

- (28) Fairthorne, R. F., *Am. J. Pharm.*, 54, 236 (1882).  
(29) Merrell, A., cited by Whitebread, C., *JOUR. A. PH. A.*, 26, 923 (1937).  
(30) Thomson, W. M., *Am. J. Pharm.*, 55, 537 (1883).  
(31) Beard, J. G., *JOUR. A. PH. A.*, 7, 964 (1918).  
(32) Macheboeuf, M. A., and Fethke, N., *Bull. soc. chim. biol.*, 15, 796 (1933); through *Chem. Abstr.*, 27, 5220 (1933).  
(33) Anon., *Pharm. Ztg.*, 79, 635 (1934).  
(34) Kessler, E., *Süddeut. Apoth.-Ztg.*, 75, 437 (1935); *Pharm. Ztg.*, 80, 1080 (1935).  
(35) Flowers, H., *PROC. A. PH. A.*, 58, 1252 (1910).  
(36) Hänle, C. F., *Magazin für die Pharmacie*, 11, 57 (1825).  
(37) Rosenwasser, N., *Am. J. Pharm.*, 53, 567 (1881).  
(38) Berry, cited by Wiegand, T. S., *Ibid.*, 55, 587 (1883).  
(39) Cohn, A. I., *Merck's Report*, 8, 4 (1899).  
(40) Husa, W. J., and Magid, L., *JOUR. A. PH. A.*, 23, 1190 (1934).  
(41) Peck, W. C., *Quart. J. Pharm. Pharmacol.*, 9, 401 (1936).  
(42) Kessler, E., *Pharm. Ztg.*, 81, 1308 (1936).  
(43) Breddin, H., *Ibid.*, 82, 78 (1937).

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## DRUG EXTRACTION. XX. THE EFFECT OF VACUUM ON THE PERCOLATION OF BELLADONNA ROOT.\*<sup>1</sup>

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In a previous study (1) it was found that the application of vacuum did not affect the efficiency of extraction of belladonna root in a maceration process.

Further research has been carried out to determine the efficiency of ordinary percolation of belladonna root as compared with a process of vacuum maceration in a percolator followed by ordinary percolation.

### EXPERIMENTAL PART.

The drug and menstruum used and the methods of analysis were the same as in a previous study (1). In all experiments reported in this paper the drug was introduced into the percolators in small portions with slight agitation to promote even distribution, and after all the drug had been thus introduced it was packed from the top, starting with light pressure which was gradually increased.

*Experiment 1.*—A 250-Gm. portion of moderately coarsely powdered belladonna root was packed in the dry state in a pyrex glass tube 64 cm. in length and 4 cm. in internal diameter. The tube containing the dry drug was evacuated to a pressure of 9 mm. of mercury for thirty minutes, by means of a vacuum pump connected to the receiving flask. The menstruum was then added under reduced pressure. When the menstruum reached the lower orifice of the percolator tube air was admitted and the mixture allowed to macerate for twenty-four hours at atmospheric pressure. Percolation was then carried out at atmospheric pressure, two successive 125-cc. portions of percolate being collected. The experiment was carried out in duplicate and at the same time two controls were conducted, following the same procedure except that vacuum was not used.

In each case the volume of the packed drug was 505 cc. and the length of the drug column was between 37 and 38 cm. In the vacuum experiments the liquid reached the lower orifice in about 210 minutes while in the controls a time of about 1415 minutes was required. The rate of flow was 0.6 to 0.7 cc. per minute in the vacuum experiments and about 0.3 cc. per minute in the controls.

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<sup>1</sup> This paper is based on part of a dissertation presented to the Graduate Council of the University of Florida by George R. Jones, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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TABLE I.—PERCOLATION OF BELLADONNA ROOT WITH AND WITHOUT PREVIOUS VACUUM MACERATION.

	Total Alkaloids Extracted in Gm.				Total Extractive in Gm.			
	Vacuum.		Control.		Vacuum.		Control.	
	A.	B.	C.	D.	A.	B.	C.	D.
First fraction	1.02	1.01	1.12	1.16	20.7	20.4	22.0	21.7
Second fraction	0.06	0.06	0.00	0.00	14.7	15.0	13.6	16.1
Total	1.08	1.07	1.12	1.16	35.4	35.4	35.6	37.8

From the results in Table I it appears that vacuum maceration has no beneficial effect on the extraction. In the controls more alkaloids and more total extractive were extracted than in the vacuum experiments. A much longer time was required for the first menstruum to reach the lower orifice in the controls than in the vacuum experiments, thus allowing a longer time in the controls for the liquid to dissolve the plant constituents. It was intended to have a rate of flow of 0.6 to 0.7 cc. per minute in all cases but the vacuum experiments were completed first and it was later found that the controls would not percolate faster than about 0.3 cc. per minute.

*Experiment 2.*—In order to duplicate the results of Experiment 1 under conditions of equal rates of flow in all tubes the entire experiment was repeated. In the vacuum experiments the liquid reached the lower orifice in about 120 minutes while in the controls a time of about 1415 minutes was required. In all cases the rate of flow was about 0.2 cc. per minute for the first fraction and about 0.29 cc. per minute for the second fraction. The other details were the same as in Experiment 1 except that the collection of percolate was interrupted for fourteen and one-half hours between the collection of the first and second percolates.

TABLE II.—PERCOLATION OF BELLADONNA ROOT WITH AND WITHOUT PREVIOUS VACUUM MACERATION.

	Total Alkaloids Extracted in Gm.				Total Extractive in Gm.			
	Vacuum.		Control.		Vacuum.		Control.	
	A.	B.	C.	D.	A.	B.	C.	D.
First fraction	1.07	1.08	1.11	1.12	20.5	20.0	20.1	19.1
Second fraction	0.08	0.08	0.00	0.00	16.5	17.2	15.2	16.2
Total	1.15	1.16	1.11	1.12	37.0	37.2	35.3	35.3

In Tables I and II it is seen that in the controls the second fraction of percolate was free from alkaloids while in the vacuum experiments the second fraction contained some alkaloids. This fact indicates definitely that extraction of alkaloids was more rapid in the controls than in the vacuum experiments. In the controls the first menstruum passed through the column of packed drug much more slowly than in the vacuum experiments, thus giving the menstruum in the controls more time to dissolve the plant constituents, or bringing about more efficient displacement of the first and most concentrated percolate.

*Experiment 3.*—It is interesting to note in Tables I and II that in the controls, using ordinary percolation in cylindrical glass tubes, all of the alkaloidal content was extracted in the first 125 cc. of percolate from 250 Gm. of drug. The first fraction of percolate was thus equivalent in alkaloidal content to a double-strength fluidextract. It was thus demonstrated that in the case of belladonna root, it is possible to prepare a standard fluidextract by ordinary percolation without collection of any weak percolate whatever.

Further experiments were carried out to determine whether a similarly high efficiency of extraction could be attained in ordinary percolation in an Oldberg percolator. The Oldberg percolators used were 56.5 cm. in length and 11.3 cm. in internal diameter at the widest part. In some cases the drug was packed in the dry state and in other tests the drug was moistened with 25 cc. of menstruum per 100 Gm. of drug and allowed to macerate for fifteen minutes before packing.

In each case 1200 Gm. of drug were packed in a percolator and twelve hours was allowed for maceration after the liquid reached the lower orifice. The percolate was collected in three

successive 600-cc. fractions, the rate of flow being 0.6 to 1.0 cc. per minute for the first fraction and about 1.0 cc. per minute for the second and third fractions. Percolation was stopped for fourteen and one-half hours between the collection of the various fractions. For the drug packed in the dry state the volume of the packed drug was about 2300 cc., the length of the drug column was about 32 cm. and about 850 minutes were required for the first liquid to reach the lower orifice. For the moistened drug the volume of packed drug was about 3150 cc., the length of the drug column was about 41 cm., and about 320 minutes were required for the first liquid to reach the lower orifice. The experiments were conducted in duplicate.

TABLE III.—ORDINARY PERCOLATION OF BELLADONNA ROOT IN OLDBERG PERCOLATORS.

	Total Alkaloids Extracted in Gm.				Total Extractive in Gm.			
	Packed after Moistening.		Packed Dry.		Packed after Moistening.		Packed Dry.	
	A.	B.	C.	D.	A.	B.	C.	D.
First fraction	5.14	4.95	5.08	5.18	79.2	82.7	87.3	77.7
Second fraction	0.24	0.45	0.18	0.17	83.0	91.4	66.1	54.2
Third fraction	0.02	0.07	0.03	0.14	53.5	53.1	57.7	58.9
Total	5.40	5.47	5.29	5.49	215.7	227.2	211.1	190.8

The data in Table III indicate that in percolating belladonna root in ordinary percolators the rate of extraction of alkaloids was not as rapid as that observed in cylindrical glass tubes. In ordinary percolators there was an important proportion of alkaloids in the second fraction and a small proportion of alkaloids in the third fraction or weak percolate. However, the results obtained show that the first 1200 cc. of percolate from 1200 Gm. of drug is capable of yielding a fluidextract of U. S. P. XI alkaloid content provided the drug used is very slightly above U. S. P. requirements as to alkaloidal content.

## DISCUSSION OF RESULTS.

*Vacuum Maceration Preparatory to Percolation.*—In the historical review of a previous paper by the present authors (1) it was shown that vacuum maceration preparatory to percolation has been advocated from time to time for many years. A recent advocate is Kessler (2), whose so-called evacolation process is essentially a percolation procedure in a single cylindrical tube, using vacuum maceration and an evacuated receiver, with careful regulation of the flow of menstruum into the percolator. In spite of the numerous advocates of vacuum methods there is surprisingly little data in the literature in which exact comparisons are made of the vacuum processes with simple percolation.

The results of the present study show that vacuum maceration preparatory to ordinary percolation gives less efficient extraction than when ordinary maceration is employed. Our results are in accord with the fact that vacuum percolators which were patented years ago have not continued in general use in drug extraction on a factory scale. In earlier work of Husa and Yates (3) it was likewise found that vacuum maceration conducted in a different manner was of no benefit.

*Preparation of Fluidextracts without Collection of Weak Percolate.*—It was previously shown by Husa and Huyck (4) that fluidextract of belladonna could be prepared without collection of weak percolate by percolation under pressure through a long column of drug. In the present paper the same objective has been attained in ordinary percolation in cylindrical glass tubes and the same result has been closely approached in ordinary percolators. It is unlikely that every drug would yield a fluidextract without collection of weak percolate since some drugs are more

difficult to extract than others. However, the results obtained indicate that ordinary percolation can be made more efficient than has been generally thought and that in some cases, at least, a fluidextract can be made without collection of weak percolate and without resorting to fractional percolation.

*Proportion of Moistening Liquid.*—The results indicating that extraction of the alkaloids of belladonna root is equally efficient when the drug is packed dry or moistened with 25 cc. of menstruum per 100 Gm. of drug are in accord with earlier work of Husa and Yates (3). It was previously shown (3), however, that excessive quantities of moistening liquid reduce the efficiency of percolation.

#### SUMMARY.

Vacuum maceration preparatory to percolation has been advocated from time to time for many years but surprisingly little data has been published in which exact comparisons are made of the vacuum processes and ordinary percolation.

The results of the present study indicate that vacuum maceration preparatory to ordinary percolation gives less efficient extraction than when ordinary maceration is employed.

It has been found that a full strength fluidextract of belladonna root can be prepared by ordinary percolation in a cylindrical glass tube without collecting weak percolate or resorting to fractional percolation.

#### REFERENCES.

- (1) Husa, W. J., and Jones, G. R., *JOUR. A. PH. A.*, 27, 852 (1938).
- (2) Kessler, E., *Süddeut. Apoth.-Ztg.*, 75, 437 (1935); *Pharm. Ztg.*, 80, 1080 (1935).
- (3) Husa, W. J., and Yates, S. B., *JOUR. A. PH. A.*, 24, 615 (1935).
- (4) Husa, W. J., and Huyck, C. L., *Ibid.*, 27, 290 (1938).

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## DRUG EXTRACTION. XXI. THE EFFECT OF VACUUM IN THE EXTRACTION OF CINCHONA.\*<sup>1</sup>

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In earlier papers by the present authors it was found that the application of vacuum in several ways was of no benefit in the extraction of belladonna root by maceration or percolation (1), (2). In the present paper a report is given of experiments on the use of vacuum in the extraction of cinchona. If reduced pressure has any general beneficial effect on the extraction of drugs it seems that it should be discernible in the extraction of belladonna, which contains a small proportion of alkaloids which are relatively easy to extract, or in cinchona which contains a high percentage of alkaloids which are comparatively difficult to extract completely.

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<sup>1</sup> This paper is based on part of a dissertation presented to the Graduate Council of the University of Florida by George R. Jones, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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