SCIENTIFIC SECTION

DRUG EXTRACTION. III. THE FUNCTION OF PRELIMINARY MACERATION IN RELATION TO THE PERCOLATION OF BELLADONNA ROOT.[1,2]

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As a part of the general study of the fundamental principles of drug extraction, which is being carried out in the Department of Pharmacy of the University of Florida, some of the factors influencing the extraction of belladonna root have been studied. The work reported in this paper deals with the function of maceration, both before and after packing the drug in the percolator, in relation to the percolation of belladonna root.

HISTORICAL REVIEW.

Variations in U. S. P. Percolation Methods.—Since the introduction of the process of percolation in the U. S. P. of 1840, changes have been made in the time of maceration.

TABLE I.—VARIATIONS IN TIME OF PRELIMINARY MACERATION IN U. S. P. PERCOLATION METHODS.

U. S. P.	Time of Maceration. Before Packing.	After Packing.
1840	24 hours	0
1850	0 to 14 days	0
1860	0	0
1870*	0	4 days
1880	0	48 hours
1890	0	48 hours
1900	0	48 hours
1910*	6 hours	48 hours
1920*	6 hours	48 hours

* Type processes are given.

Moistening and Maceration before Packing.—The moistening and preliminary maceration of a drug is one of the established steps in percolation. According to Couch (1) the purpose of preliminary maceration is to assist in packing, to allow a modification of the drug constituents and to insure the saturation of every particle of drug with menstruum so that the actual percolation may affect all the drug evenly.

In 1833 the Boullays, father and son (2), recommended that the drug be packed dry in the percolator. Dausse (3) in 1836 suggested that the powdered drug be moistened with half its

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[2] This paper is based on a thesis presented to the Graduate Council of the University of Florida by S. B. Yates, in partial fulfilment of the requirements for the degree of Master of Science in Pharmacy.

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weight of cold water, and allowed to macerate for several hours before introducing it into the apparatus for extraction. In 1841 Deane (4) stated that no further maceration was required than might be necessary to complete the swelling process. Procter (5) recommended maceration before packing when using aqueous or weakly alcoholic menstrua, but not when percolating with alcohol or ether. In 1889 J. U. Lloyd (6) advocated that, in percolation with hydro-alcoholic menstrua, the drug be macerated with water alone and that the alcohol necessary to bring the menstruum up to the proper strength be added just before packing.

In 1904 experiments were reported from Greenish's laboratory by Hooper (7) who moistened 200-Gm. portions of belladonna root with 50-, 100- and 150-cc. portions of menstruum. It was found that extraction was most rapid when 50 cc. of menstruum was used to moisten 200 Gm. of drug. Later experiments by Todd (8) in which 100 Gm. of belladonna root in No. 40 powder was packed dry, and further 100-Gm. portions moistened with 50 cc. and 100 cc., respectively, of menstruum, showed that most rapid extraction resulted from dry packing.

Bennett and Cocking (9) stated that "It is generally agreed that in small scale operations percolation proceeds more evenly, and consequently a drug is exhausted more quickly when a relatively small quantity of menstruum is used to moisten it."

Recently the purpose and necessity of the moistening and maceration of the drug prior to packing has been questioned by W. L. Scoville (10).

Maceration after Packing in the Percolator.—In 1864 Procter (11) approved of long maceration after packing the drug in the percolator. Likewise, Savage (12) in the same year showed by experiments with calumba, catechu, cinchona, cinnamon, gentian, myrrh, opium and rhubarb that long maceration produces a much more saturated first percolate. Campbell (13) in 1869 stated that the process of percolation is dependent on the important step of maceration. He moistened and packed the drug and allowed it to macerate for 4 days in a conical percolator, previous to percolation. Taylor (14) in 1869 carried out experiments which indicated that long maceration was an important requirement for thorough and complete exhaustion of a drug by percolation.

Vacuum Maceration.—In 1869 Duffield (15) advanced the idea that a more perfect maceration could be obtained if the ground drug were placed in a strong cylinder, the air pumped out, and the requisite amount of menstruum admitted. He stated that "... the pores of the comminuted drug give up the air enclosed in them, and when the menstruum is allowed to flow in, it is forced into these pores by the pressure of the air outside."

EXPERIMENTAL PART.

The drug used was from a 125-pound shipment of belladonna root previously described (16).

Variation in the Amount of Moistening Liquid.—Comparative percolations were carried out on 100-Gm. portions of belladonna root in No. 40 powder, using varying amounts of menstruum for moistening the drug, but keeping all other factors as nearly constant as possible. The U. S. P. process for the preparation of the fluidextract was followed, using the menstruum of alcohol five volumes—water one volume, but with the variation that 80 cc. of reserve percolate was set aside in each case and further percolates collected in successive 100-cc. portions. The quantities of menstruum used in moistening the various 100-Gm. portions of the drug were as follows: 0, 25 cc., 60 cc. and 90 cc. Otherwise the U. S. P. details were followed, *i. e.*, the drug was allowed to macerate for 6 hours before packing in the percolator and 48 hours after packing. The successive percolates were collected without interruption.

TABLE II.—EFFECT ON PERCOLATION OF THE AMOUNT OF LIQUID USED IN MOISTENING BELLADONNA ROOT FOR PRELIMINARY MACERATION.

A. Gm. of Alkaloid in Various Portions of Percolate.

Percolates.	0.*	25 Cc.*	60 Cc.*	90 Cc.*
80 cc.	0.411	0.434	0.460	0.281
100 cc.	0.030	0.026	0.054	0.164
100 cc.	0.004	0.008	0.006	0.006
100 cc.	0.000	0.000	0.000	0.000
100 cc.	0.000	0.000	0.000	0.000
Totals	0.445	0.468	0.520	0.451

* Quantity of menstruum used in moistening 100 Gm. of drug for preliminary maceration.

B. Gm. of Total Extractive Contained in the Various Percolates.

Percolates.	0.*	25 Cc.*	60 Cc.*	90 Cc.*
80 cc.	11.19	10.05	8.38	7.55
100 cc.	8.41	8.43	8.95	7.45
100 cc.	2.40	3.10	3.63	4.02
100 cc.	0.95	1.24	1.54	1.99
100 cc.	0.59	0.65	0.78	1.09
Totals	23.54	23.47	23.28	22.10

* Quantity of menstruum used in moistening 100 Gm. of drug for preliminary maceration.

C. Per Cent of Total Alkaloid Contained in:

Quantity of Menstruum Used for Moistening 100 Gm. of Drug.	First Percolate.	First 2 Percolates.	First 3 Percolates.
0	92.4	99.1	100.0
25 cc.	92.7	98.3	100.0
60 cc.	88.5	98.9	100.0
90 cc.	62.3	98.7	100.0

The results in Table II indicate that the rate of extraction of alkaloid is equally rapid when no liquid is used for moistening and when 25 cc. is used for 100 Gm. of drug. Using 60 cc. there is a slight reduction in yield of alkaloid in the first percolate and using 90 cc. there is a material reduction. In each case all the alkaloid is contained in the first 280 cc. of percolate. The yield of total extractive in the reserve percolate varies inversely with the quantity of moistening liquid used.

The Function of Maceration before and after Packing in Relation to Percolation of Belladonna Root.—The object of the following experiment was to determine the effect of varying the time of maceration, both before and after packing in the percolator, on the rate of extraction of belladonna root.

100-Gm. portions of belladonna root in No. 40 powder were percolated by the U. S. P. method for the preparation of fluidextract of belladonna root but varying the time of maceration as will be indicated; 80 cc. of reserve percolate was collected in each case in ten hours and set aside, after which successive portions of 100 cc. of percolate were collected, three hours being taken for collection of each portion. In each case 60 cc. of menstruum was used for moistening 100 Gm. of drug.

TABLE III.—EFFECT OF TIME OF MACERATION ON THE PERCOLATION OF BELLADONNA ROOT IN NO. 40 POWDER.

A. Gm. of Alkaloid in Various Percolates when Maceration Was as Follows:

Percolates.	0–0.*	0–24.*	0–48.*	24–48.*
80 cc.	0.387	0.419	0.396	0.417
100 cc.	0.081	0.072	0.064	0.065
100 cc.	0.010	0.009	0.009	0.094
100 cc.	0.000	0.000	0.000	0.000
100 cc.	0.000	0.000	0.000	0.000
Totals	0.478	0.500	0.469	0.576

B. Gm. of Total Extractive Contained in Various Percolates.

Percolates.	0–0.*	0–24.*	0–48.*	24–48.*
80 cc.	8.64	8.30	8.26	10.39
100 cc.	7.63	7.64	7.74	7.47
100 cc.	3.71	3.58	3.60	2.69
100 cc.	1.61	1.62	1.82	1.32
100 cc.	0.85	0.80	0.92	0.55
Totals	22.44	21.94	22.34	22.42

C. Per Cent of Total Alkaloid Contained in:

Hours of Maceration. Before Packing.	After Packing.	First Percolate.	First 2 Percolates.	First 3 Percolates.
0	0	81.0	95.8	100.0
0	24	83.8	98.2	100.0
0	48	84.4	98.1	100.0
24	48	85.8	99.6	100.0

* The first number indicates the hours of maceration before packing in the percolator and the second number shows the number of hours of maceration after packing.

The results in Table III clearly show that in the case of belladonna root in No. 40 powder maceration either before or after packing is not of appreciable value in promoting rapid extraction of alkaloids. The total extractive is higher in the reserve percolate in the batch that was macerated before and after packing; this advantage almost disappears by the time the fourth percolate is collected.

The Effect of Variations in Preliminary Maceration.—100-Gm. portions of belladonna root in No. 40 powder were subjected to varying types of preliminary maceration as will be indicated. The drug was then packed in the percolator, and percolation conducted immediately. In each case 80 cc. of percolate was collected in four hours, after which successive 100-cc. portions were collected in two-hour periods. The variations in preliminary maceration were as follows:

Sample A: The drug was macerated with 60 cc. of the official menstruum for 6 hours before packing in the percolator.

Sample B: The drug was macerated for 6 hours with water equivalent to 60 cc. of the official menstruum, the alcohol necessary to bring it up to the official menstruum strength being added just before packing.

Sample C: A flask containing the drug was evacuated for 3 hours, using a Cenco Hyvac pump. Sixty cc. of the official menstruum was then added through a separatory funnel placed through the stopper, the flask being shaken until the powder appeared uniformly damp. The mixture was macerated for 6 hours. The drug was then packed and percolated immediately.

TABLE IV.—EFFECT OF VARIATIONS IN PRELIMINARY MACERATION ON THE PERCOLATION OF BELLADONNA ROOT IN NO. 40 POWDER.

	A. Gm. of Alkaloid in Various Portions of Percolate.			B. Gm. of Total Extractive Contained in:		
Percolates.	Sample A.	Sample B.	Sample C.	Sample A.	Sample B.	Sample C.
80 cc.	0.382	0.378	0.406	8.55	7.31	8.18
100 cc.	0.074	0.094	0.065	7.25	7.33	7.22
100 cc.	0.009	0.008	0.007	6.22	5.38	6.53
100 cc.	0.000	0.000	0.000	3.62	4.61	4.40
100 cc.	0.000	0.000	0.000	2.47	2.54	2.18
Totals	0.465	0.480	0.478	28.11	27.17	28.51

C. Per Cent of Total Alkaloid Contained in:

Sample.	First Percolate.	First 2 Percolates.	First 3 Percolates.
A.	82.2	98.1	100.0
B.	78.8	98.3	100.0
C.	84.9	98.5	100.0

The results in Table IV indicate that preliminary maceration with water alone, with subsequent addition of alcohol, has little or no advantage over maceration in the usual manner. Vacuum maceration also appears to offer no particular advantage, as far as present results go. The results show that slightly more alkaloid is extracted by vacuum maceration in the first percolate than by the usual method of maceration. However, all the alkaloid is contained in the first 280 cc. in each case.

DISCUSSION OF RESULTS.

The results obtained in the present investigation show that dry packing works equally as well as moistening with 25 cc. of liquid per 100 Gm. of drug, but that extraction is slower with larger quantities of moistening liquid. Hooper's results (7) agree with these in showing that quantities above 25 cc. decrease the rate of extraction. Todd's results (8) agree with these in showing that dry packing gives more rapid extraction than moistening with large proportions of liquid, but as Todd did not try any quantities of moistening liquid between 0 and 50 cc. per 100 Gm. of drug he failed to discover that moistening with small proportions of menstruum did not hinder extraction. The lack of advantage in moistening the drug verifies Scoville's contention (10) that the 6 hours of maceration before packing is not needed on account of rate of solubility or to allow time for osmosis. It would seem that in the case of powdered drugs which swell only slightly in the menstruum used the preliminary maceration serves no useful purpose.

In regard to the results on the quantity of moistening liquid used, it is interesting to note that similar results have been found for other drugs. Thus Lenton (17) found that in the percolation of coca leaves, on reducing the amount of menstruum used for moistening the drug, more than half of the alkaloid was obtained in the reserve percolate, while with the official British Pharmacopœial quantity of moistening liquid, the greater part of the alkaloid was contained in the "weak percolate." His results on cimicifuga and aconite were similar.

The previous workers in this field have failed to explain why an increase in the amount of moistening liquid decreases the rate of extraction. Considering the results in Table II it may be said that several factors have a bearing on the results. When no moistening liquid is used, it is evident that all of the liquid appearing as reserve percolate must traverse the entire column of drug. But when the drug is moistened before packing the result is that when percolation is started most of the liquid used in moistening reaches the bottom of the percolator without passing through the entire column of drug. When 90 cc. of moistening liquid is used and 80 cc. of reserve percolate collected it is obvious that more than 10 cc. of the moistening liquid is still in the percolator when the reserve is set aside, and the portion remaining in the percolator is that which has traversed the greatest distance through the drug. However, when only 25 cc. of moistening liquid was used, extraction of alkaloid was just as efficient as when the drug was packed dry. This would indicate that small quantities of moistening liquid may become rather fully saturated so that nothing would be gained by passing through more of the drug. But when more moistening liquid is used than can become saturated, the reserve percolate is less concentrated. From Table II, Part B, it is possible that certain easily soluble extractives dissolve in a very small amount of moistening liquid so that even 25 cc. of moistening liquid results in dilution as far as these constituents are concerned, since the total extractive in the reserve percolate is reduced even by 25 cc. of moistening liquid.

It is interesting to note that maceration after the liquid has begun to drop from the percolator is of very little benefit in the percolation of belladonna root with the official menstruum. This result is in accord with Husa and Magid's findings (16) that equilibrium is quickly attained in maceration with an excess of liquid. The results cast considerable doubt on the necessity and wisdom of the 48-hour macera-

tion period after packing as specified in the U. S. P. X type processes A, B and C for fluidextracts. In the present tests, the results with 19 hours of percolation were equally as good as with 91 hours of combined maceration and percolation. This saving of time is of importance. J. U. Lloyd (18) found that percolation without maceration was best for the preparation of fluidextract of cimicifuga. It remains to be seen whether maceration in connection with percolation is important for other drugs. Probably the most logical way for the U. S. Pharmacopœial Revision Committee to handle this problem would be to introduce a type process for percolation without any maceration either before or after packing. This type process could be specified for only those drugs which are found from time to time to be extracted equally as rapidly and completely without maceration as with maceration.

SUMMARY.

Percolation experiments indicate that maceration before or after packing is of no advantage in promoting more rapid extraction of powdered belladonna root. When the amount of moistening liquid is not kept down to a low proportion there is a decrease in rate of extraction. No advantage is apparent in (*a*) vacuum maceration, or (*b*) preliminary maceration with water alone, with subsequent addition of alcohol.

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PHYTOCHEMICAL NOTES.*

No. 113. AN UNUSUAL PEPPERMINT OIL.

BY SISTER M. FRANCIS XAVIER.

As a preliminary to the study of a number of Mentha materials, largely hybrids of which only small amounts were available, a lot of about 370 cc. of peppermint oil,

* From the Laboratory of Edward Kremers.