

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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## EXPERIMENTAL PART.

*Materials Used.*—All of the drug used was from a thoroughly mixed fifty-pound portion of moderately coarsely powdered yellow cinchona containing 8.26 per cent of alkaloids and 8.95 per cent of moisture. The menstruum used was a mixture of 100 volumes of glycerin, 100 volumes of diluted hydrochloric acid and 800 volumes of alcohol as Menstruum I, and a mixture of 4 volumes of alcohol and 1 volume of distilled water as Menstruum II, as specified in the U. S. P. X for fluidextract of cinchona.

*Analytical Methods.*—Alkaloids were determined by the U. S. P. X assay for fluidextract of cinchona, using asbestos fiber as the absorbent. Determinations of moisture and total extractive and calculations of imbibed liquid were made as in a previous study (1).

*Experiment 1. Effect of Vacuum Maceration Previous to Percolation.*—Portions of 300 Gm. each of moderately coarsely powdered yellow cinchona were packed in cylindrical glass tubes 64 cm. long and 4 cm. in internal diameter. The drug in the dry state was introduced into the percolator in small portions with slight agitation of the percolator to promote even distribution, and after all the drug was in the percolator it was packed from the top, starting with light pressure which was gradually increased. This method of packing was used for all the vacuum experiments. In the controls it was found that the menstruum would not pass through the drug column and it was necessary to omit forcible packing. In the vacuum experiments the pressure in the tubes containing the dry drug was reduced to 8 mm. of mercury for thirty minutes by means of a vacuum pump attached to the receiving flask. The menstruum was then added under reduced pressure. When the first menstruum reached the lower orifice air was allowed to enter and the mixture was macerated for seventeen hours at atmospheric pressure. Percolation was then carried out at atmospheric pressure, three successive 150-cc. portions of percolate being collected. The experiment and a control without vacuum were conducted in duplicate.

The tightly packed drug in the vacuum experiments had a volume of about 535 cc. and the length of the drug column was about 41 cm. The less tightly packed drug in the controls had a volume of about 665 cc. and the length of the drug column was about 49.5 cm. It seemed desirable to retain the tight packing in the vacuum experiments since the menstruum was able to pass through the drug column with sufficient rapidity under these conditions. In the vacuum experiments the liquid reached the lower orifice in about 255 minutes while in the controls a time of about 1860 minutes was required.

TABLE I.—PERCOLATION OF YELLOW CINCHONA WITH AND WITHOUT PREVIOUS VACUUM MACERATION.

	Rate of Flow of Percolate in Cc. per Minute.							
	Vacuum.		Control.					
	A.	B.	C.	D.				
First fraction	0.11	0.07	0.26	0.17				
Second fraction	0.19	0.10	0.48	0.27				
Third fraction	0.28	0.17	0.51	0.36				
	Total Alkaloids Extracted in Gm.				Total Extractive in Gm.			
	Vacuum.		Control.		Vacuum.		Control.	
	A.	B.	C.	D.	A.	B.	C.	D.
First fraction	7.37	7.34	7.27	7.14	48.4	47.1	47.3	45.2
Second fraction	5.33	5.32	4.84	6.05	32.7	34.9	31.9	36.7
Third fraction	3.16	3.53	3.23	2.98	18.1	20.6	18.2	16.5
Total	15.86	16.19	15.34	16.17	99.2	102.6	97.4	98.4

The results in Table I indicate that vacuum maceration previous to percolation is of no benefit in the extraction of yellow cinchona, the differences between the vacuum experiments and the controls being within the experimental error.

*Experiment 2. Effect of Vacuum in Extraction by a Maceration Process.*—In the percolation of drugs many factors, such as the rate at which the menstruum is added to the drug and the rate at which the percolate is collected, must be considered. In maceration with an excess of menstruum such factors as mentioned are eliminated, hence more definite conclusions can be drawn as to the effect of other factors, such as reduced pressure, on the efficiency of extraction.

Four hundred grams of moderately coarsely powdered yellow cinchona were placed in a five-liter, round-bottomed flask. The flask was fitted with a two-holed rubber stopper in which was placed a separatory funnel and a glass tube for connection to the vacuum pump. The flask was evacuated for thirty minutes to a pressure of 12 mm. of mercury. Sixteen hundred grams of menstruum I were gradually added through the separatory funnel to the evacuated drug, with occasional shaking, taking fifteen minutes for the addition of the menstruum. When all the menstruum had been added the vacuum gage showed a pressure of 45 mm. of mercury. Air was then allowed to enter the flask and the contents were thoroughly shaken. The mixture was allowed to stand at atmospheric pressure for ten minutes with occasional shaking. A partial vacuum (pressure of 45 to 50 mm. of mercury) was applied for ten minutes, with occasional shaking. The mixture was then allowed to stand at atmospheric pressure for ten minutes after which a partial vacuum was reapplied for ten minutes. The mixture was filtered and the macerate weighed. The damp marc was also weighed. The above procedure and a control using no vacuum were carried out in duplicate.

TABLE II.—EFFECT OF REDUCED PRESSURE ON EXTRACTION AND IMBIBITION OF 400-GM. PORTIONS OF YELLOW CINCHONA.

Liquid Imbibed in Marc.	Dry Marc.	Weight in Gm. of		Total Extractive.	Total Alkaloids.
		Macerate.	Loss of Menstruum.		
A. Vacuum Experiments.					
883.8	188.2	881.5	36	176.0	14.36
829.1	187.9	928.0	37	176.3	15.06
<b>Av.</b> 856.5	188.1	904.8	36.5	176.2	14.71
B. Controls (No Vacuum).					
869.9	188.6	926.5	0	175.6	13.74
832.0	178.0	973.0	1	186.2	15.22
<b>Av.</b> 850.9	183.3	949.8	0.5	180.9	14.48

From Table II it is seen that the use of vacuum is of no benefit in the extraction of yellow cinchona, the differences between the averages of the vacuum experiments and the controls being within the experimental error.

#### DISCUSSION OF RESULTS.

*Effect of Vacuum on Extraction by Maceration.*—The results indicating that vacuum is of no benefit in the extraction of yellow cinchona in a maceration process are in accord with earlier results on belladonna root (1). Taken together these results show rather conclusively that the application of vacuum is not of general benefit in extraction by maceration.

*Effect of Vacuum on Imbibition.*—In accordance with earlier results on belladonna root (1) it was found that vacuum maceration with an excess of liquid does not increase the proportion of menstruum imbibed by the drug. It may be possible that larger pieces of vegetable tissue, such as chips or blocks, would imbibe a greater amount of liquid in vacuum maceration but such is definitely not the case with the powdered drugs which were studied. However, it was noticed that in vacuum maceration with an excess of liquid the drug appeared to settle better than in the controls. Since this is not due to a greater quantitative absorption of menstruum it may possibly be due to removal of adsorbed air from the surface of the drug particles.

*Effect of Vacuum Maceration Preparatory to Percolation.*—The present results indicate that vacuum maceration preparatory to percolation is not beneficial in the case of yellow cinchona. Similar results were obtained by the present authors in

research on belladonna root (2). The results on yellow cinchona are in accord with the results of Büchi and Feinstein (3) who found that slight variations of the evacuation process gave results on cinchona which were inferior in some cases and equal in other cases to the results obtained by ordinary percolation.

*Loss of Menstruum.*—It is to be expected that in using vacuum there will be a greater loss of menstruum than occurs at atmospheric pressure and this expectation is borne out by the experimental data. Because of this loss of menstruum and the expense of operating vacuum pumps it is clearly inadvisable to use vacuum in drug extraction, particularly since no real advantage can be demonstrated relative to efficiency of extraction.

#### SUMMARY.

Experiments show that the application of vacuum in several ways does not increase the efficiency of extraction of yellow cinchona by maceration or percolation. Various authors have presumed that vacuum maceration increases the proportion of menstruum imbibed by the drug but quantitative studies show that this process does not increase imbibition in the case of yellow cinchona. These results are in accord with earlier results by the present authors on belladonna root. Taken together, these results indicate rather conclusively that the application of vacuum is of no general advantage in drug extraction. Disadvantages of vacuum methods are the greater loss of menstruum and the cost of operating the vacuum pumps.

#### REFERENCES.

- (1) Husa, W. J., and Jones, G. R., *Jour. A. Ph. A.*, 27, 852 (1938).
- (2) Husa, W. J., and Jones, G. R., *Ibid.*, 27, 859 (1938).
- (3) Büchi, J., and Feinstein, K., *Pharm. Acta Helv.*, 11, 121, 341 (1936).

## PREPARATION OF ALPHA-PHENYLALKANOIC ACIDS AND A STUDY OF THEIR BACTERICIDAL AND PHYSICAL PROPERTIES.\*

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Many organic acids are known to possess some antiseptic and germicidal power, and attempts have been made at various times to correlate both the structure and the physical properties of some of these acids with their bactericidal action. Kuroda and others (1) have found that certain acids were effective antiseptics in dilute solutions if the  $p_H$  was below 4.5, but were ineffective in the neutral range. Daniel and Lyons (2) found that, in an homologous series of acids, there was some correlation between bactericidal power and oil-water distribution, solubility and adsorption on charcoal.

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