested a phenomenological log-log relationship between absolute height and time for the phase following the initial settling.

Ward and Kammemeyer (9) tested the model in different types of systems (carbonates, silicates and magnesium oxide) and found fair agreement with respect to the shape of curves, but large (20-40%) quantitative deviation in the second phase of sedimentation.

Most recently, in the works of Carstensen and Su (14, 15) the mathematical approach was improved. By considering the sedimentation to be composed of two phases and each phase subjected to be treated separately. The approach taken by them is to account for the forces involved, even though all of them could not be expressed explicitly, and thus, lead to the following conclusion.

For the first phase, the height of sediment (x) will be a function dependence of time (t) and can be expressed as [$x = \underline{a} + \underline{b}$] provided that a diminishes at the expense of b when the time goes by. The decrease in a-value may be considered to be of the form,

$$a = x_o e^{-kt} \qquad (2)$$

and the height of cake (b) experiences an increase at the expense of a and a decrease due to (exponential) contraction:

$$\frac{db}{dt} = - w_1 \cdot b \qquad (3)$$

where w_1 is the first phase contraction rate constant.

After grouping, rearranging and integration, the equation to be fitted for graph plotting is:

$$\text{Log}\left(\frac{x - x_o e^{-kt}}{1 - e^{-kt}}\right) = -\frac{w_1}{2.3} \cdot t + \text{Log } C \qquad (4)$$

With the proper k-value, by using the iteration computerized procedure, linearity prevails to within 15 cm of critical height. The k-value is inversely proportional to viscosity of the system and is speculated to be related to floc formation rate constant.

For the sedimentation below the critical height, however, the rate would change and be much slower. The forces exerted on the sediment are gravitational forces, frictional and reactional forces, and forces that are electrical in nature. The gravitational force has a magnitude of $M[1 - \rho_o/\rho]g$ where ρ and ρ_o are densities of solid and liquid, $\underline{M}$ is mass of the sediment, and $\underline{g}$ is the gravitational acceleration. The frictional and reactional forces must be related to the viscosity and the wall effect (i.e., to the geometry of the vessel), and can be described as a velocity dependent $[-B(\eta, R)\, dy/dt]$ and a velocity independent $[-\Psi(R)]$ component. The electrical force is assumed to be a repulsion, and with regard to magnitude it is assumed to increase the closer the floc-aggregates are to one another, they are assumed to be of the form $[\theta y]$. The sum of all the forces thus equals the mass of the sediment times its acceleration, i.e.,

$$M[1 - \rho_0/\rho]g - B(\eta,R)\,\frac{dy}{dt} - \psi(R) - \theta y \;=\; M\,\frac{d^2y}{dt^2} \qquad (5)$$

By inserting the appropriate solution into the above homogeneous differential equation, one may obtain the characteristic roots as,

$$w \;=\; \frac{B(\eta,R)}{2M} \pm \quad [\frac{B(\eta,R)}{2M}]^2 - \frac{\theta}{M} \qquad (6)$$

The roots may be simplified if $\frac{B(\eta,R)}{M} >> \frac{\theta}{B(\eta,R)}$ which yields,

$$w_1 \;=\; \frac{B(\eta,R)}{M} \qquad (7)$$

$$w_2 \;=\; \frac{\theta}{B(\eta,R)} \qquad (8)$$

Upon rearranging and integration, the sedimentation of the second phase then assumes the biexponential relation of the form,

$$(x - H_\infty) \;=\; A_1e^{-w_1\tau} + A_2e^{-w_2\tau} \qquad (9)$$

where $\underline{w_1}$ and $\underline{w_2}$ have the meaning signified above (w_2 is, however, the so-called contraction rate constant of the second phase). $\underline{w_1}$ was shown to be the same here as in equation (3) (15), and its magnitude is higher than $\underline{w_2}$.

As t gets bigger the first term on the right hand will become vanishingly small and the equation takes the form of,

$$\log (x - H_{\infty}) = -\frac{w_2}{2.3} \cdot \tau + \log A_2 \qquad (10)$$

From this relation, it can be realized at once that the nature of the final phase sedimentation should be predominantly governed by the electrical forces of the system in terms of the w_2-function. Based on this assumption, one might think about sedimentation of the flocculated suspension under normal gravity as compressing the sack of marbles. Comparatively small forces can compress the sack until the marbles are randomly closely packed. Unlike the marbles, however, the floc aggregates can repel one another by interparticular forces and prevent them from tumbling into a closed packed array of their own accord, except they are forced in by the weight of overlying solid. Aside from mechanical factors, ultimate height, H_{∞}, which corresponds to the final volume of cake in flocculated suspensions would be influenced by the electrostatic repulsions forces also. Combining both factors, of course, one would expect the ultimate height (H_{∞}) of the sediment to be a function (will be discussed in detail later) of the form,

$$H_{\infty} = \Phi[\theta, B(\eta, R)] \qquad (11)$$

Since the particle double layer potentials, responsible for the repulsive interaction, are related to the Zeta-potential of the system (19), varying of the Zeta-potential of flocculated suspension would have some influence on the sedimentation behavior, and also on the final height (H_∞) of the cake as well.

From a pharmaceutical point of view, it is important to determine the pattern and predict the ultimate height (H_∞) of suspension sedimentation.

It is one of the objectives of this study to establish the graphical means describing the influence of Zeta-potential on the flocculation constant of the early phase prior to the critical height. Another objective is to attempt to find the dependence of the ultimate height and the rate constant of the second phase sedimentation upon the Zeta-potential of the flocculated suspension in the intermediate concentration range.

EXPERIMENTAL

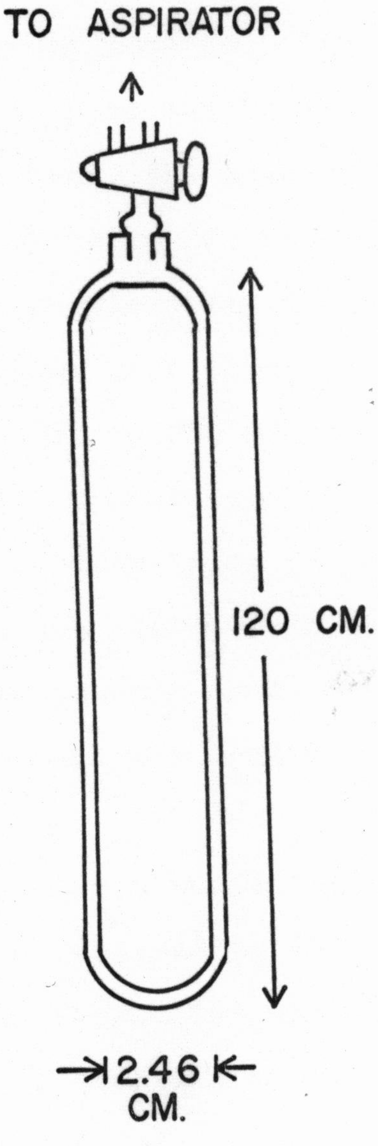
Materials

5 u Min-u-Sil was obtained from Pennsylvania Glass and Sand Corp. and purified by HCl-wash as described shortly. Min-u-Sil is an air separated natural silica; the maximum size particle is 5 µ in long dimension, and the average size is 1 µ (20); the size distribution is quite narrow. Calcium carbonate precipitated was U.S.P. grade, and obtained from Diamond Shamrock Chem. and not purified further. The rest of the chemicals (i.e., sodium chloride, calcium chloride and methyl p-hydroxy benzoate) were analytical reagent grade and obtained from Mallinckrodt Chemical Works. It should be noted here that $CaCl_2 \cdot 2H_2O$ (granular) was used in the experiments instead of $CaCl_2$ (anhydrous) but the final concentration used was calculated based on anhydrous calcium chloride.

Apparatus

For the sedimentation of suspensions at high concentration, air entrapment might be a source of variation (10), and an apparatus set-up such as shown in the picture (Figure 1) has been used throughout the experiment.

Figure 1. Sedimentation Apparatus.


TO ASPIRATOR
120 CM.
2.46 CM.

Methods

All the suspensions were made under high shear rate by using a Waring blender in order to obtain a relatively uniform size of floc-aggregates. Preventing the variation in initial settling (which may be due to the initial turbulence) is important, the method of providing a uniform starting suspension has been used by turning the suspension tube end-over-end ten times for each experiment.

One of the systems used here was a concentrated suspension of Min-u-Sil in 25% w/v concentration.

Several batches of this product were tested and reproducibility of sedimentation patterns were only possible by washing the silica with diluted hydrochloric acid. The following general procedure gave reproducible sedimentation curves and was used for all the experiments with Min-u-Sil.

121 gm of silica were suspended in doubly distilled water and the volume adjusted to 485 ml with doubly distilled water; the suspension was sheared for five minutes in a Waring blender, 1 cc of concentrated hydrochloric acid was added and the suspension left in a sedimentation tube for 12 hours. The supernatant was then siphoned off, and 500 cc of doubly distilled water added, the suspension shaken, left for 12 hours, the supernatant siphoned off, etc. until the silica has been washed five times. After the last decantation, the suspension was brought up to a volume of 484 cc with

doubly distilled water and 242 cc of 0.1% w/v aqueous methyl p-hydroxy benzoate solution, so that the solution was 0.05% with respect to preservative.

The preservative was incorporated due to the long periods (3 months) necessary to attain final heights. The system could not be tested at zero percent electrolyte concentration since a clear interface is not formed; small amount of sodium and calcium chloride, however, leave the supernatant clear. These two substances were used to adjust Zeta potential.

Suspensions of $CaCO_3$ were used in another experiment. Various concentrations of $CaCO_3$ in the range of 5% to 25% w/v concentration were preliminarily tested and the 7.5% w/v concentration of calcium carbonate suspension was found to be in an intermediate concentration range. The procedure of preparation was similar to that of Min-u-Sil suspension except no concentrated hydrochloric acid was added. 34.9 gm of calcium carbonate were again suspended in doubly distilled water and the total volume was adjusted to 465 cc; calcium carbonate then was washed by doubly distilled water five times following the same method as previously described. Methyl p-hydroxy benzoate was also employed as a preservative in this system at the same concentration.

In both systems, the final suspensions were thoroughly deaerated by applying aspirator vacuum to one of the outlets of the two-way stopcock (Figure 1). The tube was occasionally turned end-over-end, and finally after no more visible escape of air, the tube was turned end-over-end ten times, then opened to the atmosphere and placed vertically; the movement of the interface was followed by use of a high precision cathetometer[1] and an electric timer. The set-up of the sedimentation tube was such that the bottom positions appeared at the same mark on the cathetometer at all times.

All experiments were carried out in a constant-temperature room ($24\pm0.5^{\circ}$).

All the preliminary sedimentation curves obtained were reproducible. Incorporations of electrolytes of various concentrations were accomplished through substitution of supernatant. A calculated volume of supernatant was withdrawn and replaced by the same volume of electrolyte solution (in 0.05% aqueous methyl p-hydroxy benzoate solution) that would give the desired concentration.

The Zeta-potential of the system was checked with a Zeta-meter[2] (and in the case of Min-u-Sil with a Numinco Electrophoretic Mass Transport Analyzer[3]). In measuring the

---

[1] Gaertner Scientific Corp., Chicago, Ill.

[2] Produced by Zeta-Meter, Inc., 1720 First Avenue, New York, N.Y. 10028.

[3] Produced by Numinco-Numec Instruments and Controls Corp., 300 Seco Road, Monroeville, Pa. 15146.

Table I

Amount of electrolytes consumed in sedimentation study of Min-u-Sil suspension

Number of run	Electrolyte	Concentration of solution (%)	Amount of solution used (cc)	Final concentration in suspension (mM)
1	NaCl	1	1.42	0.50
2	NaCl	1	4.83	1.00
3	$CaCl_2 \cdot 2H_2O$	1	5.35	0.75 ($CaCl_2$)
4	$CaCl_2 \cdot 2H_2O$	1	10.70	1.50 ($CaCl_2$)
5	$CaCl_2 \cdot 2H_2O$	5	4.28	3.00 ($CaCl_2$)

Table II

Amount of electrolytes consumed in sedimentation study of calcium carbonate suspension

Number of run	Electrolyte	Concentration of solution (%)	Amount of solution used (cc)	Final concentration in suspension (ppm)
1	NaCl	1	1.16	25
2	$CaCl_2 \cdot 2H_2O$	1	3.08	50 ($CaCl_2$)
3	$CaCl_2 \cdot 2H_2O$	2	3.08	100 ($CaCl_2$)
4	$CaCl_2 \cdot 2H_2O$	2	6.15	200 ($CaCl_2$)
5	$CaCl_2 \cdot 2H_2O$	5	9.85	800 ($CaCl_2$)

ζ-potential of the system by using Zeta-meter, the operating instruction (21) was strictly followed. Very diluted suspension of both substances (0.1% w/v concentration Min-u-Sil, $CaCO_3$) were prepared each at a time, following the same procedure as used in preparing the tested system. Appropriate concentrations of electrolytes were added to the system, then each one of them was analyzed separately under the Zeta-meter.

RESULTS AND DISCUSSION

Table III

Sedimentation Data of Min-u-Sil Suspension at Various Concentrations of Electrolytes

NaCl 0.5×10^{-3} M		NaCl 1.0×10^{-3} M		$CaCl_2$ 0.75×10^{-3} M		$CaCl_2$ 1.5×10^{-3} M		$CaCl_2$ 3.0×10^{-3} M	
Height (cm)	Time (hr)	Height (cm)	Time (hr)	Height (cm)	Time (hr)	Height (cm)	Time (hr)	Height (cm)	Time (hr)
95.240	0.00	95.500	0.00	97.375	0.00	96.700	0.00	96.635	0.00
94.520	0.50	94.960	0.50	96.610	0.50	96.200	0.50	96.245	0.50
93.920	1.00	94.590	1.00	96.155	1.00	95.775	1.00	95.835	1.05
93.355	1.50	94.250	1.50	94.990	2.00	94.995	2.00	95.115	2.15
92.820	2.00	93.875	2.00	93.900	3.35	94.535	2.50	94.610	3.02
91.845	3.00	93.290	3.00	81.775	18.79	94.290	3.06	83.985	21.15
89.740	5.20	83.650	23.00	78.165	24.40	89.990	9.33	77.935	32.82
84.015	11.15	80.240	29.50	74.480	30.46	82.300	21.92	65.690	56.80
76.010	22.90	71.200	48.28	59.950	57.52	76.160	31.42	58.740	71.24
70.205	34.60	67.850	55.50	53.800	69.97	63.525	54.92	49.190	93.05
62.400	59.50	63.050	70.68	44.025	93.48	44.660	94.70	47.420	97.57
52.320	83.80	55.240	82.83	34.310	118.12	30.675	141.91	36.705	129.65
33.025	130.10	37.450	125.40	27.530	174.93	28.110	183.00	29.325	185.10
24.870	150.70	24.530	173.40	25.165	235.04	26.204	214.60	26.574	214.75
24.357	171.32	23.167	228.45	24.087	283.73	25.594	230.60	24.916	225.25
23.656	215.46	22.682	245.91	23.450	331.06	24.981	249.06	24.246	246.58
22.968	268.70	22.226	289.10	23.190	368.90	24.185	288.25	24.000	261.25
22.455	347.55	21.442	258.97	22.665	415.33	23.450	360.16	23.820	299.87
21.930	392.18	20.500	332.42						

Table IV

Sedimentation Data of Second Phase for High Value of t when w_2 is the Predominant Term

Height (x)	$(x - H_\infty)$	$\mathrm{Log}(x - H_\infty)$	Time (t_x)	$\tau = (t_x - t_o)$
26.370	-	-	136.50	-
24.870	2.940	.468	150.70	14.20
24.357	2.427	.335	171.32	34.82
23.656	1.726	.212	215.46	78.96
22.968	1.038	.016	268.70	132.20
22.455	0.525	- .280	347.55	211.05
21.930	-	-	-	-
26.500	-	-	153.20	-
24.530	4.030	.605	173.40	20.20
23.167	2.667	.426	228.45	75.25
22.682	2.182	.339	245.91	92.71
22.226	1.726	.212	289.10	135.90
21.442	0.942	- .026	258.97	205.77
20.500	-	-	-	-
30,425	-	-	136.40	-
27.530	4.865	.687	174.93	38.53
25.165	2.500	.398	235.04	98.64
24.087	1.422	.153	283.73	147.33
23.450	.785	- .105	331.06	194.66
23.190	.525	- .280	368.90	232.50
22.665	-	-	-	-
31.400	-	-	132.10	-
28.110	4.660	.668	188.00	55.90
26.204	2.754	.440	214.60	82.50
25.594	2.144	.331	230.60	98.50
24.981	1.531	.185	249.06	116.96
24.185	.735	- .133	288.25	156.15
23.450	-	-	-	-
31.500	-	-	146.00	-
29.325	5.505	.740	185.10	44.10
26.574	2.754	.248	214.75	68.75
24.916	1.096	.040	225.25	79.25
24.246	.426	- .371	246.58	100.58
24.000	.180	- .744	261.25	120.25
23.820	-	-	-	-

Table V

Sedimentation Parameters at Various ζ-Potentials

Electrolyte	Concentration (mM)	ζ-Potential (mV)	Sedimentation Rate Constants (hr^{-1}) k	w_1	w_2	Final Height H_∞ (cm)
$CaCl_2$	3.00	-12.0	0.052	0.065	0.0450	23.820
$CaCl_2$	1.50	-14.5	0.065	0.070	0.0186	23.450
$CaCl_2$	0.75	-18.3	0.08	0.075	0.0116	22.665
NaCl	0.5	-38.1	0.125	0.056	0.0089	21.930
NaCl	1.0	-40.0	0.132	0.064	0.0080	20.500
NaCl	2.5	-40.0	0.132	0.064	0.0080	20.555

Table VII

Sedimentation Data of Second Phase for High Value of t when w_2 is the Predominant Term

Height (**X**)	$(X - H_\infty)$	$\log(x - H_\infty)$ + 1.5000	Time (t_x)	$\tau = (t_x - t_o)$
66.755	-	-	58.01	-
66.000	2.110	1.8243	89.30	31.29
64.982	1.092	1.5381	138.77	80.29
64.535	.645	1.3096	170.57	112.56
64.283	.393	1.0947	190.00	131.99
64.165	.275	.9394	211.41	153.40
63.890	-	-	-	-
67.190	-	-	56.90	-
66.831	.976	1.4893	94.58	32.68
66.340	.485	1.1856	129.58	72.68
66.161	.306	.9862	153.66	96.76
66.124	.269	.9302	160.33	103.43
66.025	.170	.7305	187.45	130.55
65.855	-	-	-	-
68.825	-	-	55.15	-
68.790	.560	1.2475	82.56	27.41
68.510	.280	.9480	109.06	53.91
68.431	.201	.8030	120.31	65.16
68.387	.157	.6969	135.81	80.66
68.310	.080	.4030	161.56	106.41
68.230	-	-	-	-
69.650	-	-	53.75	-
69.280	.560	1.2482	98.47	44.72
69.055	.335	1.0252	116.39	62.64
69.009	.289	.9610	124.72	70.97
68.953	.233	.8672	131.59	77.84
68.815	.095	.4778	164.23	110.48
68.720	-	-	-	-
73.650	-	-	49.90	-
73.477	.812	1.4098	71.28	21.38
73.246	.581	1.2644	81.78	31.88
73.112	.447	1.1503	89.92	40.02
72.885	.220	.8425	110.25	60.35
72.815	.150	.6760	125.25	75.35
72.665	-	-	-	-

Table VIII

Sedimentation Parameters at Various ζ-Potentials

Electrolyte	Concentration	ζ-Potential	Sedimentation Rate Constants (hr^{-1})			Final Height
	(ppm)	(mV)	k	w_1	w_2	H_∞ (cm)
NaCl	25	-11.098	0.070	0.0377	0.01665	63.890
$CaCl_2$	50	- 8.990	0.062	0.0347	0.01832	65.855
$CaCl_2$	800	- 7.980	0.059	0.0433	0.01981	68.230
$CaCl_2$	100	- 7.850	0.055	0.0389	0.02045	68.720
$CaCl_2$	200	- 5.455	0.050	0.0396	0.03298	72.665

Figure 2. Typical sedimentation curve of Min-u-Sil suspension in intermediate concentration range.

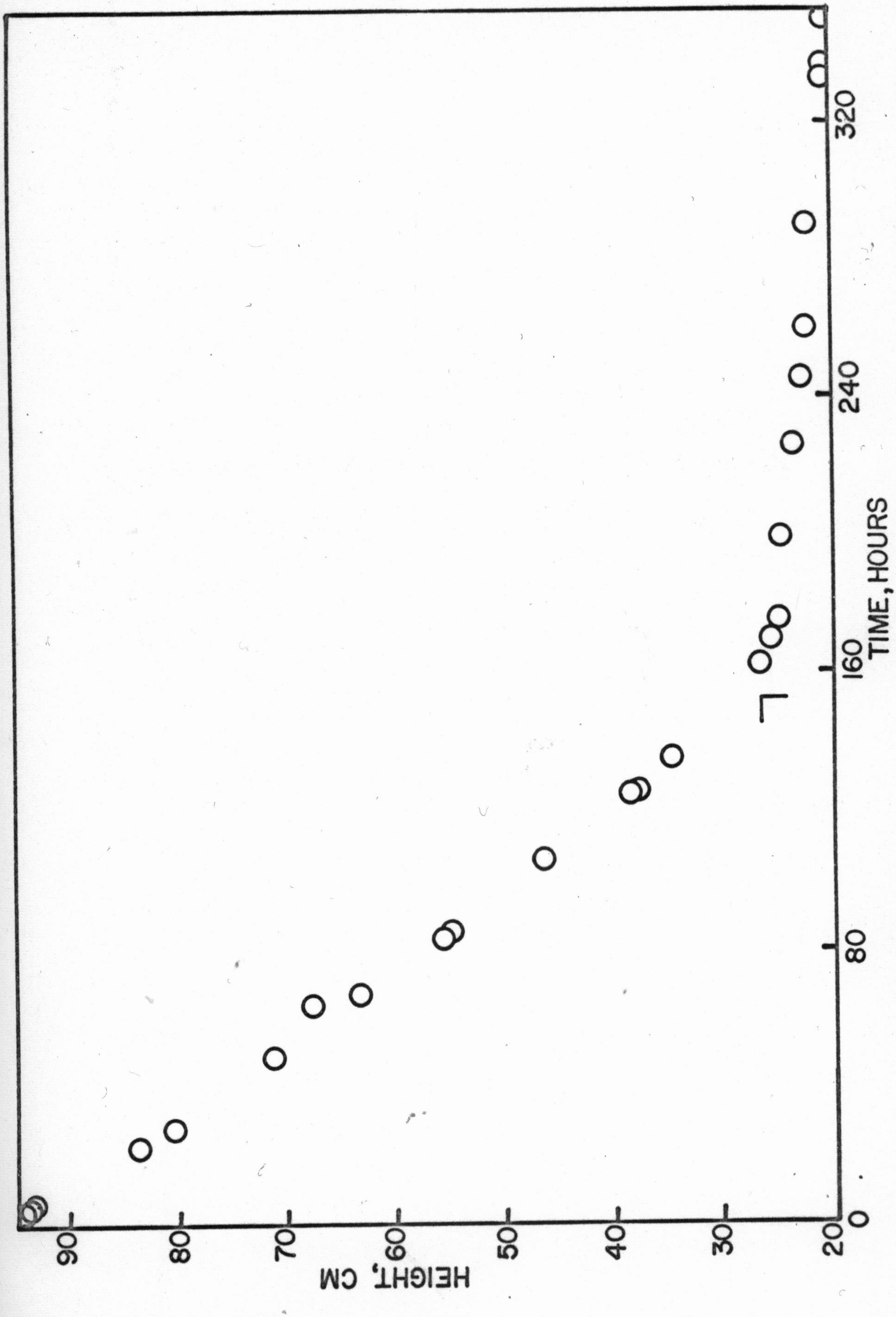

HEIGHT, CM
90
80
70
60
50
40
30
20
TIME, HOURS
0
80
160
240
320

Figure 3. Typical sedimentation curve of calcium carbonate suspension in intermediate concentration range.

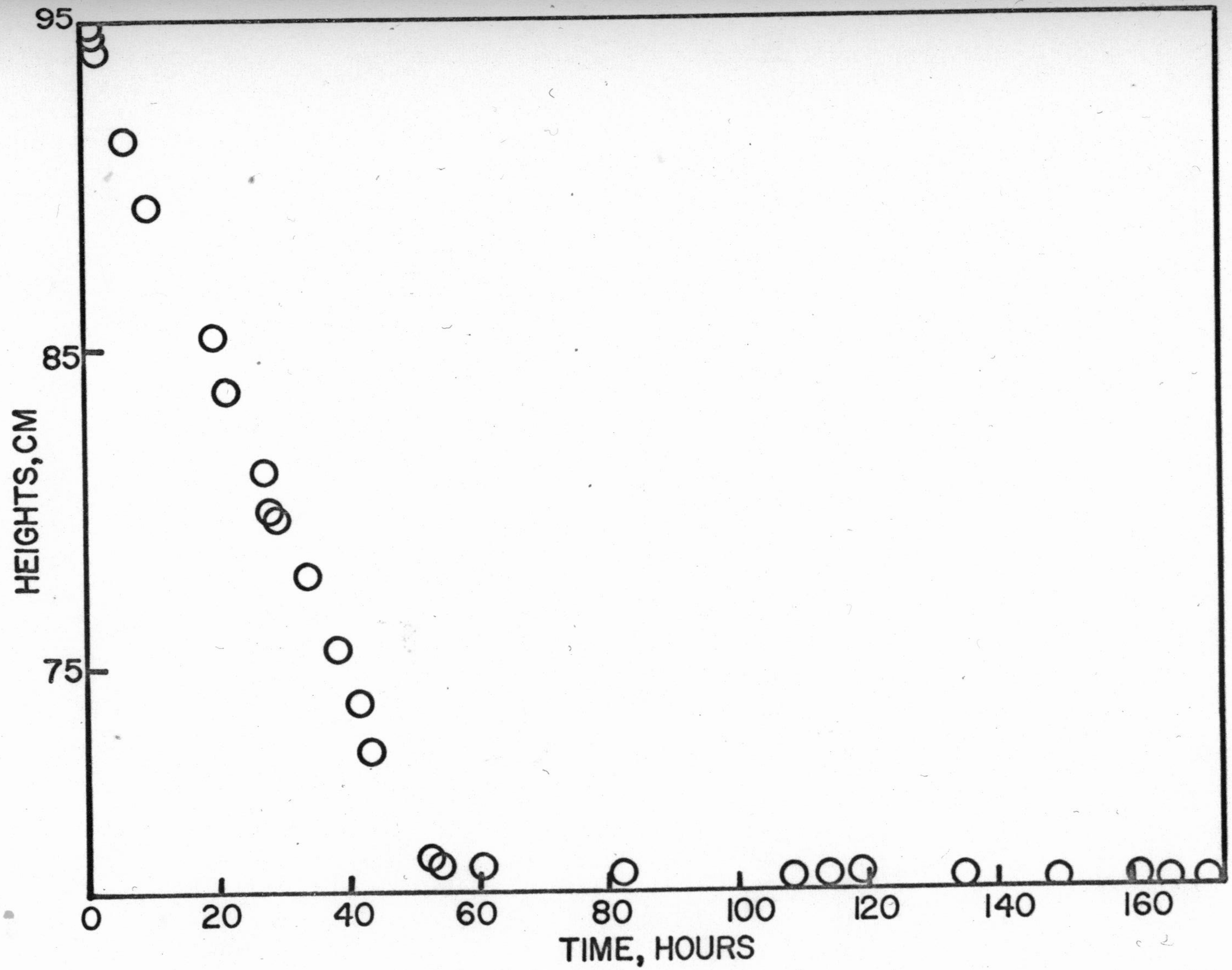

95
85
75
HEIGHTS, CM
0
20
40
60
80
100
120
140
160
TIME, HOURS

Figure 4. First phase sedimentation curve of Min-u-Sil suspension.

Key

● 3.00 mM of $CaCl_2$ is added
◑ 1.50 mM of $CaCl_2$ is added
⊕ 0.75 mM of $CaCl_2$ is added
◒ 1.00 mM of NaCl is added
○ 0.50 mM of NaCl is added

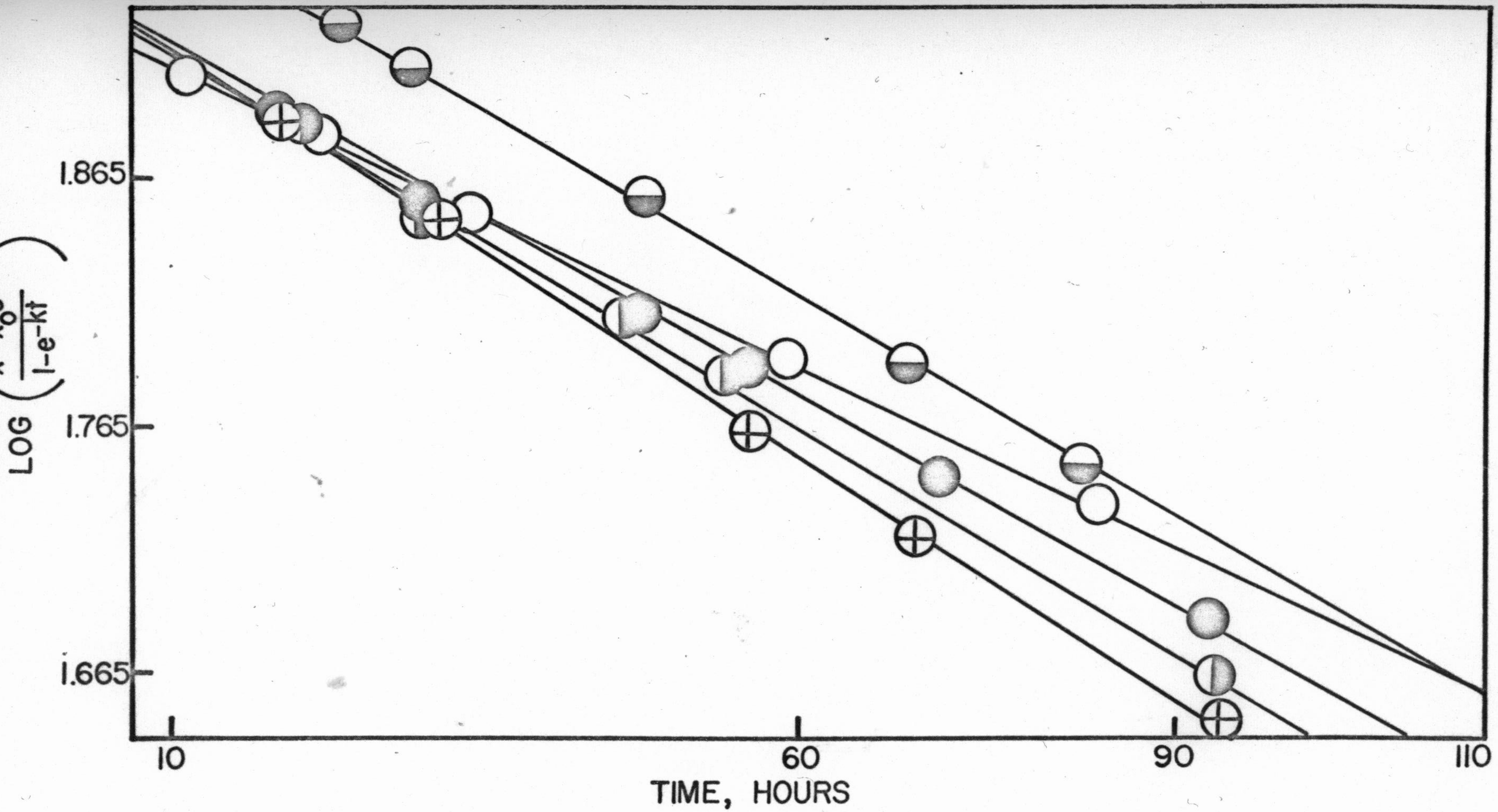

LOG $\left(\frac{x - x_o e^{-kt}}{1 - e^{-kt}}\right)$
1.865
1.765
1.665
10
60
90
110
TIME, HOURS

Figure 5. First phase sedimentation curve of calcium carbonate suspension.

Key

◓ 800 ppm of $CaCl_2$ is added
○ 200 ppm of $CaCl_2$ is added
◐ 100 ppm of $CaCl_2$ is added
● 50 ppm of $CaCl_2$ is added
⊕ 25 ppm of NaCl is added

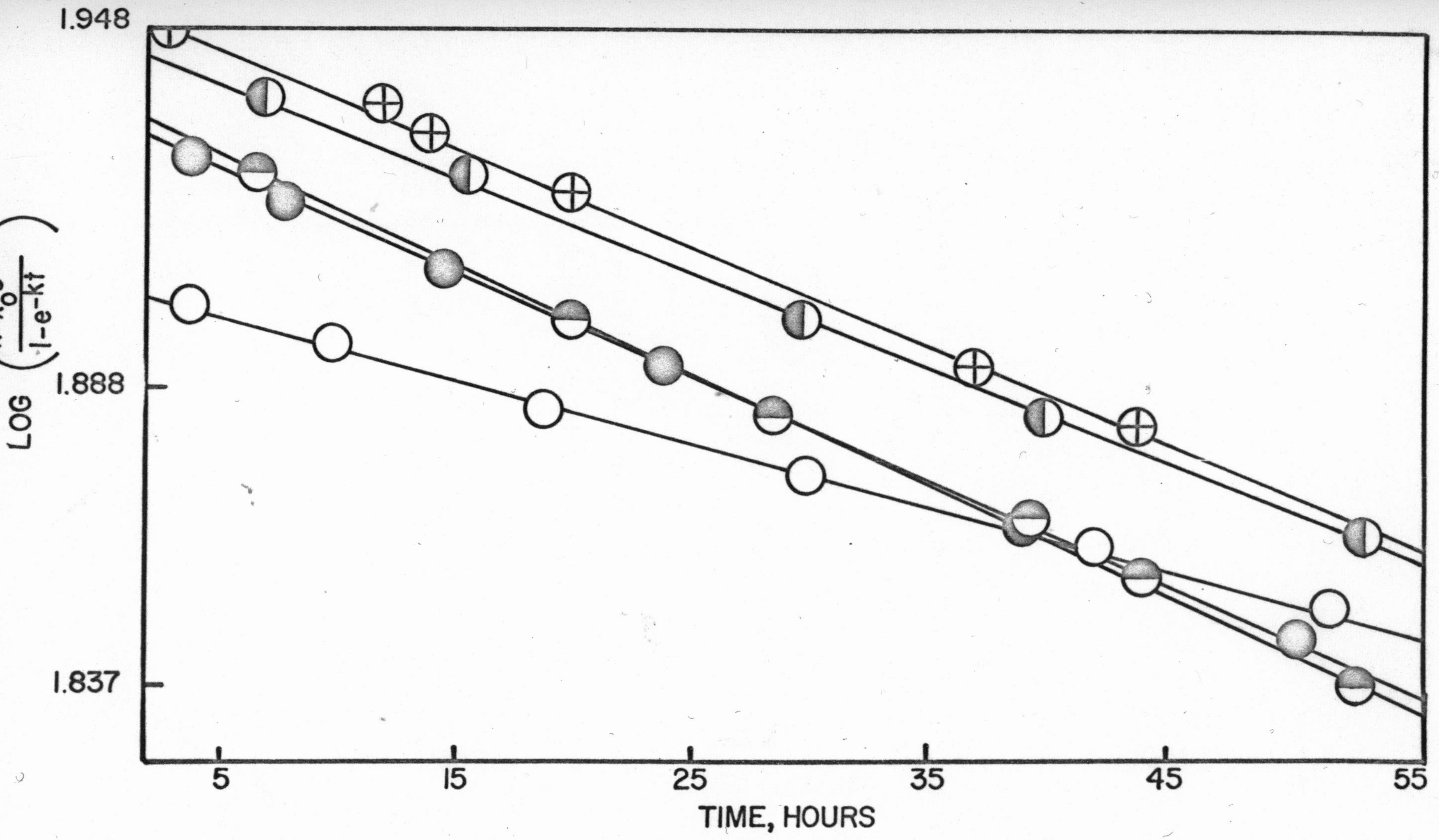

1.948
1.888
1.837
$\mathrm{LOG}\left(\frac{x-x_o e^{-kt}}{1-e^{-kt}}\right)$
5
15
25
35
45
55
TIME, HOURS

Figure 6. Second phase sedimentation curve of Min-u-Sil suspension.

Key

◓ 3.00 mM of $CaCl_2$ is added

◑ 1.50 mM of $CaCl_2$ is added

⊕ 0.75 mM of $CaCl_2$ is added

○ 1.00 mM of NaCl is added

● 0.50 mM of NaCl is added

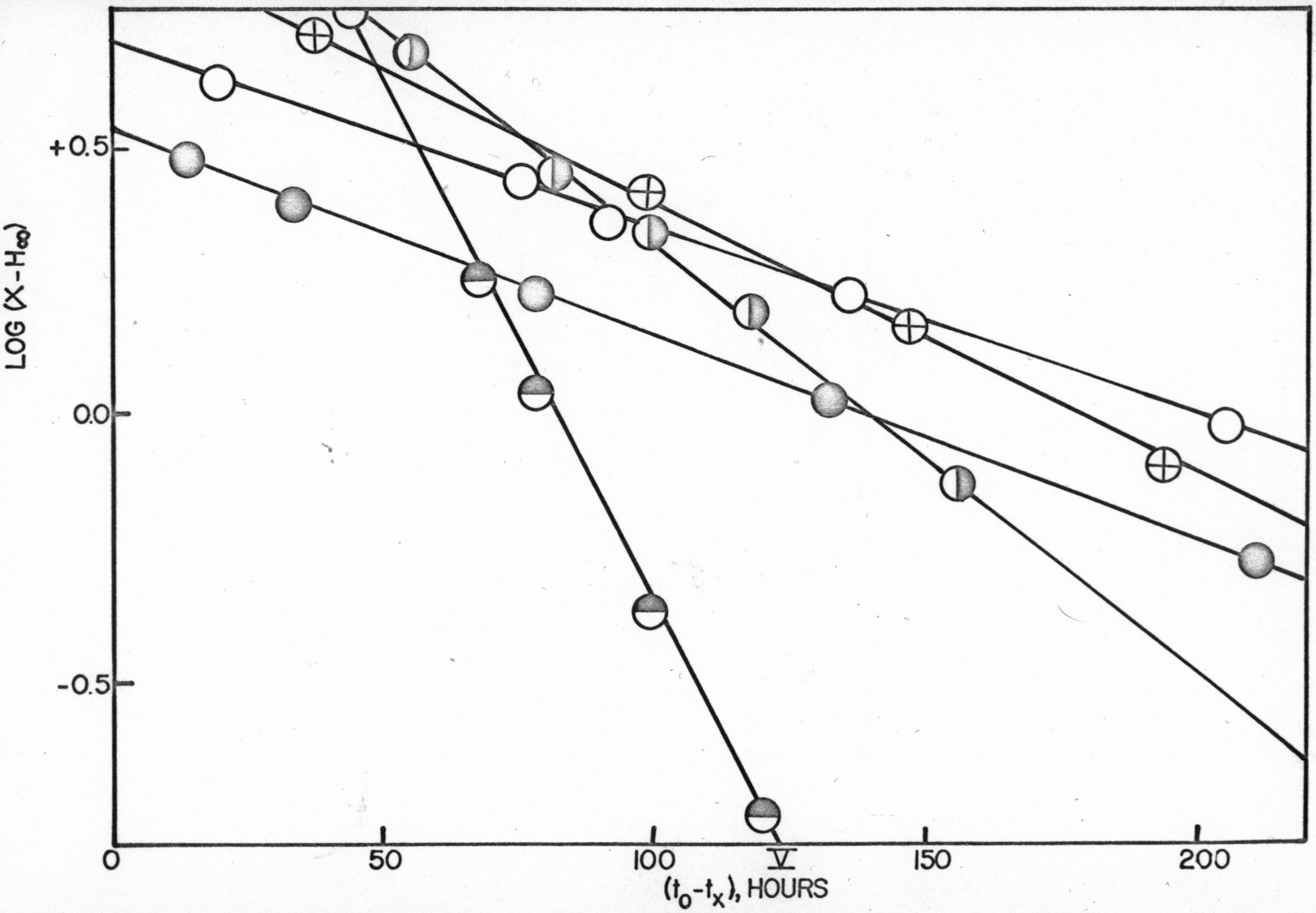

LOG (X-H∞)
+0.5
0.0
-0.5
0
50
100
V
150
200
(t_0-t_x), HOURS

Figure 7. Second phase sedimentation curve of calcium carbonate suspension.

Key

⊕ 800 ppm of $CaCl_2$ is added

○ 200 ppm of $CaCl_2$ is added

● 100 ppm of $CaCl_2$ is added

◑ 50 ppm of $CaCl_2$ is added

◒ 25 ppm of NaCl is added

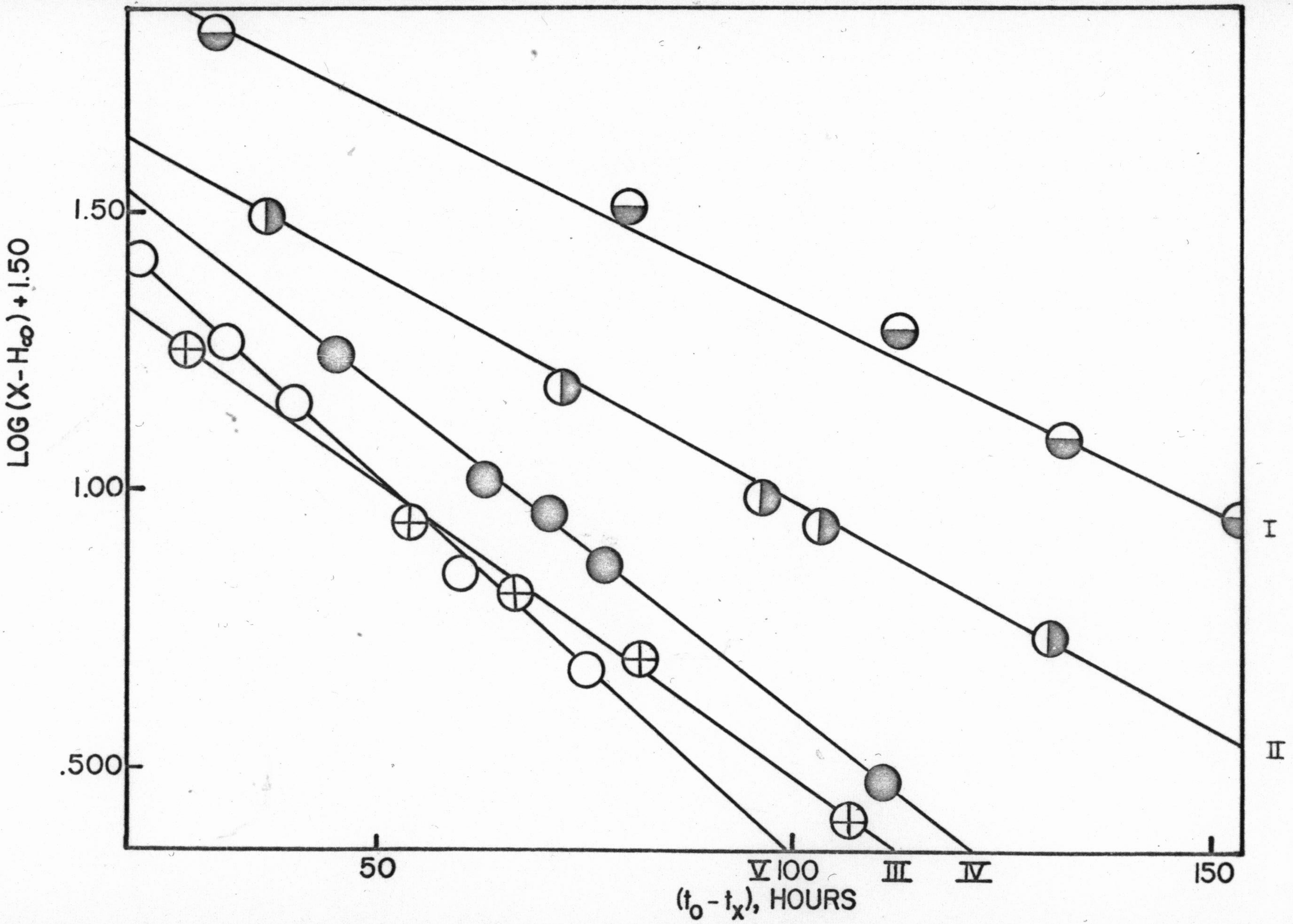
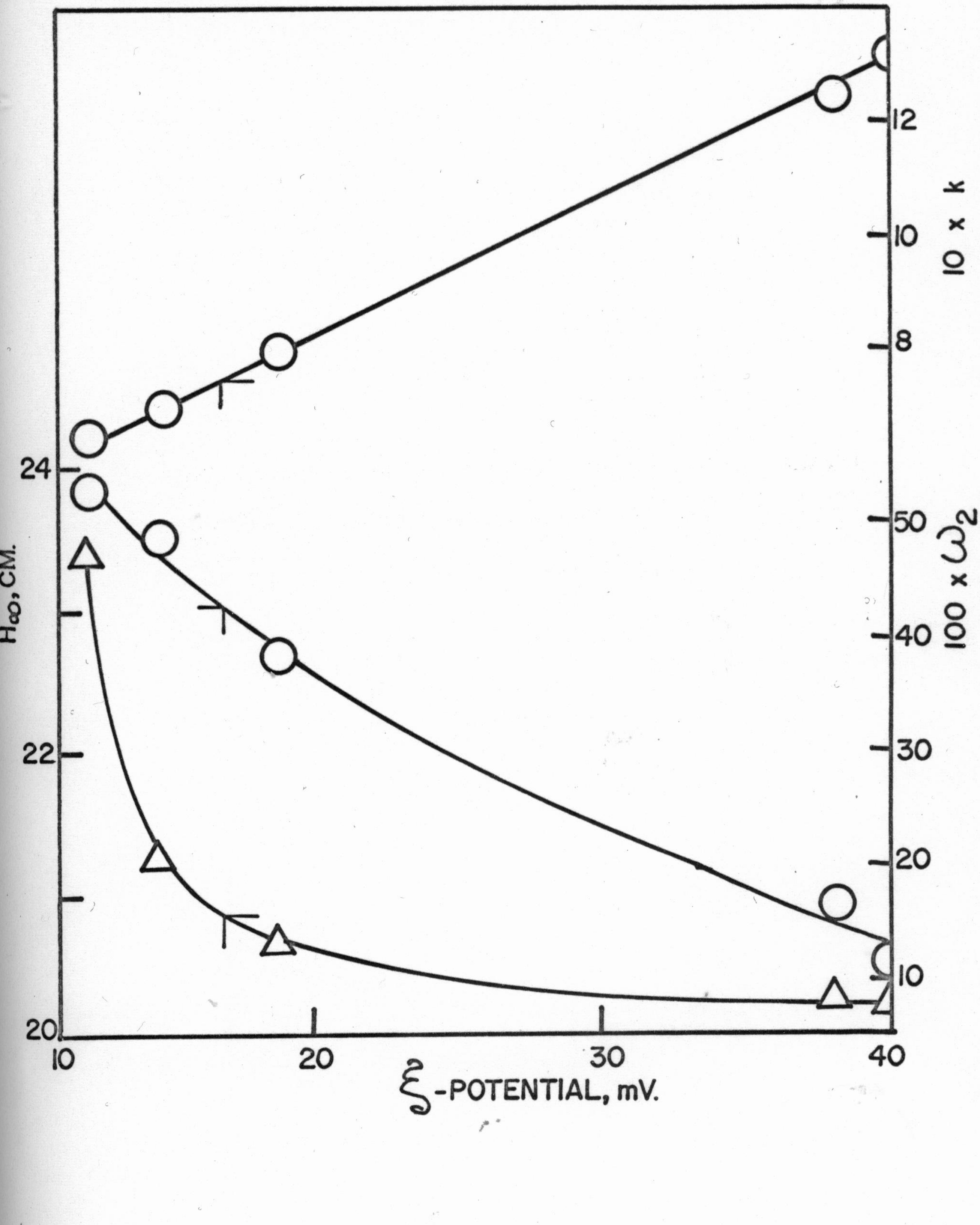

LOG (X-H_∞) + 1.50
1.50
1.00
.500
50
100
150
$(t_o - t_x)$, HOURS
I
II
III
IV
V

Figure 8. Plots of various sedimentation parameters versus Zeta-potentials of Min-u-Sil suspension.



H∞, CM.
24
22
20
10
20
30
40
ξ-POTENTIAL, mV.
12
10
8
10 x k
50
40
30
20
10
100 x ω2

Figure 9. Plots of various sedimentation parameters versus Zeta-potentials of calcium carbonate suspension.

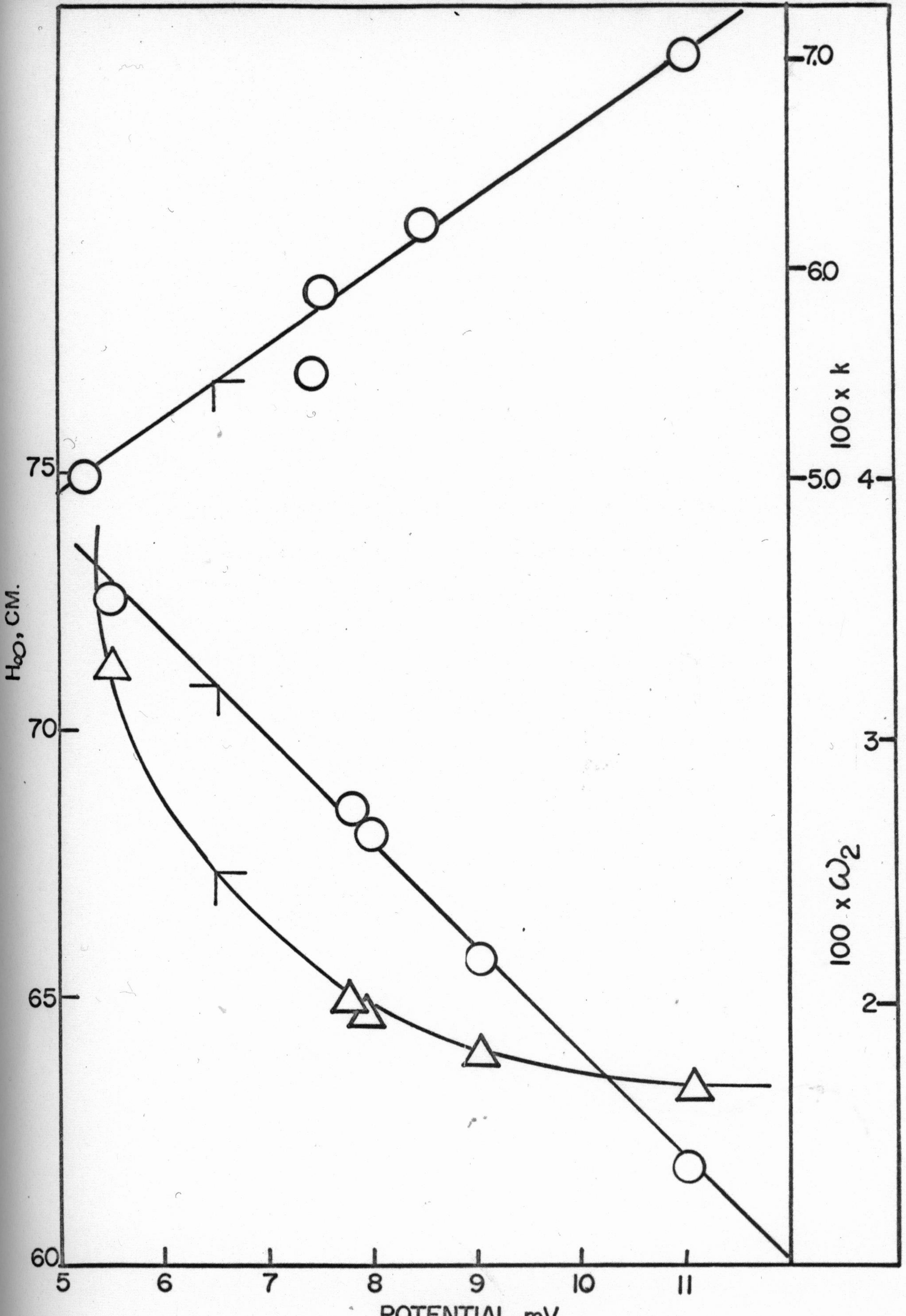

H∞, CM.
75
70
65
60
5
6
7
8
9
10
11
POTENTIAL, mV
100 x k
7.0
6.0
5.0
100 x ω2
4
3
2

Figure 10. Relation between reciprocal of w_2-rate constant and Zeta-potential of Min-u-Sil suspension.

Equation of the line is:

$$\frac{1}{w_2} = -\frac{1600}{|\zeta|} + 160$$

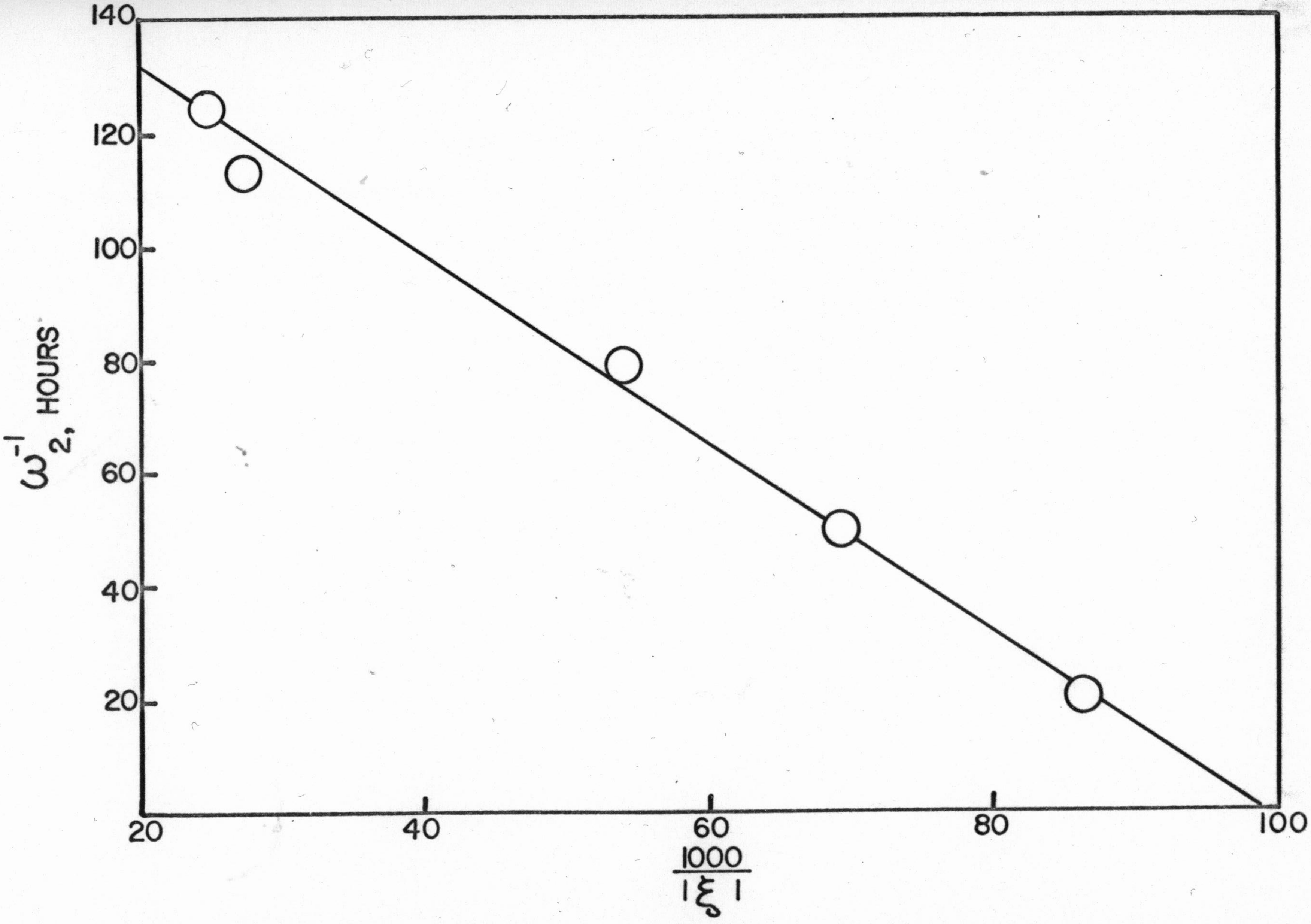

140
120
100
80
60
40
20
ω_2^{-1}, HOURS
20
40
60
80
100
$\frac{1000}{|\xi|}$

Figure 11. Relation between reciprocal of w_2-rate constant and Zeta-potential of calcium carbonate suspension.

Equation of the line is:

$$\frac{1}{w_2} = \frac{40.51}{|\zeta|} + 67.69$$

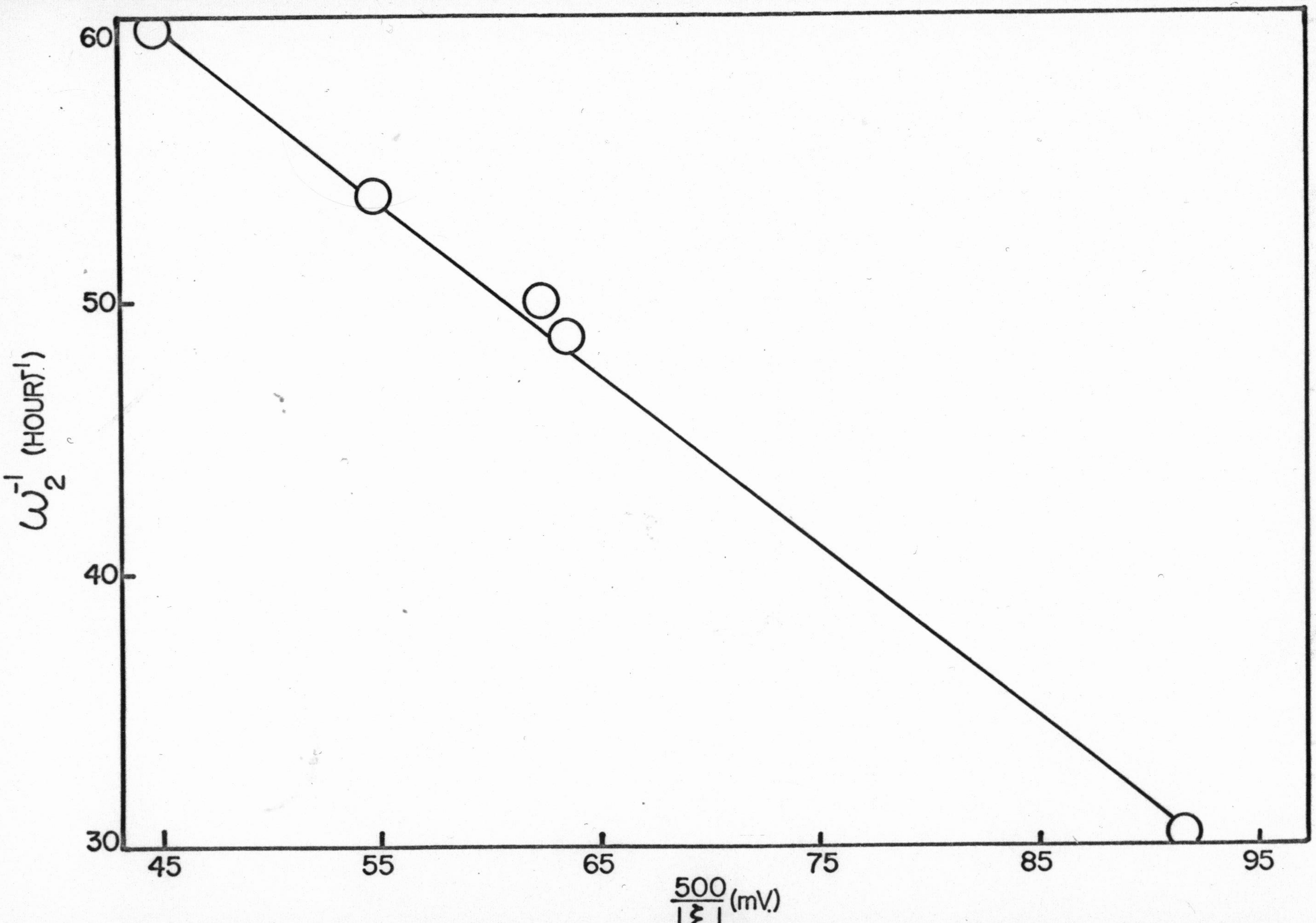

ω_2^{-1} (HOUR^{-1})
60
50
40
30
45
55
65
75
85
95
$\frac{500}{|\xi|}$ (mV)

Figure 12. Relation between flocculation rate constant (k) and ultimate height (H_∞) of Min-u-Sil suspension.

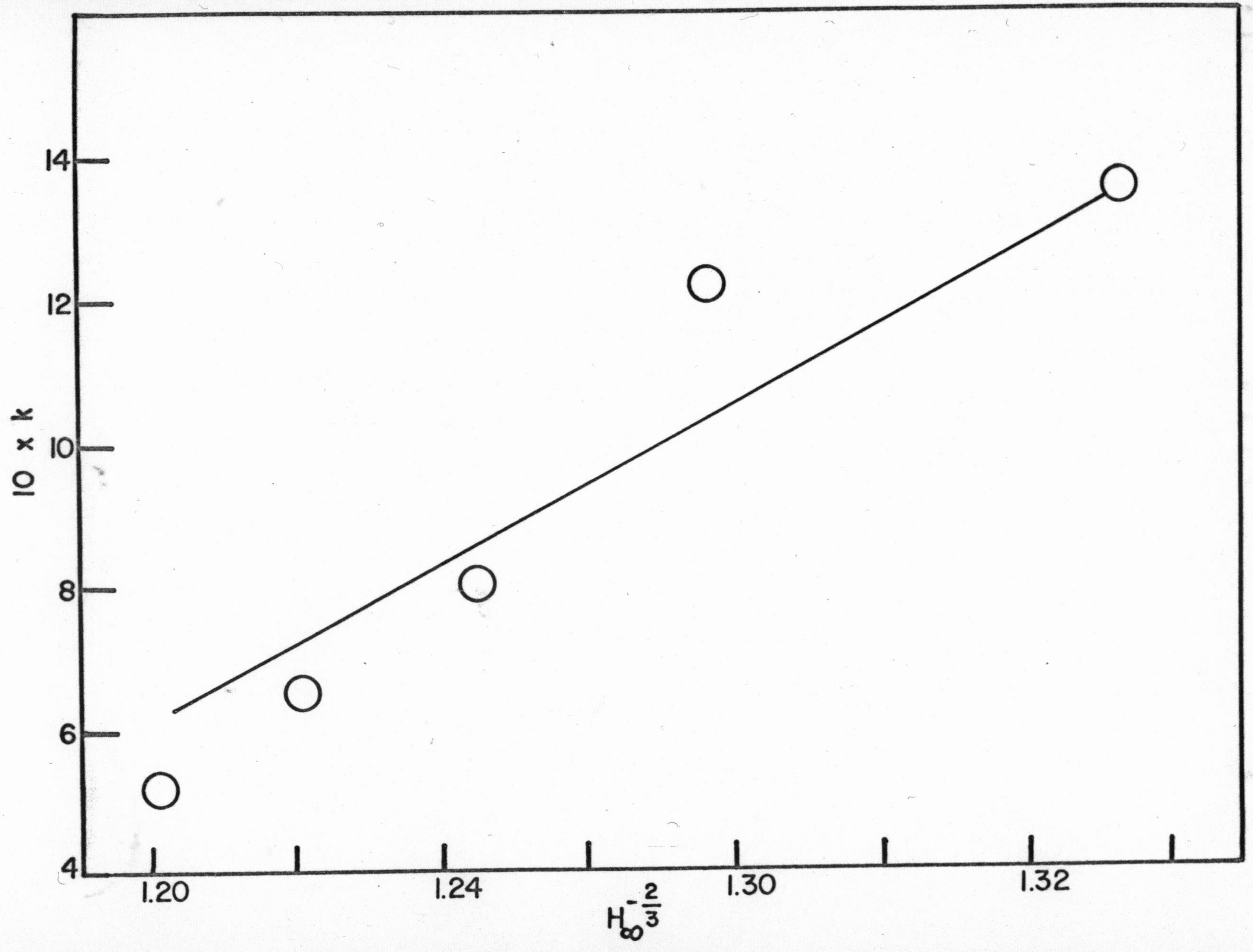

14
12
10
8
6
4
10 x k
1.20
1.24
1.30
1.32
$H_{\infty}^{-\frac{2}{3}}$

Figure 13. Relation between flocculation rate constant (k) and ultimate height (H_∞) of calcium carbonate suspension.

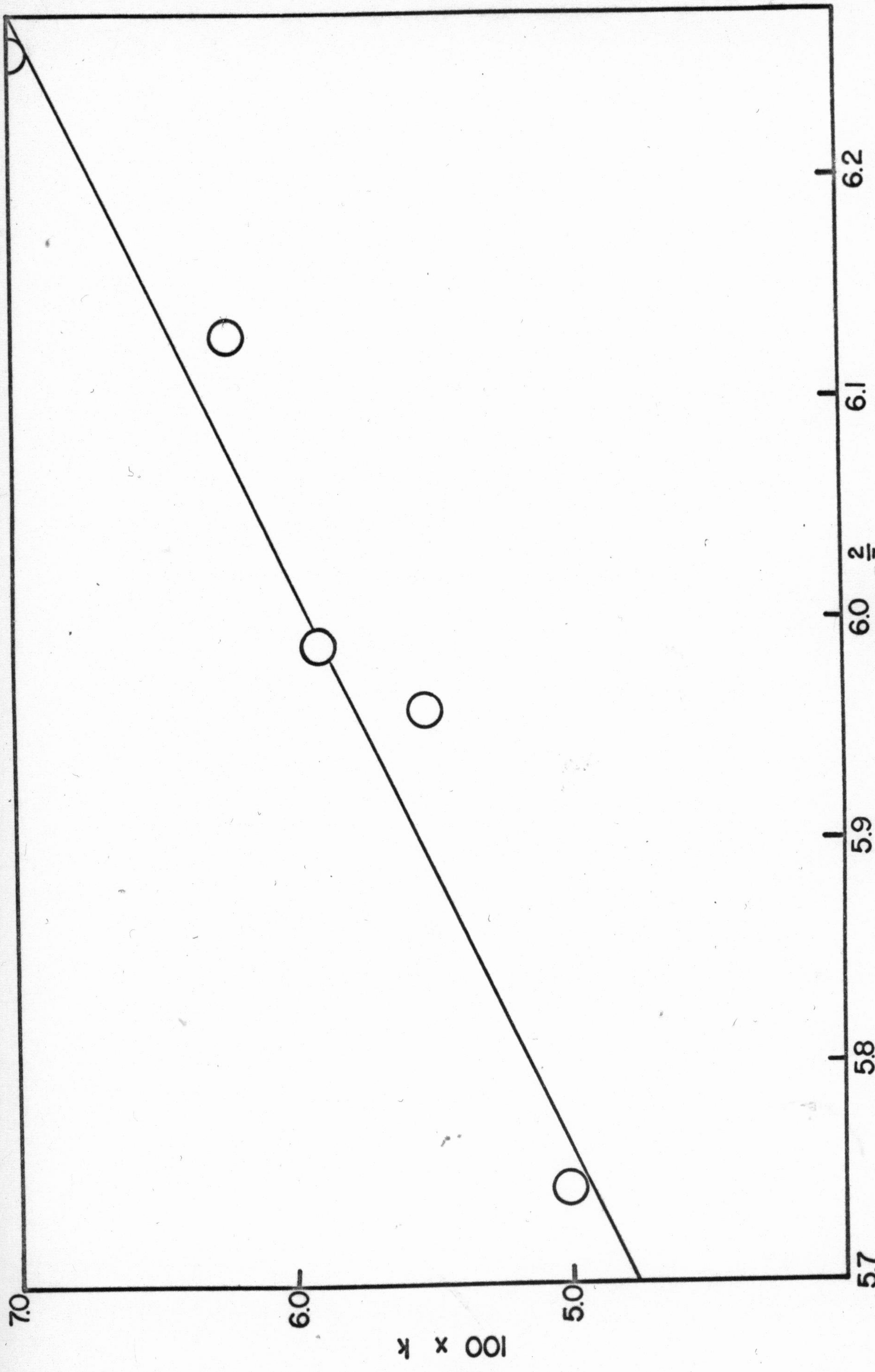
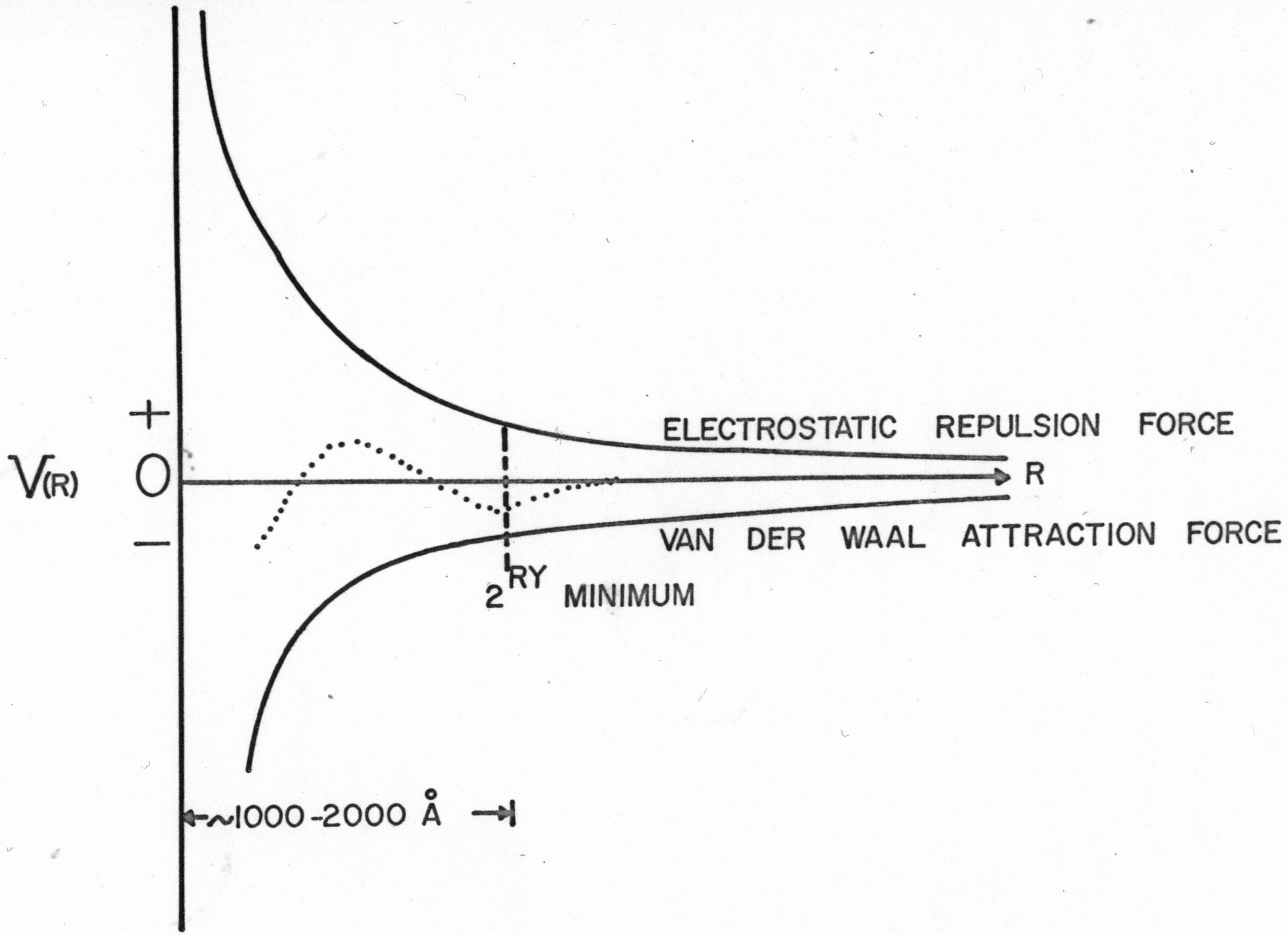

100 x k
7.0
6.0
5.0
5.7
5.8
5.9
6.0
6.1
6.2
$100 \times H_{\infty}^{-\frac{2}{3}}$

Figure 14. Hypothetical potential energy curve of flocculation formation.


V(R)
+
O
−
ELECTROSTATIC REPULSION FORCE
R
VAN DER WAAL ATTRACTION FORCE
2RY MINIMUM
~1000-2000 Å

General Pattern of Sedimentation Kinetics of Suspensions in an Intermediate-Concentration Range

Sedimentation curves were drawn for one of the experiments with Min-u-Sil and of calcium carbonate suspensions in the presence of electrolytes. As shown in Figure 2 and Figure 3, both systems obey the general pattern of Michael and Bolger (10), and Carstensen and Su (14) in the intermediate concentration range of tested materials. The sedimentation curves at other electrolyte concentrations in both systems were also generated, but have not been displayed here because of their similarity.

Preliminary tests had been done at the beginning of each experiment to insure reproducibility of the curves. Care should be taken in determination of the ultimate height (H_∞), thus, in all this study the values were obtained when a point in time had been reached where less than 0.2 mm. change occurred in a 24-hr period; this usually required 9-16 days. Evaluation of critical heights (H_o) and times (t_o) in each run were done via the sedimentation curves with a fair amount of accuracy ($\pm$9.1%).

First Phase Sedimentation Behavior

Values of absolute heights (x) and corresponding time (t) were used, in each run, to estimate the best-fitted k-constant (an initial rate constant), and enable one to exhibit the semilogarithmic linearity behavior of first phase sedimentation. The mathematic derivation (Eq. 4) by Carstensen and Su were used in all calculations related to the initial rate constant. Following an iteration method many k-values were chosen and tested until curve-plotting of the yielded numbers generated straight lines (Figures 4 and 5). Then w_1-values would be obtained from the slope of these lines by using least-square fitted method. Desired parameters were then taken and utilized in exploring the relation between initial rate constants and variation of the Zeta-potentials of the system. From Figure 8 and Figure 9 plots of one of the initial rate constants (k-value) versus Zeta-potential in both systems yielded very good straight lines, which shows the primary effect on the rate constant-k (flocculation rate of the suspension).

Values of w_1, however, are insensitive to the change in Zeta-potential and thus, appear to be independent of it.

Sedimentation Below Critical Height (H_o)

Rate constants of the second phase sedimentation consists of two separate rate constants, w_1 and w_2; as noted before, value of w_1 appears to be the same as what was obtained from the first phase. w_2, however, can be determined from the biexponential equation (Eq. 9). $(A_1 + A_2)$ is equal to the value of critical height (H_o) in each case, as shown in Figures 6 and 7.

The effect of Zeta-potential on w_2-rate constant is obvious; Figure 10 and Figure 11 show that for both systems linearity relation can be obtained via an equation:

$$[w_2]^{-1} = -\frac{D}{|\zeta|} + E \qquad (12)$$

where D and E are specific constants for each system. Equation (12) is compatible with equation (8) in the sense that increase in Zeta-potential increases the electrostatic repulsion between floc-aggregates.

Various Influences on the Ultimate Height (H_∞) of the Sediment

The effect of electrolytes on the ultimate height (H_∞) of flocculated suspensions has been reported before (16). In this study, H_∞, is plotted versus the Zeta-potential of the system, and the excellent straight lines are obtained; as appeared on Figure 8 and Figure 9. It is obvious here that in general H_∞ is maximum when Zeta-potential is close to zero.

There is also an influence from the mechanical forces on the final height of the cake as was partly discussed in the study of Higuchi and Stehle (22). Since the value of k-rate constant might be considered to be a function of floc-size in the sense that it depends linearly on $\underline{r}^2$, where '$\underline{r}$' is the "<u>radius</u>" of the final floc-aggregates, then, if it is also considered to depend on flocculation rates, it may be put in the form:

$$k = a \cdot r^2 + b \qquad (13)$$

$$\text{or,} \quad r = (\alpha \cdot k + \beta)^{0.5} \qquad (14)$$

If each floc is separated on the average by ℓ-cm, then the number of flocs in a cross-sectional area is:

$$m = \pi (1.23)^2 / \ell^2 \qquad (15)$$

The total number of particles is:

$$N = \frac{M}{\rho} \cdot \frac{1}{4\, r^3/3} = \frac{3\, M}{4 \pi \ell \cdot (\alpha \cdot k + \beta)^{0.5}} \qquad (16)$$

If each cross-section is ℓ-cm apart the total number of particles is also given by $[H_\infty \cdot m/\ell]$, so that:

$$(\alpha \cdot k + \beta)^{1.5} = \frac{3 M\ell^2}{4(1.23)^2 H_\infty \pi \varrho} \qquad (17)$$

$(\alpha \cdot k + \beta)$ should, therefore, be proportional to $\underline{\ell}^2$ and inversely proportional to $(H_\infty)^{2/3}$.

Figure 12 and Figure 13 show that the latter relationship holds fairly well.

CONCLUSION

In the colloid literature, the word 'stable' as applied to colloidal solutions or suspensions is synonymous with 'deflocculated'. A flocculated suspension, consisting of large fluffy clumps which settle rapidly, is considered as "unstable." Accordingly, the industrial chemist and pharmacist have often concluded that a suspension should be maintained in the deflocculated condition. In many systems, dispersed particles, which eventually do settle even in the presence of the most effective suspending agents, tend to form permanent caked masses. Moreover, very frequently the suspending agent increases rather than prevents the caking in the sediment. Since the permanent cake may contain the active ingredients, uniform dosage distribution cannot be assured even after vigorous shaking in contrast to the flocculated system. Therefore, minimizing this condition is a necessary step in the compounding of suspensions.

The investigations reported here represent preliminary studies aimed at elucidating the sedimentation nature of the flocculated suspensions.

Most of the important sedimentation parameters have been found and certain relations among them have been established. Min-u-Sil and calcium carbonate were chosen as test materials because a fair amount of information about these two substances (such as their sizes and particular nature of the particles surface) are reported.

In aqueous medium, dispersed particles are surrounded by an ionic cloud and will create an electrical potential when they settle under normal gravity. Incorporation of various amounts of electrolytes into the system reduce Zeta potential, by shrinkage of the double layer's distance. The data presented confirm that variation of Zeta potential does affect the sedimentation kinetics of our system. This includes the fluctuation of the values of k, w_1 and w_2. Moreover, the final height of the sediment, which partly dictates the stability of the suspension, was shown to respond to the influences from both Stokes' and electrical forces. Although, direct effect of electrolytes on the ultimate height of the sediment was treated before, there have been no previous explanations suggesting variation of H_∞ due to other factors, such as mechanical forces.

Matthews and Rhodes (16), in their papers, have discussed the nature of flocculation in concentrated suspension, based on a preceding suggestion by Kruyt (23), as the trapping of two particles into the secondary van der Waals minimum (vicinity of about 1000-2000 Å separation), as shown in Figure 14.

Thus, they reached the conclusion that H_∞ is highest when the Zeta-potential is closest to zero. The effect of different types of electrolytes [i.e., NaCl (1:1) and $CaCl_2$ (2:1) are used instead of $AlCl_3$ (3:1)] used in this study on the final height of the sediment appear to confirm the result of Matthews and Rhodes. It is worth noting that values of H_{∞} obtained from calcium carbonate suspensions are much more sensitive to variation of Zeta potential than Min-u-Sil. Obviously, this should be due to the difference in the particle surfaces (function B in equation 8) that reflects the variation in sedimentation characteristics.

In conclusion, more study is required on this subject before one can gain a full understanding of the nature of flocculated suspensions sedimentation. A sequel to this study might be to study the effect of other types of electrolytes on the sedimentation behavior, and also the effect of the nature of particle surfaces. Rigorous treatment in this study aims specifically on the suspensions in an intermediate range of concentration, which is the most frequently encountered in pharmaceutical work.

This work, it is hoped, may provide some qualitative idea in dealing with the manufacturing of pharmaceutical suspensions in the most probable concentration range.

BIBLIOGRAPHY

(1) R. Stokes, Proc. Cambridge Phil. Soc., 9, 5 (1856).

(2) G. Kynch, Trans. Faraday Soc., 48, 166 (1952).

(3) T. Higuchi, J. Amer. Pharm. Ass., Sci. Ed., 47, 657 (1958).

(4) E. N. Hiestand, J. Pharm. Sci., 53, 1 (1964).

(5) H. Steinour, Ind. Eng. Chem., 36, 540 (1944).

(6) Ibid., 35, 901 (1944).

(7) C. S. Robinson, Ind. Eng. Chem., 18, 869 (1926).

(8) L. K. Benedict, G. S. Banker, and W. V. Kessler, J. Pharm. Sci., 54, 1659 (1965).

(9) H. Ward and K. Kammermeyer, Ind. Eng. Chem., 32, 622 (1940).

(10) A. S. Michaels and J. C. Bolger, Ind. Eng. Chem., Fundamentals, 1, 24 (1962).

(11) A. M. Gaudin and M. C. Fuerstenau, Eng. Mining J., 159, 110 (1958).

(12) A. M. Gaudin and M. C. Fuerstenau, and S. R. Mitchell, Mining Eng. (London), 11, 613 (1959).

(13) A. M. Gaudin and M. C. Fuerstenau, Int. Mining Proc. Congr., London, England, Apr. 1960.

(14) J. T. Carstensen and K. Su, J. Pharm. Sci., 59, 666 (1970).

(15) Ibid., 59, 671 (1970).

(16) B. A. Matthews and C. T. Rhodes, J. Pharm. Sci., 57, 569 (1968).

(17) E. Verway and J. Overbeek, "Theory of the Stability of Lyophobic Colloids," Elsevier, Amsterdam, The Netherlands, 1948.

(18) C. B. Egolf and W. L. Mc Cabe, Trans. Amer. Inst. Chem. Eng., 33, 620 (1937).

(19) O. Stern, Z. Elektrochem., 30, 508 (1924).

(20) V. K. LaMer, J. C. Kane and H. B. Linford, J. Am. Chem. Soc., 86, 3450 (1964).

(21) Zeta-Meter Manual, Zeta-Meter Inc., 2nd ed., 1968.

(22) W. I. Higuchi and R. G. Stehle, J. Pharm. Sci., 54, 265 (1965).

(23) H. R. Kruyt, "Colloid Science," vol. I, Elsevier, Amsterdam, The Netherlands, 1952.