SUMMARY.

The effects produced by peimine and peiminine are practically the same. When perfused through the inferior vena cava in frogs, they induce decrease in the heart rate, complete A-V block and periodicity. They cause a fall of blood pressure (cats), and inhibit the activity of isolated rabbits' intestines. There is a moderate hyperglycemic action in rabbits. The minimal lethal dose to white mice, by intravenous injection, of both peimine and peiminine, is 9 mg. per Kg., death being preceded by tonic convulsions.

BIBLIOGRAPHY.

(1) S. C. Li, Pentsao Kang Mu (1596), Chapter 13.
(2) G. A. Stuart, Chinese Materia Medica, American Presbyterian Mission Press, Shanghai (1911) 178.
(3) Botanical Nomenclature, Commercial Press, Shanghai (1917), 474.
(4) S. Yagi, *Kyoto Igaka Zassi*, 10 (1913), 175.
(5) M. Fukuda, *Sci. Repts. Tôhoku Imp. Univ.*, 18 (1929), 323.
(6) T. Q. Chou, *Chinese J. Physiol.*, 6 (1932), 265.

STUDIES IN PERCOLATION.*

A. Anomalies Observed in the Percolation of Cinchona.

BY MILTON WRUBLE.

As one of the first tests of the mechanism of percolation, it seemed desirable to learn something about the nature of the extraction as the menstruum passes down from stratum to stratum in the percolator. The ideal way to carry out this test experimentally on a percolator containing 1000 Gm. of drug, would be to segment the drug in layers of 100 Gm. and stop the tincture at the bottom of each segment. To carry out this idea practically it seemed unsatisfactory to devise a means giving even approximate results. Hence, in place of a single percolator, a number of percolators were used, each representing a hypothetical segment of the larger percolator as suggested above.

The unit adopted for the first test of this scheme was that of 100 Gm. and the unit of percolate to be tested that of 100 cc. Inasmuch as 10 cc. were to be removed from each percolate for the tests planned, it was necessary to charge the second percolator with 90 Gm. of drug and to draw 90 cc. of percolate, to charge the third percolator with 80 Gm. of drug and to draw 80 cc. of percolate, etc.

Cinchona was selected for this experiment, not only because its alkaloidal content could be determined quantitatively with a considerable degree of accuracy even in mere traces, but because this drug presented problems in connection with the keeping qualities of both tincture and fluidextract that were worth while investigating.

The drug in question was obtained from J. L. Hopkins & Co., in December 1930, in powdered form, approximately a No. 20 powder.

Experiment I.—The 100-Gm. batch was moistened with 75 cc. of 95 p. c. alcohol, and the other batches with equivalent amounts. Each such moistened batch was allowed to stand in a closed container for 6 hours before packing in the per-

* Scientific Section, A. Ph. A., Toronto meeting, 1932.

colator. After packing, maceration was allowed to take place for 24 hours before percolation was commenced. In the case of the 100-Gm. batch the drawing off of the percolate lasted approximately 200 minutes. In other cases corresponding periods were allowed.

As already indicated 10 cc. of percolate were set aside in each case. Of this reserved portion, 5 cc. were allowed to evaporate spontaneously at room temperature until of constant weight in order to determine the amount of extractive. The other 5 cc. were used for density determination by means of a pycnometer and for alkaloidal assay. The latter was carried out with modifications,[1] according to the U. S. P. X process described under Fluidextract of Cinchona. The results are herewith tabulated:

Amt. of Drug, Gm.	Rate of Percolation,[1] Minutes.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Total Alkaloids,[2] Wt., Gm.	Total Alkaloids,[2] Per Cent.
100	200	0.852	0.59	13.8	0.02	0.59
90	180	0.864	0.75	17.3	0.01	0.29
80	160	0.876	0.89	20.3	0 008	0.23
70	140	0.876	0.97	22 2	0.01	0.29
60	120	0.866	0.81	18.7	0.02	0.59
50	100	0.856	0.64	14.9	0.02	0.59

[1] The rate was set at as close to ten drops per minute as was possible and from time to time this rate had to be increased or decreased to this figure.

[2] No alkaloidal assay on this bark was made.

Experiment IIa.—A second series of percolators was started, this time using ten and following out the same general scheme as in the first set of experiments. In each case the material was macerated for twenty-four hours in the percolator before the actual percolation, as before.

The results are tabulated as follows:

Amt. of Drug, Gm.	Rate,[1] Minutes.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Total Alkaloids, Wt., Gm.	Total Alkaloids, Per Cent.
100	200	0.835	0.45	10.7	0.03	0 89
90	180	0 856	0.64	14.9	0.02	0.58
80	160	0.863	0.80	18.5	0.02	0.57
70	140	0.884	0.90	20.4	0.02	0.56
60	120	0.880	0.87	19.7	0.02	0.57
50	100	0.868	0.86	19.8	0.03	0.86
40	80	0.866	0.84	18.9	0.07	2.02
30	60	0.885	0.80	18 2	0.05	1.41
20	40	0.887	0.87	19.6	0.06	1.41
10	20	0.863	0.58	13.4	0.06	1.73

[1] The rate was set as close to ten drops per minute as was possible. Invariably the rate slowed down and required frequent attention. In the case of the 100-Gm. and 90-Gm. percolators the percolation stopped several times unexpectedly hence the time in these two cases is approximate.

Experiment IIb.—Extraction was resumed September 24th on the same set of percolators used in Experiment IIa after they had been corked and left standing since June 14th. The same general scheme was followed out in this case as before. The results are tabulated as follows:

[1] No absorbent material was used but the alcoholic extract added directly to the ether-chloroform mixture.

Amt. of Drug, Gm.	Rate, Hours.	Sp. Gr., 20°.	Extractive,[1] Wt., Gm.	Extractive,[1] Per Cent.	Total Alkaloids,[2] Wt., Gm.	Total Alkaloids,[2] Per Cent.
100	18 1/2	0.796	0.15	3.7	0.02	0.63
90	18	0.803	0.30	7.4	0 03	0.93[3]
80	12 1/2	0.814	0.31	7.6	0.04	1.22
70	11 1/4	0.828	0.39	9.4	0.055	1.66
60	9 1/4	0.820	0.44	10.7	0.05	1.52
50	6 3/4	0.830	0.46	11.0	0.05	1.50
40	4	0.840	0.55	13.0	0.06	1.64
30	3 1/4	0.828	0.45	10.8	0.05	1.50
20	2 3/4	0.825	0.37	8.9	0.04	1.21
10	2	0.822	0.47	11.4	0.03	0 91

[1] U. S. P. X method for total extractive, page 466.

[2] U. S. P. X method for total alkaloids, page 453.

[3] No doubt the increases in these alkaloidal contents are due to the maceration period which intervened.

Experiment III.—The same scheme as had been carried out with the smaller quantities was now extended to larger quantities of drug.[1] In the first percolator 1000 Gm. of drug were used, in the second 900 Gm. and so on to the tenth percolator containing 100 Gm. From the percolator containing 1000 Gm., 1000 cc. of tincture were collected, 100 cc. of this amount were reserved and the 900 cc. of the remaining tincture used in percolating the next batch containing 900 Gm. of drug. This was repeated throughout just as was done in the earlier experiments. Ten such series of experiments were made and the determinations carried out as outlined in the U. S. P. X.

p_H determinations were attempted with the use of the quinhydrone electrode in conjunction with a Leeds and Northrup potentiometer set-up. Because of the high alcoholic content of the solutions these values are not to be relied upon.[2] The results of ten such series of extractions are herewith tabulated:

SERIES I.

Amt. of Drug, Gm.	p_H.[1]	Rate, Hours.	Sp. Gr., 20°.	Extractive,[2] Wt., Gm.	Extractive,[2] Per Cent.	Alkaloidal Content,[2] Wt., Gm.	Alkaloidal Content,[2] Per Cent.
1000	3.72	78 3/4	0.8572	0.772	9.05	0.04	1.17
	3.27						
900	3.87	71 1/4	0.8699	1.03	11.09	0.54	1.59
	3.52						
800	4 22	61 1/2	0 8703	1.10	12.50	0.55	1.58
	3.44						
700	3.98	52 3/4	0.8725	1.14	13.00	0.56	1.63
	3.28						
600	3.75	48 1/2	0.8787	1.27	14.50	0.58	1.63
	3.32						
500	3.69	41	0.8685	1.14	13.20	0.53	1.54
	3.32						
400	3.80	34 3/4	0.8691	1.07	12.40	0.53	1.53
	3.77						
300	3.78	22 1/2	0.8691	1.07	12.65	0.48	1.41
	3.73						

[1] Received from J. L. Hopkins & Co. in 1931, No. 20 powder, alkaloidal assay 4.70 p. c., 4.32 p. c. and 4.26 p. c. of total alkaloids in as many assays (U. S. P. X).

[2] It is possible that the apparatus did not admit of the sensitivity that should be required when working under such conditions.

200	4.12 3.73	13 1/2	0.8681	1.14	13.24	0.52	1.50
100	4.26 3.80	7 3/4	0.8761	1.38	15.80	0.61	1.74

[1] The second figures in the p_H column were obtained 72 hours after the first readings were taken.

[2] The total extractive was determined by drying in an oven exactly as outlined in the U. S. P. X and not as was carried out in earlier experiments. Alkaloidal determinations were also made according to U. S. P. X methods.

SERIES II.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt., Gm.	Alkaloidal Content, Per Cent.
1000	3.80 3.15	77 1/4	0.8320	0.310	3.72	0.02	0.60
900	3.90 3.12	72 1/2	0.8555	0.714	8.35	0.031	0.91
800	4.24 3.65	62 3/4	0.8613	0.926	10.67	0.045	1.33
700	4.22 3.73	50 1/2	0.8612	0.911	10.60	0.042	1.24
600	3.92 3.46	47 1/2	0.8616	0.878	10.11	0.035	1.02
500	3.95 3 35	37 3/4	0.8519	0.749	8.75	0.027	0.79
400	3.95 3.25	32 1/4	0.8489	0.685	8.10	0.024	0.71
300	4.02 3.31	24	0.8508	0.743	8.75	0.031	0.93
200	4.15 3.31	10 3/4	0.8549	0.803	9 40	0.028	0.82
100	4.02 3.22	6 1/2	0.8555	0.793	9.30	0.034	0.01

SERIES III.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt., Gm.	Alkaloidal Content, Per Cent.
1000	4.20 3.87	76 1/4	0.8177	0.167	2.05	0.013	0.39
900	3.72 3.73	70	0.8240	0.256	3.10	0.020	0.62
800	3.97 4 05	58 1/2	0.8339	0.437	5.23	0.027	0.81
700	4.04 4.10	51 1/4	0.8335	0.491	5.88	0.033	0.99
600	4.17 3.82	42 1/2	0.8379	0.414	5.95	0.023	0.69
500	3.93 3.68	38 1/2	0.8387	0.512	6.12	0.026	0.78
400	3.76 3.40	30 3/4	0.8334	0.426	5.12	0.038	0.84
300	3.67 3.58	22 1/2	0.8329	0.394	4.72	0.021	0.65
200	3.72 3.47	14 1/2	0.8335	0.434	5.20	0.022	0.68
100	4.21 3.96	8 1/2	0.8349	0.574	6.87	0.025	0.76

SERIES IV.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt., Gm.	Alkaloidal Content, Per Cent.
1000	3.78 3.74	58 3/4	0.8167	0.124	1.52	0.010	0.30
900	3.53 3.57	49 1/2	0.8217	0.234	2.84	0.015	0.47
800	3.53 3.20	44 1/2	0.8312	0.372	4.46	0.023	0.69
700	3.63 3.20	40	0.8337	0.432	5.10	0.021	0.65
600	3.35 3.57	37 1/4	0.8347	[1]		0.025	0.76
500	3.36 3.15	34 1/2	0.8368	0.493	5.90	0.034	0.77
400	3.18 3.07	28 1/2	0.8368	0.477	5.70	0.025	0.79
300	3 22 3.10	23 1/4	0 8323	0.385	4.74	0.024	0.72
200	3.15 3.48	16 3/4	0.8307	0.391	4.72	0.023	0.70
100	3.47 3.48	9	0.8412	0.582	6.90	0.027	0.80

[1] Sample lost.

SERIES V.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt., Gm.	Alkaloidal Content, Per Cent.
1000	3.58 3.52	50 1/2	0.8148	0.095	1.16	0.013	0.41
900	3.29 3.56	44 3/4	0.8210	0.164	2.01	0.015	0.47
800	3.14 3.93	41 1/2	0.8267	0.273	3.32	0.025	0.77
700	3.22 3.88	39 3/4	0.8320	0.387	4.64	0.026	0.79
600	3.54 3.85	36 1/2	0.8344	0.453	5.42	0.020	0.61
500	3.34 3.68	34 1/2	0.8371	0.493	5.88	0.020	0.61
400	3.44 3.87	26 1/4	0.8371	0.514	6.15	0.032	0.97
300	3.23 3.77	22 1/4	0.8336	0.450	5.40	0.021	0.64
200	3.26 3.62	14 3/4	0.8325	0.407	4.88	0.017	0.51
100	3.42 3.75	8 1/2	0.8353	0.472	5.65	0.025	0.76

SERIES VI.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt., Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt., Gm.	Alkaloidal Content, Per Cent.
1000	3.87 4.10	53	0.8131	0.075	0.93	0.009	0.29
900	3.67 4.10	47 1/2	0.8169	0.140	1.70	0.010	0.31

800	3.52 4.23	44 1/2	0.8253	0.235	2.85	0.016	0.48
700	3.26 4.55	41	0.8303	0.382	4.60	0.023	0.54
600	3.34 3.07	36 1/4	0.8349	0.452	5.42	0.021	0.64
500	3.28 3.32	32 3/4	0.8367	0.477	5.70	0.022	0.66
400	3.38 3.35	27 1/4	0.8364	0.531	6.35	0.023	0.71
300	4.13 3.35	23 3/4	0.8345	0.470	5.62	0.023	0.70
200	3.55 3.75	17 3/4	0.8343	0.478	5.72	0.022	0.67
100	3.61 3.87	8 3/4	0.8336	0.425	5.10	0.023	0.69

SERIES VII.

Amt. of Drug, Gm.	p_H.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt. Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt. Gm.	Alkaloidal Content, Per Cent.
1000	3.32 3.67	52 1/2	0.8096	0.058	0.72	0.008	0.24
900	3.28 3.80	45 1/2	0.8145	0.119	1.46	0.012	0.37
800	2.98 3.87	43	0.8188	0.197	2.40	0.016	0.59
700	3.00 3.62	41 3/4	0.8242	0.300	3.63	0.020	0.62
600	3.45 3.47	37 1/4	0.8296	0.427	5.18	0.024	0.72
500	3.23 3.65	34 1/4	0.8320	0.463	5.45	0.026	0.78
400	3.26 3.42	25 3/4	0.8345	0.521	6.25	0.027	0.81
300	3.22 3.50	22 1/2	0.8336	0.512	6.15	0.027	0.82
200	3.42 3.38	19 1/4	0.8298	0.428	5.12	0.026	0.79
100	3.49 3.43	7 3/4	0.8318	0.457	5.50	0.028	0.86

SERIES VIII.

Amt. of Drug, Gm.	Rate, Hours.	Sp. Gr. 20°.	Extractive, Wt. Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt. Gm.	Alkaloidal Content, Per Cent.
1000	50 3/4	0.8098	0.043	0.54	0.008	0.24
900	44 1/2	0.8138	0.115	1.42	0.017	0.32
800	41 1/2	0.8175	0.183	2.23	0.0125	0.38
700	37 1/2	0.8226	0.275	3.33	0.0200	0.60
600	34 1/4	0.8302	0.415	5.00	0.022	0.68
500	30	0.8321	0.483	5.80	0.025	0.74
400	27 1/4	0.8346	0.570	6.82	0.027	0.82
300	23 1/2	0.8352	0.565	6 70	0.022	0.67
200	18 1/4	0.8342	0.535	6.40	0.026	0.79
100	8 1/2	0.8386	0.584	7.00	0.028	0.83

SERIES IX.

Amt. of Drug, Gm.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt. Gm.	Extractive, Per Cent.	Alkaloidal Content. Wt. Gm.	Alkaloidal Content. Per Cent.
1000	44 1/2	0.8183	0.038	0.47	0.008	0 24
900	41 1/4	0.8198	0.075	0.92	0.0085	0.26
800	37 1/4	0.8229	0.1345	1.63	0.0130	0.39
700	34	0.8268	0.209	2.53	0.0190	0.59
600	32 1/2	0.8298	0.282	3.39	0.022	0.66
500	31 1/4	0.8373	0.408	4.87	0.024	0.72
400	26 3/4	0.8414	0.484	5.72	0.025	0.75
300	21 1/2	0.8519	0.736	8.65	0.031	0.90
200	11 1/2	0.8706	0.890	9.30	0.031	0.90
100	6	0.8598	0.763	8.90	0.029	0.86

SERIES X.[1]

Amt. of Drug, Gm.	Rate, Hours.	Sp. Gr., 20°.	Extractive, Wt. Gm.	Extractive, Per Cent.	Alkaloidal Content, Wt. Gm.	Alkaloidal Content, Per Cent.
1000	46 1/2	0.8162	0.038	0.46	0.006	0.18
900	40	0.8171	0.075	0.90	0.012	0.28
800	37 3/4	0.8213	0.119	1.44	0.016	0.48
700	33	0.8239	0.187	2.23	0.017	0.50
600	31 1/2	0.8224	0.190	2.32	0.013	0.39
500	27 3/4	0.8323	0.321	3.85	0.040	0.49
400	25 1/2	0.8310	0.355	4.26	0.022	0.66
300	20	0.8406	0.548	6.62	0.026	0.79
200	10 3/4	0.8403	0.472	5.62	0.016	0.47
100	7 1/4	0.8373	0.479	5.72	0.021	0.62

[1] The ninth and tenth series in these experiments were run after an approximately three-month period of rest.

Discussion.—From these many results it is to be noted that certain anomalies are present. In every series the maximum point is reached followed by a decrease. Such results are not readily explainable. No doubt, however, certain surface phenomena, such as adsorption, absorption and perhaps others of which we know little, are responsible in a great measure for this anomaly.

Errors.—These experiments presented a number of difficulties in technique some of which were only realized during the procedure. It must be admitted that at their best they represent only an approach to ideal conditions. While as many of the variables in percolation were controlled as nearly as possible to be identical in each of the ten percolators, it was found quite impossible to maintain them at comparative rates of flow for any length of time. The rates would generally decrease after being adjusted, sometimes increase and in a number of instances stop flowing altogether.

Where the rate decreased it was adjusted to run faster so that the final volumes in all percolators would be collected at comparative rates and if it increased the percolator was allowed to run slower in like manner. If a percolator stopped and was not noticed soon thereafter (this did not occur frequently), the rate at which it was set was determined by the judgment developed in carrying out the rather large number of extractions.

Percolators were started at approximately the same time each morning and stopped at a fixed time every day. Experimentation was not interrupted at any

other time but was carried out seven days a week. Here again, the ideal manner of conducting such extractions would have been to continue percolation from the very beginning without a single interruption. While we may assume that the intervening maceration periods, having been the same in each case would tend to equalize this error, it must not be forgotten that during these macerations numerous changes took place. (See Series IX and X.)

Throughout the many months in which these experiments were conducted the changes in temperature[1] must have affected the solubility of the constituents more or less. Some of the latter series were made in the warmer months of the year, the earlier in the fall months while those in between during the winter months. The room temperature during these various periods of the year must of necessity have varied somewhat.

In spite of the errors that have been enumerated it is believed that inasmuch as the large number of extractions made show strikingly the repetition that has already been pointed out, we can feel justified in believing that such an anomaly exists in the case of cinchona.

It was only after the experimental results had been tabulated that Searby's discussion of Seifert's paper on "interrupted" percolation (*Proc. Cal. Pharm. Soc.*, 22 (1892), 125) came to the notice of the writer. When a year ago the anomalies observed were discussed with Professor Wilbur Scoville and Dr. F. O. Taylor of Parke, Davis & Co., both stated that they had observed them in factory practice. Inasmuch as their observations have not been published, hence their data are not available, it seemed best to complete the series of experiments recorded above and to report in detail. No one appears to have attempted an explanation of these anomalies thus far. It certainly is imperative that they be given due consideration even though they complicate a situation already sufficiently difficult of understanding.

WISCONSIN PHARMACEUTICAL EXPERIMENT STATION.

[1] Goris, who has recently made a comprehensive theoretical analysis of percolation, states in this connection: *"Il est surtout important au cours d'une lixiviation, d'éviter les changements de temperature."* (*Bull. des Sciences Pharmcol.*, 26 (1919), 477.)

STRYCHNINE POISONING.

M. C. Wheelock (*J. A. M. A.*, 99 (1932), 1862) reports on a case of attempted suicide in which probably about 1 grain of strychnine sulphate was taken as recorded, in which the patient ultimately recovered under prompt treatment with sodium phenobarbital and sodium amytal. The immediate treatment, twenty minutes after the first seizure, was the administration of 5 grains of phenobarbital by hypodermic injection. Subsequent to this, any attempt to move the patient caused violent convulsions; 5 grains more sodium barbital was then injected by vein but without complete relief. Therefore, 15 grains of sodium amytal, dissolved in 10 cc. of water, was injected intravenously at the rate of 1 cc. a minute. The patient was sound asleep in ten minutes and could then be moved to bed. There were only slight spasms during the subsequent day. Further treatment consisted in the administration of the three bromides. Subsequently recovery was uneventful. No attempt was made to wash the stomach. The antidotal action of phenobarbital sodium on experimental strychnine poisoning in animals has been recorded previously, but no case of its use for this purpose in man has been recorded. In this one case the results were so dramatic as to suggest that the remedy should at least be tried when needed.—Through *Quarterly Journal of Pharmacy.*