SCIENTIFIC SECTION

DRUG EXTRACTION. II. THE EFFECT OF FINENESS OF POWDER AND OF VARIATION IN SOLVENTS ON THE PERCOLATION OF BELLADONNA ROOT.[1,2]

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In connection with 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 it seemed desirable to investigate the extraction of a series of drugs of different types. Belladonna root was selected as representing a simple type of plant structure containing alkaloids as the active constituents. The work reported in this paper covers research on the swelling of belladonna root in various solvents and the effect of fineness of powder and variation in solvents on the percolation of belladonna root.

EXPERIMENTAL PART.

Materials Used.—Except where otherwise specified, the belladonna root used was from the 125-lb. shipment previously described (1). A thorough pharmacognostic study was made and it was found that the shipment conformed to the U. S. P. description.

Swelling of Strips.—Using the technique (1) of making measurements with a filar micrometer of the width of thin strips of cross sections before and after the addition of solvents, the swelling of the wood of belladonna root in various liquids was determined. Cross sections 0.10 to 0.15 mm. thick were cut by means of a sharp carpenter's plane. The results, which in each case are the average of several determinations, have been expressed on a percentage basis, taking the width of the dry strips as 100.

TABLE I.—THE EFFECT OF ALCOHOL-WATER MIXTURES ON THE WOOD OF BELLADONNA ROOT.

Vol. of Alcohol.	Vol. of Water.	Average Width of Strips of Cross Sections (Dry = 100) after Time Intervals in Minutes. 0.	1.	3.	10.	20.	40.	60.	90.
0	1	100	110	109	110	110	110	113	112
1	3	100	110	109	109	110	110	112	110
1	2	100	106	105	109	111	111	111	112
1	1	100	105	105	105	106	106	106	
3	2	100	102	101	102	102	103	104	103
7	3	100	102	101	102	102	104		
4	1	100	101	101	101	101	103	103	
5	1	100	101	101	102	102	102	101	101
9	1	100	101	102	102	102	102	102	
1	0	100	101	100	100	100	100		

Table I shows that a mixture of 1 vol. of alcohol and 3 vol. of water gave the same swelling curve as water alone. As the percentage of alcohol increased there was an increasing tendency to-

[1] Scientific Section, A. PH. A., Washington meeting, 1934.

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

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ward a smaller primary swelling and a smaller total swelling during the period of the test. Alcohol has practically no effect of swelling or shrinking on the wood of belladonna root. Tests made with drug from another shipment gave similar results with the exception that the initial swelling in water was about 30% instead of 10%. It seems likely that the percentage swelling may vary according to the age of the root and the extent to which it has been dried. According to Gortner (2) bio-colloids show a decrease in imbibition capacity with age, old plant tissues being in general less highly hydrated than are the younger tissues.

TABLE II.—THE EFFECT OF GLYCERIN–WATER MIXTURES ON THE WOOD OF BELLADONNA ROOT.

Vol. of Glycerin.	Vol. of Water.	Average Width of Strips of Cross Sections (Dry = 100) after Time Intervals in Minutes. 0.	1.	5.	10.	30.	60.	90.	120.
1	0	100	100	100	101	103	104	105	106
4	1	100	103	103	105	108	108	108	108
3	2	100	105	106	106	107	107	107	107
1	1	100	108	108	108	108	108	109	109
1	3	100	108	110	110	110	110	111	112
1	7	100	108	109	109	110	110	110	110

The above results indicate that glycerin causes a gradual swelling of the wood of belladonna root, amounting to 6% in two hours. With increasing proportions of water, the primary rise increases and there is a more rapid approach to equilibrium.

TABLE III.—THE EFFECT OF GLYCERIN–ALCOHOL MIXTURES ON THE WOOD OF BELLADONNA ROOT.

Vol. of Glycerin.	Vol. of Alcohol.	Average Width of Strips of Cross Sections (Dry = 100) after Time Intervals in Minutes. 0.	1.	3.	30.	60.	120.
9	1	100	101	101	102	103	106
4	1	100	100	100	101	103	105
3	2	100	99	99	101	103	105
1	1	100	97	97	98	99	100
1	3	100	99	98	99	99	102
1	7	100	99	99	99	100	100

As to the effect of alcohol–glycerin mixtures on the swelling of belladonna root it may be said that the swelling in a mixture of these liquids is practically an average of the effects of the liquids themselves when allowance is made for the relative proportions of the two liquids in the mixture.

The Effect of the Fineness of Powder on the Percolation of Belladonna Root.—100 Gm. portions of belladonna root in Nos. 20, 40, 60 and 80 powders were percolated by the U. S. P. process for the fluidextract, 80 cc. of reserve percolate being set aside in each case and the further percolate being collected in successive 100-cc. portions.

Numerous tests were carried out to determine the amount of menstruum necessary to render powdered belladonna root "evenly and distinctly damp" as specified in the U. S. P. Naturally this would vary with different samples of drug according to moisture content. For the drug used in this experiment containing about 10% moisture, 90 cc. of menstruum seemed right for moistening 100 Gm. of drug. Accordingly this amount of menstruum (alcohol 5 vol.—water 1 vol.) was used for moistening each 100-Gm. portion of drug, and the drug macerated for six hours. The drug was then packed in the percolators as uniformly as possible, and, following the U. S. P. directions, macerated for 48 hours. The reserve portions of 80 cc. were then collected at the rate of 10 drops per minute, and then four successive 100-cc. portions were collected at the rate of 20 drops per minute. Wherever it was neces-

sary to stop the percolation for a few hours, such as over night, the time factor was held constant for each portion of drug.

The various fractions of percolate were assayed for total alkaloids and total extractive.

TABLE IV.—EFFECT OF FINENESS OF POWDER ON PERCOLATION OF BELLADONNA ROOT. GM. OF ALKALOID IN VARIOUS PORTIONS OF PERCOLATE.

Percolate.	No. 20 Pwd.	No. 40 Pwd.	No. 60 Pwd.	No. 80 Pwd.
80 cc.	0.301	0.307	0.305	0.300
100 cc.	0.109	0.149	0.160	0.160
100 cc.	0.015	0.027	0.016	0.019
100 cc.	0.001	0.009	0.003	0.004
100 cc.	0.002	0.003	0.002	0.002
Total	0.428	0.495	0.486	0.485
	Gm. Total Extractive in Various Portions of Percolate.			
80 cc.	6.91	6.73	8.27	7.46
100 cc.	6.76	6.70	7.23	7.49
100 cc.	3.52	3.88	4.47	4.73
100 cc.	1.83	1.95	3.10	2.42
100 cc.	0.86	1.05	1.90	0.91
Total	19.88	20.31	24.97	23.01

The results in Table IV indicate that within the limits of No. 20 and No. 80 powder, the fineness of powder is of minor importance as to its effect on rate of extraction of alkaloids by percolation. In each case the amount of alkaloid beyond the third percolate was comparatively unimportant. The data as to total extractive agree with the previous findings (1) that the yield of total extractive increases as the size of powder decreases down to and including No. 60 powder and that with the No. 80 powder there is a decrease in yield of total extractive.

No extensive work has previously been done on the relation of the fineness of powder to the extraction of belladonna root. At the present time the British Pharmacopœia uses a No. 22 powder and the U. S. P. specifies a No. 40 powder.

The Effect of Variation of Solvents on the Percolation of Belladonna Root.—100-Gm. portions of belladonna root in No. 40 powder were percolated by the U. S. P. process for the fluidextract but using various alcohol-water mixtures in two series of percolations. In each case 80 cc. of reserve percolate were set aside and the further percolate collected in successive 100-cc. portions. The amount of moistening liquid used was 90 cc. for each 100-Gm. portion of drug.

TABLE V.—PERCOLATION OF BELLADONNA ROOT WITH VARIOUS ALCOHOL-WATER MIXTURES.

(FIRST SERIES.)

Gm. Alkaloid in Various Fractions of Percolate.

Percolate.	Alcohol.	Alc. 95 Vol.—Water 5 Vol.	Alc. 9 Vol.—Water 1 Vol.	Alc. 7 Vol.—Water 1 Vol.	Alc. 5 Vol.—Water 1 Vol.
80 cc.	0.154	0.159	0.172	0.265	0.296
100 cc.	0.095	0.186	0.201	0.122	0.175
100 cc.	0.011	0.015	0.014	0.007	0.015
100 cc.	0.002	0.002	0.002	0.003	0.001
100 cc.	0.001	0.001	0.001	0.001	0.000
Marc	0.122	0.033	0.004	0.005	0.000
Total	0.385	0.396	0.394	0.403	0.487

Gm. Total Extractive in Various Fractions of Percolate.

80 cc.	3.22	3.47	4.31	6.37	7.10
100 cc.	1.25	3.31	6.01	6.10	8.46
100 cc.	0.65	1.88	3.49	3.79	3.59
100 cc.	0.55	1.61	2.36	1.86	1.66
100 cc.	0.57	2.10	2.36	1.35	0.92
Total	6.24	12.37	18.53	19.47	21.73

TABLE VI.—PERCOLATION OF BELLADONNA ROOT WITH VARIOUS ALCOHOL-WATER MIXTURES.

(SECOND SERIES.)

Gm. Alkaloid in Various Fractions of Percolate.

Percolate.	Alc. 5 Vol.—Water 1 Vol.	Alc. 4 Vol.—Water 1 Vol.	Alc. 7 Vol.—Water 3 Vol.	Alc. 1 Vol.—Water 1 Vol.	Alc. 1 Vol.—Water 2 Vol.
80 cc.	0.295	0.241	0.303	0.304	0.233
100 cc.	0.164	0.182	0.153	0.158	0.186
100 cc.	0.006	0.001	0.021	0.040	0.019
100 cc.	0.000	0.001	0.001	0.001	0.002
100 cc.	0.000	0.000	0.000	0.000	0.001
Total	0.465	0.425	0.478	0.503	0.441

Gm. Total Extractive in Various Fractions of Percolate.

80 cc.	6.59	7.06	9.51	14.20	16.09
100 cc.	7.66	8.41	10.99	10.95	12.46
100 cc.	3.45	3.47	2.71	2.48	0.81
100 cc.	1.63	1.26	1.12	0.33	0.19
100 cc.	1.05	0.66	0.61	0.11	0.14
Total	20.38	20.86	24.94	28.07	26.69

The results in the preceding tables indicate that as the alcoholic strength of the menstruum decreases, extraction of alkaloids becomes more rapid and the yield of extractive becomes greater. It is evident that the four highest alcoholic strengths used do not make good menstrua for belladonna root. The next four proportions, *i. e.*, alcohol 5 vol.—water 1 vol., alcohol 4 vol.—water 1 vol., alcohol 7 vol.—water 3 vol., alcohol 1 vol.—water 1 vol., have approximately the same efficiency, resulting in extraction of substantially all of the alkaloid. As far as our present results go the official menstruum for the U. S. P. fluidextract appears to be well chosen. The results of the U. S. P. menstruum (Alcohol 5 vol.—Water 1 vol.) carried out two different times in the two different series of percolations agree fairly well. This indicates that the two series of percolations are comparable and that no important differences have arisen from differences in conditions such as temperature, degree of packing and time consumed in percolation. The discrepancy in the total alkaloid shown in case of the higher percentages of alcohol has previously been investigated and explained (1).

DISCUSSION OF RESULTS.

Water caused an immediate swelling of thin strips of the wood of belladonna root, the swelling curves being of the same type as those observed in case of thin strips of chestnut wood (1). The results of the tests of alcohol-water mixtures on

the wood of belladonna root are fully comparable with the results on chestnut wood on the more aqueous mixtures. With the more highly alcoholic liquids there is less swelling in the case of belladonna wood than in the case of chestnut wood. It would seem that woody tissues may differ more in behavior to alcohol than to water. The effects of mixtures of liquids on the swelling of the wood of belladonna root are in accord with previous conclusions that the effect of a mixture of two liquids is practically an average of the effects of the liquids themselves when allowance is made for the relative proportions. It is noteworthy that glycerin causes considerable swelling of the belladonna wood in two hours (60% as much as caused by water) whereas glycerin causes only a very slight swelling of chestnut wood (5% as much as caused by water). It should be noted that alcohol had exactly the reverse effect, causing no swelling in the case of belladonna wood but giving considerable swelling with chestnut wood (75% as much as caused by water). The opposite behavior of the two liquids with the two kinds of woody tissue is an example of a principle of colloidal chemistry, *i. e.*, that the swelling of gels is a process of highly selective character. Each gel shows an ability to take up a certain particular liquid (3). Further study of the swelling of drugs should lead to a better understanding of the fundamental principles involved and of their significance in the processes of drug extraction.

The results on percolation of belladonna root with alcohol-water mixtures are in general agreement with the work of Farr and Wright (4). A search of the literature shows that alcohol alone has not been favored as a menstruum for this drug, the trend having been toward the use of 50% to 85% alcohol.

SUMMARY.

A study has been made of the swelling of the wood of belladonna root in binary mixtures of water, alcohol and glycerin. Percolation tests show that within the limits of No. 20 and No. 80 powder, the finess of powder is of minor importance in the extraction of belladonna root. By a series of percolations of belladonna root, using various alcohol-water mixtures, it was found that mixtures ranging from alcohol 5 vol.—water 1 vol. to alcohol 1 vol.—water 1 vol. give the best results.

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COMPARATIVE STUDIES ON THE UTILIZATION OF DIFFERENT MAGNESIUM SALTS.*

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Although considerable work has been done on magnesium metabolism little data are available concerning the relative utilization of the naturally occurring

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