2. All of these compounds were potent local anesthetics but showed no measurable vasopressor action.

REFERENCES.

(1) Cherbuliez, Neumeier and Lorenz, *Helv. Chim. Acta*, 14, 186 (1931).

(2) Beaufour, *Bull. soc. chim.* (4), 11, 648 (1912); cf. also *Bull. soc. chim.* (4), 13, 349 (1913); (4), 14, 354 (1913).

STUDIES IN THE EXTRACTION OF CINCHONA.*

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The experiments which are recorded in this report were undertaken primarily for the purpose of obtaining specific facts relative to extraction in general and to the extraction of cinchona in particular, because it was known to offer numerous extraction difficulties and because, being an alkaloidal drug, it presented an opportunity for basing the study upon something more tangible and of more relative importance than so-called extractive matter, which might or might not be indicative of drug activity and extraction efficiency.

Reports of other workers and the results of this study indicate that each drug must be considered as a specific problem and that what proves of value in one instance may be utterly lacking in another. Studies of the literature and the results of this study on cinchona bear evidence of both of these conditions. Consequently the results as here reported may or may not be indicative of what might be found with other drugs under similar conditions.

A carefully selected whole red cinchona bark was used in this study. The bark was ground to meet the specifications of numbers 10, 20, 40, 60 and 100 powders, and assays upon these showed the presence of 7.524, 7.436, 7.600, 7.416 and 6.872 per cent of alkaloids of cinchona, respectively.

Due to the nature of the experiments, U. S. P. alcohol was selected as the menstruum throughout, since a multiple-phase menstruum would not have worked satisfactorily under certain conditions and comparative results could not have been obtained unless a uniform menstruum was used in all cases.

EXPERIMENTAL PROCEDURE.

I and II.—To study the effects of vacuum and agitation on extraction in relation to the degree of comminution of the drug, the following maceration experiments were conducted with powders Nos. 10, 20, 40, 60 and 100: (*a*) vacuum but no shaking; (*b*) vacuum with shaking; (*c*) no vacuum and no shaking (plain maceration); (*d*) no vacuum but with shaking (plain maceration with shaking). Each of the experiments was performed in duplicate, and flasks of similar shape and size were used.

The experiments with vacuum were carried out in 250-cc. conical suction flasks whereas those without vacuum were made in similar, plain, conical flasks. Twenty grams of accurately weighed powder were placed in each flask. The suction flasks were closed with stoppers, each carrying a separatory funnel, the side arm of the flask was connected with the vacuum line and 100 cc. of alcohol were placed in the separatory funnel. The dry powders in the flasks were first subjected to a vacuum of 27 inches and maintained under such conditions for ten minutes; then the vacuum connection was closed and sufficient of the alcohol from the funnel was allowed to

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enter the flask by opening the cock until the powder was completely covered, a small part of the alcohol being allowed to remain in the funnel so as not to break the vacuum. The powder and the alcohol in each flask were mixed by gentle rotation of the flask and allowed to stand for five minutes. Then the remaining alcohol from the funnel was allowed to pass into the flask and the vacuum was broken. In the experiments without vacuum, after putting the powders into the flasks, 100 cc. of alcohol were added and mixed with the powder by gentle rotation. All of the flasks were then tightly stoppered and the powder was allowed to macerate for one hour. The flasks of the experiments in which the shaking was used, were, after half an hour, placed on a mechanical agitator and shaken for the remaining half hour. The flasks of the experiments with no shaking were, at intervals of fifteen minutes, *i. e.*, three to four times during the experiment, gently rotated for momentary mixing of the contents. At the end of the hour, after shaking the flasks, about 50 cc. of the liquid was decanted through a filter paper and analyzed for both extractive and total alkaloids. In all cases alkaloidal analysis was carried out by the U. S. P. method. The results are given in Tables I to III.

TABLE I.—PER CENT OF EXTRACTIVE MATTER IN THE EXTRACT BY PLAIN AND VACUUM MACERATION, WITH AND WITHOUT SHAKING.

Powder No.:		10.	20.	40.	60.	100.
A. Vacuum, no shaking	I	1.3425	1.956	2.214	3.178	3.110
	II	1.3525	1.946	2.206	3.248	3.118
Average		1.3475	1.951	2.210	3.213	3.114
B. Vacuum, with shaking	I	1.3650	1.904	2.398	3.348	3.076
	II	1.3175	1.834	2.376	3.346	3.002
Average		1.3413	1.869	2.387	3.347	3.039
C. No vacuum, no shaking	I	1.2125	1.772	2.328	3.196	3.126
	II	1.2350	1.814	2.358	3.242	3.098
Average		1.2238	1.793	2.343	3.219	3.162
D. No vacuum, with shaking	I	1.3300	1.822	2.396	3.312	3.024
	II	1.3275	1.834	2.293	3.266	3.028
Average		1.3288	1.828	2.394	3.289	3.026

TABLE II.—PER CENT OF TOTAL ALKALOIDS IN THE EXTRACT (ALSO EXPRESSED IN PERCENTAGE OF THE TOTAL AVAILABLE ALKALOIDS IN THE PORTION OF DRUG EXTRACTED) BY PLAIN AND VACUUM MACERATION, WITH AND WITHOUT SHAKING.

Powder No.:		10.	20.	40.	60.	100.
A. Vacuum, no shaking	I	0.2450	0.3353	0.3710	0.5215	0.5160
	II	0.2377	0.3365	0.3725	0.5285	0.5180
Average		0.2414	0.3359	0.3718	0.5250	0.5170
Per cent of total available alkaloids		16.04	22.72	24.46	35.40	37.63
B. Vacuum, with shaking	I	0.2450	0.3340	0.4005	0.5370	0.5073
	II	0.2341	0.3120	0.4000	0.5385	0.4993
Average		0.2396	0.3230	0.4003	0.5378	0.5033
Per cent of total available alkaloids		15.92	21.72	26.34	36.26	36.63
C. No vacuum, no shaking	I	0.2215	0.3117	0.3875	0.5260	0.5240
	II	0.2179	0.3145	0.3960	0.5305	0.5233
Average		0.2197	0.3131	0.3918	0.5283	0.5237
Per Cent of total available alkaloids		14.6	21.06	25.78	35.62	38.11
D. No vacuum, with shaking	I	0.2415	0.3246	0.4015	0.5420	0.5080
	II	0.2355	0.3210	0.4055	0.5325	0.5113
Average		0.2385	0.3228	0.4035	0.5373	0.5097
Per Cent of total available alkaloids		15.85	21.71	26.55	36.23	37.10

NOTE.—Alkaloids available from 20 Gm. of powder. From No. 10, 1.505 Gm.; from No. 20, 1.487 Gm.; from No. 40, 1.520 Gm.; from No. 60, 1.483 Gm.; from No. 100, 1.374 Gm. (on the basis of analysis by U. S. P. method).

TABLE III.—GM. OF ALKALOID PER ONE GM. OF EXTRACTIVE (CALCULATED FROM C AND D, TABLES I AND II).

Powder No.:	10.	20.	40.	60.	100.
C	0.18	0.175	0.167	0.164	0.166
D	0.18	0.177	0.169	0.163	0.168

From these results it appears that the degree of comminution of the drug is of great importance in the effects of vacuum and shaking on extraction. Whereas vacuum maceration has helped somewhat in powders Nos. 10 and 20, *i. e.*, coarser powders, it has shown no advantage in extraction of powders Nos. 40, 60 and 100.

As regards the effects of mechanical shaking, no better results are shown in conjunction with vacuum in the case of coarse powders (Nos. 10 and 20), although in these powders, without vacuum, it has demonstrated some advantage over plain maceration. In the case of fine powders, however (Nos. 40, 60 and 100), while vacuum did not show any advantage in extraction, mechanical shaking indicates a somewhat more favorable result.

The efficiency of extraction to the degree of comminution of the powder will be seen readily by comparing the results obtained, for instance, in C, Table II. If these results are expressed in such a way that a comparison can be made of the alkaloids extracted (taking the No. 10 powder as the unit) the extraction ratios with powders Nos. 10, 20, 40, 60 and 100 will be 1, 1.44, 1.77, 2.44 and 2.6. That is, due to the size of powder, the No. 60 yields about two and one-half times as much alkaloid as does a No. 10 powder. Therefore it will be seen that the finer the powder the better the extraction, the rate of extraction increasing notably as the size of particle decreases. There is no appreciable difference in the extraction between Nos. 60 and 100 powders, indicating that a No. 60 is the optimum size for the extraction of cinchona.

These results also tend to show that there is no advantage in grinding the powder finer than No. 60, and in the case of this drug at least, the possibility of grinding the drug to such a fine condition as to wash or dissolve the active principles, as in the making of a solution in a single operation, seems to be far remote or at least impractical.

From the results of the effects of vacuum on extraction using the different size powders, it seems that for practical penetration of the solvent, in the case of cinchona, the cells in a No. 40 or finer powder are sufficiently damaged or crushed to allow easy penetration of the solvent, and vacuum offers no added advantage.

The ratio of Gm. of alkaloid per Gm. of extractive, Table III, primarily shows a gradual decrease in the order of the fineness of powder indicating an increase of extractive per Gm. of alkaloid. However, this increase apparently reaches its maximum with No. 60 powder, as No. 100 shows a slight change in the opposite direction. This finding is in line with that of Husa and Huyck (1) who found with belladonna root that the yield of extractive increases as the size of powder decreases down to and including No. 60 powder and that with No. 80 powder there is a decrease in yield of total extractive.

III.—To study the effect of time on the rate of extraction of drug of different degrees of comminution, 20 Gm. of cinchona in Nos. 10, 20, 40 and 60 powders were accurately weighed and placed into 250-cc. conical flasks. One hundred cc. of alcohol were added to each flask and the flasks tightly stoppered. The contents were well mixed by gentle rotation of the flasks for a few minutes and then allowed to macerate, being shaken by gentle rotation for a few minutes at about two-hour intervals, four times during the day. At the end of 24, 48 and 144 hours of such treatment, about 50 cc. of the extracts were filtered and analyzed for extractive and total alkaloids. The results are given in Tables IV to VII.

TABLE IV.—PER CENT OF EXTRACTIVE ON BASIS OF TIME.

Powder No.:	10.	20.	40.	60.
24 hours	2.272	2.688	3.100	3.510
48 hours	2.532	2.924	3.330	3.594
144 hours	2.680	3.114	3.426	3.658

TABLE V. PER CENT OF TOTAL ALKALOIDS BY U. S. P. METHOD, ON BASIS OF TIME.

Powder No.	10.	20.	40.	60
24 hours	0.3680	0.4375	0.4970	0.5455
48 hours	0.4055	0.4580	0.5115	0.5500
144 hours	0.4400	0.4965	0.5585	0.5655

TABLE VI. PER CENT OF TOTAL AVAILABLE ALKALOIDS EXTRACTED (CALCULATED FROM TABLE V).

Powder No.:	10.	20.	40.	60.
24 hours	24.45	29.42	32.70	36.78
48 hours	26.94	30.13	33.65	37.09
144 hours	29.24	33.40	36.74	38.13

TABLE VII.—GM. OF ALKALOID PER ONE GM. OF EXTRACTIVE (CALCULATED FROM TABLES IV AND V).

Powder No.:	10.	20.	40.	60.
24 hours	0.162	0.163	0.160	0.155
48 hours	0.160	0.157	0.154	0.153
144 hours	0.164	0.159	0.163	0.155

These results indicate that within the time limit of six days it does not seem possible to extract the total available alkaloids of the drug by a single maceration, the maximum extraction being about 38 per cent of the available alkaloids.

From Table VI it appears that there is a saturation point at which the rate of extraction tends to remain stationary, such saturation being easily obtained by optimum fineness of the powder in the shorter period of time, coarser powders requiring longer maceration. Thus while powders Nos. 10, 20 and 40 in the initial extraction at one hour (Table II, C) showed percentages of 14.6, 21.06 and 25.78, respectively, these percentages gradually increased with longer maceration until at the end of 144 hours they showed 29.24, 33.40 and 36.74 per cent extraction, respectively. However, with No. 60 powder the increase in extraction with time is not appreciable, increasing from 35.62 per cent in one hour to 38.13 per cent at the end of 144 hours, the saturation point having been quickly attained during the first hour of maceration. Thus it shows that the extraction of cinchona in coarser powders is uneconomical and time-consuming. Powder No. 40, with longer maceration, gives results similar to powder No. 60 and so may be used with advantage where powder No. 60 is found to be too fine for use as in percolation. On the other hand, powders Nos. 10 and 20, *i. e.*, very coarse powders, are unsatisfactory for extraction purposes.

Table VII shows that during the earlier period of maceration the rate of solution of the extraneous matter is greater than that of the alkaloids. However, upon further maceration the ratio of alkaloids to the extraneous matter increases. This finding is in agreement with that of Bull (2), who, by study of the percolation fractions of cinchona, reported that the inert material is extracted more quickly than the alkaloids.

IV.—To study the influence of a single maceration with a large quantity of menstruum, and to note the effects of using the same quantity of the menstruum in divided portions, 20 Gm. of the No. 60 cinchona powder were introduced into a conical flask and 200 cc. of alcohol were added. The flask was then stoppered, the contents well mixed by gentle rotation and allowed to macerate for two hours with frequent agitation. After two hours' maceration, 50 cc. of the extract were filtered and analyzed. Similarly 20 Gm. of cinchona were placed in another flask 100 cc. of alcohol added, the flask stoppered and the contents mixed. After one hour, 80 cc. of the extract were filtered through a Gooch crucible, the residue returned to the flask, and 50 cc. of fresh alcohol added. The flask was stoppered, the contents mixed by gentle rotation, and again after one-half hour 50 cc. of the extract were filtered, the residue returned and the process repeated with another 50-cc. portion of alcohol, finally filtering an additional 50 cc. of the extract. Thus, a total of 200 cc. of alcohol was used. The three fractions of the filtered extract were analyzed and the results are as follows.

The total alkaloids in 200 cc. of the extract obtained by a single maceration amounted to 0.6144 Gm., equivalent to 41.43 per cent of the total available alkaloids.

Total Alkaloids by Fractional Maceration.—0.4292 Gm. in the first extract of 80 cc.; 0.1480 Gm. in the second extract of 50 cc.; 0.0945 Gm. in the third extract of 50 cc.; 0.0378 Gm. estimated as being present in the 20 cc. of menstruum remaining with the marc.

Total.—0.7095 Gm. in 200 cc. of extract obtained by fractional maceration, and equivalent to 47.86 per cent of the total available alkaloids.

These results indicate that for cinchona, in the extraction of the alkaloids by maceration, better results are obtained by maceration with divided portions of menstruum rather than with one single portion of menstruum. Furthermore, in comparison with the results recorded in Table II, C, the extraction of alkaloids by maceration is not directly proportional to the quantity of menstruum used. In Table II, C, for instance, one-hour maceration with 100 cc. of menstruum yielded 35.62 per cent of total available alkaloids while by two hours' maceration with 200 cc. of menstruum the total available alkaloids extracted was increased only to 41.43 per cent.

V.—In order to determine the effect of vacuum and different degrees of comminution of drug by continuous extraction, 10 Gm. of Nos. 10 and 20 cinchona powder were placed in separate flasks and evacuated for ten minutes at 27 inches' vacuum. Fifty cc. of alcohol were added through a separatory funnel carried by the stopper, the contents were mixed and after five minutes the vacuum was broken. After maceration for one hour the contents were transferred to a Soxhlet apparatus, the flasks were rinsed with about 50 cc. of alcohol and extraction over a water-bath was carried on for four hours. A similar set of experiments was performed evacuating the powders for a period of 20 minutes, and extracting in the Soxhlet apparatus for $4^1/_2$ hours. Powders Nos. 10, 20, 40 and 60 were also similarly extracted both for 4 and $4^1/_2$ hours in the Soxhlet apparatus but without evacuation. The results are given in Tables VIII and IX.

TABLE VIII.—TOTAL ALKALOIDS OBTAINED BY EXTRACTION IN THE SOXHLET APPARATUS.

	4 Hours Extraction.		$4^1/_2$ Hours Extraction.	
Powder No.	Alkaloids Obtained from the Extract.	Equivalent Per Cent of the Total Available Alkaloids.	Alkaloids Obtained from the Extract.	Equivalent Per Cent of the Total Available Alkaloids.
10 with vacuum	0.4866 Gm.	64.67%	0.5312 Gm.	70.6 %
20 with vacuum	0.5628 Gm.	75.69%	0.6145 Gm.	82.64%
10 without vacuum	0.5025 Gm.	66.78%	0.5262 Gm.	69.94%
20 without vacuum	0.5292 Gm.	71.17%	0.6252 Gm.	84.08%
40 without vacuum	0.5892 Gm.	77.53%	0.7101 Gm.	93.43%
60 without vacuum*	0.4296 Gm.	.....	0.5341 Gm.	.....

* Powder No. 60 did not show proper extraction as the menstruum did not percolate readily through the powder.

TABLE IX.—TOTAL EXTRACTIVE BY CONTINUOUS EXTRACTION IN THE SOXHLET APPARATUS.

Powder No.	4 Hours Extraction.	$4^1/_2$ Hours Extraction.
10 with vacuum	2.45 Gm.	2.7439 Gm.
20 with vacuum	2.8588 Gm.	3.1523 Gm.
10 without vacuum	2.5819 Gm.	2.7265 Gm.
20 without vacuum	2.7581 Gm.	3.1955 Gm.
40 without vacuum	2.9848 Gm.	3.5797 Gm.

From these results, it appears that extraction of cinchona in very coarse powder is not satisfactory as previously stated. Even vacuum does not seem to offer any advantage under a continuous extraction process, although it seems to be slightly favorable for extraction during a short period of one hour. It appears that the customary procedure of the commercial extraction of drugs by vacuum with coarser powders averaging from Nos. 12 to 16 is not advisable in the extraction of cinchona. Powder No. 40 seems to be practical for percolation or continuous extraction methods even without vacuum. This finding of No. 40 powder as a suitable size for such extraction is in agreement with the findings of Bull (3) in percolation studies of cinchona. He reported that percolation of a moderately fine (44/85) powder gave better extraction of both alkaloids and total solids than either a fine powder No. 85 or a moderately coarse powder (22/60).

VI.—To study the effect of columns of drug of various heights upon extraction by percolation, and also the comparative value of upward (counter-current) extraction, five sets of percolators in duplicate were prepared as follows, each being charged with 50 Gm. of No. 40 cinchona powder.

(A) American type percolator; $^1/_2$ pint capacity; height of powder column about 3 inches; (B) glass tubing of $22^1/_2$ mm. internal diameter; height of powder column about $11^1/_2$ inches; (C) glass tubing of $17^1/_2$ mm. internal diameter; height of the powder column about 21 inches; (D) glass tubing of $11^1/_2$ mm. internal diameter; height of powder column about 43 inches. (E) glass tubing of $17^1/_2$ mm. internal diameter for upward (counter-current) extraction; height of the powder column about 20 inches.

In each case the powder was packed in a dry condition in order to avoid difficulties in packing through narrow tubes, and to make the conditions uniform in all. In set E, the menstruum entered the bottom of the cylinder through a tube attached to the stock container which was

raised to a height of four feet to provide the necessary pressure for a gravity feed. Stoppers, to which glass tubing was attached for delivery of the percolate, were inserted in the tops of the tubes, flush with the powder, providing a solid column of drug. Pinch-cocks at both the bottom and the top served to control the flow of the menstruum and the rate of the percolation.

Sufficient alcohol was poured on top of sets A, B, C and D to moisten and cover the powders completely. In set E alcohol was allowed to enter from below until the drug became saturated, at which time the source of supply was shut off. After allowing the drug to macerate over night, 25 cc. of percolate were collected from each, and thereafter, 25-cc. portions of percolate were collected daily until an equivalent of 200 cc. had been collected The first four fractions of 25 cc. each were analyzed separately for total extractive and alkaloids, and then the additional four fractions of 25 cc. each were combined and similarly analyzed.

The standard percolators (group A) required about 15 minutes for the collection of 25 cc. of percolate. The broadest tubing (set B) required about 25 minutes, the medium tubing (C) took about 60 minutes, the narrowest tubing (D) and the medium tubing (E), upward percolation, about 5 to 6 hours, for the collection of 25 cc. of percolate.

The results of analysis of the various fractions are given in Tables X to XIV.

TABLE X.—TOTAL GM. OF ALKALOIDS IN THE VARIOUS PERCOLATE FRACTIONS.

Fraction:	1.	2.	3.	4.	Combined 5, 6, 7, 8.	Total.
A	0.6770	0.3676	0.2432	0.1795	0.4674	1.9347
(Standard Percolation)	0.5980	0.4288	0.2572	0.1672	0.4494	1.9006
B	0.6660	0.4004	0.2548	0.1571	0.4122	1.8905
(22.5 mm. tubing)	0.5620	0.4316	0.2796	0.1648	0.4374	1.8754
C	0.7370	0.4096	0.2252	0.1528	0.4278	1.9524
(17.5 mm. tubing)	0.6980	0.4488	0.2408	0.1533	0.4170	1.9579
D	0.8360	0.4092	0.1956	0.1509	0.4308	2.0225
(11.5 mm. tubing)	0.9600	0.3317	0.1760	0.1413	0.4368	2.0458
E	0.7360	0.4000	0.2162	0.1509	0.4260	1.9261
(17.5 mm. tubing upward percolation)	0.5690	0.3992	0.2952	0.2021	0.4674	1.9329

TABLE XI.—PER CENT OF ALKALOIDS IN THE VARIOUS PERCOLATE FRACTIONS EXPRESSED IN PER CENT OF TOTAL AVAILABLE ALKALOIDS.

Fraction:	1.	2.	3.	4.	Combined 5, 6, 7, 8.	Total.
A	17.82	9.67	6.40	4.72	12.3	50.91
	15.74	11.28	6.77	4.4	11.83	50.02
B	17.53	10.54	6.71	4.13	10.85	49.74
	14.79	11.36	7.36	4.34	11.51	49.35
C	19.39	10.78	5.93	4.02	11.26	51.4
	18.37	11.81	6.34	4.03	10.97	51.52
D	22.0	10.77	5.15	3.97	11.34	53.22
	25.26	8.73	4.63	3.72	11.49	53.84
E	19.37	10.53	5.66	3.97	11.21	50.74
	14.97	10.51	7.77	5.32	12.30	50.87

TABLE XII.—GM. OF EXTRACTIVE IN THE VARIOUS PERCOLATE FRACTIONS.

Fraction:	1.	2.	3.	4.	Combined 5, 6, 7, 8.	Total.
A	3.7010	2.1680	1.3888	0.9328	2.151	10.3416
	3.6825	2.5648	1.4464	0.7920	1.983	10.4687
B	4.1010	2.3808	1.3376	0.7360	1.887	10.4424
	3.3825	2.4752	1.5984	0.7904	2.043	10.2895
C	4.3130	2.3232	1.1856	0.7792	1.977	10.5780
	4.0015	2.7152	1.3040	0.7712	1.965	10.7569
D	4.8080	2.4784	1.0096	0.6944	1.947	10.9374
	5.7445	1.8416	0.8656	0.6672	1.905	11.0239
E	4.3940	2.3696	1.1472	0.7280	1.944	10.5828
	3.3060	2.3424	1.8400	1.0352	2.202	10.7256

TABLE XIII. PERCENTAGE OF TOTAL AVAILABLE EXTRACTIVE OBTAINED.

	A.	B.	C.	D.	E.
Per cent total available extractive	57.77	58.34	59.10	61.10	59.12
	58.48	57.48	60.09	61.59	59.92

The figures in Table XIII represent the percentage of the total available extractive obtained in the various percolation processes. The total available extractive was derived from the results obtained by use of the Soxhlet apparatus, being in the proportion of 17.9 Gm. per 50 Gm. of drug (see Table IX).

TABLE XIV.—GM. OF ALKALOIDS PER 1 GM. OF EXTRACTIVE (CALCULATED FROM TABLES X AND XII) OF THE FIRST PERCOLATE FRACTION AND OF THE COMBINED 5, 6, 7 AND 8 FRACTIONS.

Fraction:	1.	Combined 5, 6, 7, 8.
A	0.183	0.217
	0.162	0.227
B	0.162	0.218
	0.166	0.214
C	0.171	0.216
	0.174	0.212
D	0.174	0.221
	0.167	0.229
E	0.168	0.219
	0.172	0.212

The results of these experiments show that for practical extraction of cinchona the usual method of percolation with standard percolators is quite satisfactory. The long column tube-type of percolator as is adopted in diacolation and its modified forms, either in downward or upward percolation and even with the rate of percolation as slow as about one drop per minute, offers no appreciable advantage in the continuous extraction of the drug to exhaustion. Of course if the first fraction or two of a percolate is considered, the slow extraction in the taller columns gives somewhat better results than is obtained by the ordinary percolator (15 to 18 per cent by ordinary percolators as compared to 22 to 25 per cent by the tallest columns and slowest percolation, sets A and D, Table XI). Subsequently, however, this advantage decreases and all types tend to similarity upon continued extraction (50 to 51 per cent as compared to 53 to 54 per cent, Table XI, A and D). This shows that there is no particular advantage in such methods over the usual type of percolator when percolation is carried to complete exhaustion of the drug. This can be explained by assuming that even though the long-column diacolation-type method of extraction helps in the earlier stages to dissolve the surface constituents, the final rate of extraction by outward diffusion from within the drug tissues is not different.

Results from Table XIV show that the ratio of alkaloid to the extractive matter gradually increases in progressive fractions of percolate. Non-alkaloidal extractive dissolves more readily than the alkaloids themselves which is in confirmation of an earlier statement concerning maceration. However, although the extractive matter is more readily removed than the alkaloids, for complete extraction there is not a great amount of difference between the removal of alkaloids and extractive matter, 58 to 62 per cent of total available extractive (see Table XIII) as compared to 50 to 54 per cent of total available alkaloids (see Table XI).

SUMMARY.

Extraction of red cinchona bark in various degrees of comminution has been studied using U. S. P. alcohol as the menstruum, and the following observations have been made.

1. It has been found that, for cinchona, in extraction by maceration, vacuum has some favorable effect for powders Nos. 10 and 20 for the initial extraction,

although on continued extraction it does not show any advantage over ordinary methods. Vacuum has no advantage in extraction of powders Nos. 40, 60 and 100 and actually has been found, during the initial extraction, to be less favorable.

2. It has been found that, for cinchona, prolonged shaking offers some advantage in all powders by ordinary maceration methods, but under vacuum it does not show any merit with coarse powders Nos. 10 and 20.

3. It has been found that, for cinchona, upon continuous extraction in a Soxhlet apparatus, No. 60 powder is too fine for such extraction while No. 40 powder gives the best results. Powders Nos. 10 and 20 do not show favorable results, apparently being too coarse for exhaustive extraction.

4. It has been found that, for cinchona, in maceration experiments, No. 60 powder is of the optimum degree of fineness on a basis of the rate of extraction, the extraction in the first hour being practically as complete as that after 144 hours. With a longer period of maceration, the extraction of No. 40 powder gradually becomes nearly as complete as that of No. 60 and since the No. 60 powder is too fine for percolation, the No. 40 can be used with advantage for such purposes. Nos. 10 and 20 powders show only a partial increase in the rate of extraction and are too coarse for practical purposes. Furthermore, these extraction studies seem to show that there is an equilibrium stage of saturation after which the extraction becomes practically stationary.

5. It has been found that, for cinchona, the use of menstruum in divided portions is more effective for extraction than a single maceration with a large quantity of menstruum.

6. It has been found that, for cinchona, the usual type of ordinary percolator is, for practical purposes, as effective as the narrow tube often used to provide a longer column of drug. In tubes where the menstruum passes as slowly as about one drop per minute through a column of powder more than 40 inches high, in contrast to the usual percolator with a column about 3 inches high, and at a rate of about 25 drops per minute, there is no appreciable difference in the final total extraction. Using a narrow tube, there is a slightly better extraction obtained in the first few fractions, but this advantage is not maintained throughout, the final sum total being about the same in each instance.

The alkaloidal and total extractive content of the various percolate fractions show that the total extractive material is removed more readily than are the alkaloids, the difference, however, not being very great.

REFERENCES.

(1) Husa, W. J., and Huyck, C. L., JOUR. A. PH. A., 24, 448 (1935).
(2) Bull, A. W., *Quart. J. Pharm.*, 8, 378 (1935).
(3) Bull, A. W., *Ibid.*, 8, 378 (1935).

VISITORS AT AMERICAN INSTITUTE OF PHARMACY.

During the month of June the following visited the American Institute of Pharmacy: J. S. Davis, New Orleans, La.; P. G. Brigandi, Washington, D. C.; Miss Daisy Coty, St. Anne, Ill.; Miss Margaret Cregan, Chicago, Ill.; Stewart T. McGee, Piedmont, Calif.; Murray W. Miller, Houston, Texas; J. L. Savage, Charlottesville, Va.; E. K. Weinstein, Roxbury, Mass.; Miss Edna Zimmerman, Fergns Falls, Minn.