Dilute solutions produced typical tail-curves, marked depression rather than stimulation, and blindness.

CONCLUSIONS.

1. Physiological actions upon mice serve to detect heroin in saliva, as well as in pharmaceutical preparations.
2. Heroin is more effective than morphine on mice.
3. After administering heroin, the saliva of horses contains a substance giving a morphine reaction on mice.

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FOOT-NOTE: The technical assistance of Harry J. Pratt and Aaron B. Sloane is gratefully acknowledged.

DRUG EXTRACTION. I. A STUDY OF VARIOUS MENSTRUA FROM THE STANDPOINT OF SWELLING EFFECTS, PENETRATION AND EXTRACTION.

BY WILLIAM J. HUSA AND LOUIS MAGID.

(*Concluded from page 1103, November Journal.*)

EXTRACTION OF BELLADONNA ROOT OF DIFFERENT DEGREES OF FINENESS.

Filtration Method.—A technique was used by Husa and Fehder (14), whereby imbibition and extraction of powdered drugs could be determined in a process of maceration. An outline of the method as applied to powdered belladonna root is as follows:

Ten grams of powdered belladonna root were macerated for 15 minutes with 90 Gm. of menstruum in a 250-cc. Erlenmeyer flask in a thermostat at 30° C., during which time it was agitated every five minutes. The mixture was then filtered and after allowing 15 minutes for completion of draining, the filtrate was weighed and the weight of the filter paper with the wet marc was also determined. Similar macerations were made for periods of 1 hour, 5 hours and 24 hours, with less frequent agitation during the longer intervals.

In the filtrate, the percentage of dissolved solids was determined by weighing exactly ten Gm. of filtrate in a tared 50-cc. beaker, evaporating to dryness on a water-bath and drying to constant weight in an oven at 105° C. The filtrate was assayed for alkaloidal content according to the U. S. P. X assay for Tincture of Belladonna except that 25 Gm. of the filtrate were used. The wet marc was also assayed for alkaloidal content according to Type Process B, designated for belladonna root by the U. S. P. X.

The amount of moisture in the powdered drug was determined by the U. S. P. X method for drugs containing no constituents volatile at 100° C. The amount of dry marc was calculated as follows: (weight of drug taken for extraction) minus (weight of moisture in drug) minus (weight of dissolved solids in filtrate) = (weight of dry marc). The weight of the liquid imbibed by the marc was calculated as

follows: (weight of wet filter paper + wet marc) minus (weight of filter paper and liquid imbibed by the filter paper) minus (weight of dry marc) = (weight of liquid imbibed by the marc). The loss of menstruum during the process was determined by comparing the total weight of the materials used with the combined weight of the filtrate and wet marc.

Work has been carried out using exactly 10.00 Gm. of powdered belladonna root of different degrees of fineness and exactly 90.00 Gm. of an alcoholic menstruum consisting of a mixture of alcohol 5 vol.—water 1 vol., this being the menstruum official in the U. S. P. X for Fluidextract of Belladonna Root.

TABLE XXV.—EFFECT OF A MIXTURE OF ALCOHOL 5 VOL.—WATER 1 VOL. ON POWDERED BELLADONNA ROOT OF DIFFERENT DEGREES OF FINENESS.

Period of Maceration.	Liquid in Marc.	Dry Marc.	Weight in Grams of Filtrate.	Loss of Menstruum.	Total Extractive.	Filtrate.	Alkaloids in Marc.	Total.
a. Belladonna Root in No. 20 Powder; moisture content = 11.12 per cent.								
15 min.	21.4	7.81	68.2	1.0	1.09	0.028	0.015	0.043
1 hr.	21.2	7.68	68.8	1.3	1.22	0.034	0.011	0.045
5 hrs.	20.9	7.65	68.9	1.0	1.24	0.034	0.010	0.044
24 hrs.	20.6	7.64	67.9	2.3	1.26	0.032	0.012	0.044
b. Belladonna Root in No. 40 Powder; moisture content = 10.27 per cent.								
15 min.	19.7	7.63	70.0	1.1	1.35	0.037	0.013	0.050
1 hr.	19.7	7.58	69.9	1.2	1.39	0.036	0.013	0.049
5 hrs.	20.1	7.57	69.9	0.8	1.40	0.036	0.013	0.049
24 hrs.	20.3	7.57	69.5	1.0	1.40	0.035	0.013	0.048
c. Belladonna Root in No. 60 Powder; moisture content = 8.10 per cent.								
15 min.	16.3	7.39	73.9	0.8	1.81	0.035	0.013	0.048
1 hr.	16.1	7.37	74.1	0.8	1.82	0.037	0.012	0.049
5 hrs.	15.8	7.39	74.1	1.1	1.81	0.036	0.013	0.049
24 hrs.	16.0	7.33	74.1	0.9	1.86	0.036	0.013	0.049
d. Belladonna Root in No. 80 Powder; moisture content = 10.35 per cent.								
15 min.	18.4	7.37	71.9	0.7	1.60	0.036	0.009	0.045
1 hr.	17.9	7.34	72.3	0.9	1.63	0.036	0.009	0.045
5 hrs.	17.3	7.30	73.0	0.9	1.67	0.036	0.009	0.045
24 hrs.	18.2	7.29	72.0	1.0	1.68	0.036	0.009	0.045

Using the official U. S. P. X menstruum for the Fluidextract of Belladonna Root (mixture of alcohol 5 vol.—water 1 vol.) and belladonna root in No. 20, 40, 60 and 80 powder, it is seen that imbibition is complete in each case in 15 minutes. The relative amounts of liquid imbibed and the yield of total non-volatile extractive (listed as "total extractive" in the tables) by the different powders offer interesting comparisons.

TABLE XXVI.—EFFECT OF FINENESS OF POWDER OF BELLADONNA ROOT ON YIELD OF TOTAL EXTRACTIVE AND ON IMBIBITION USING MIXTURE OF ALCOHOL 5 VOL.—WATER 1 VOL.

Fineness of Powder.	Grams of Solvent Imbibed by 10-Gm. Drug. Maceration Method.	Centrifuge Method.	No. Gm. of Total Extractive from 10-Gm. Drug after 24 Hrs.
No. 20	21	21	1.26
No. 40	20	17	1.40
No. 60	16	15	1.86
No. 80	18	16	1.68

In Table XXVI the figures under the centrifuge method represent the average of results after 60, 120, 360, 720 and 1440 minutes. The data on imbibition by the centrifuge method were originally stated in terms of the number of cc. of solvent imbibed by 1 Gm. of drug; for the preceding table the results given in Table XXIII were recalculated on the basis of the number of Gm. of solvent imbibed by 10 Gm. of drug. The results in Table XXVI indicate that with increasing fineness of powder, imbibition decreases until No. 80 powder is reached where *there is an increase in imbibition*. A hypothesis to explain this phenomena has already been given earlier in the paper.

The amount of total extractive obtained from the filtrate in the maceration process offers the same anomaly as observed in imbibition. The yield of total extractive increases with increasing fineness of powder down to and including the No. 60 powder, but when the fineness is increased to a No. 80 powder, the yield of extractive decreases. By powdering the drug more finely more surface is exposed, giving the solvent more ready access to the constituents, and the slowly diffusible substances have greater opportunity to enter the solvent phase; these factors would account for the increased yield of extractive in passing from a No. 20 to a No. 40 and No. 60 powder. As the total surface of the particles increases, an opposing tendency would assume greater importance, *i. e.*, the tendency for the drug constituents to be adsorbed on the surfaces of the particles. In the No. 80 powder, it appears that the greater adsorptive power due to increased surface overcomes the advantage gained by greater accessibility of solvent so that the net result is a decrease in yield of total extractive as shown in Table XXVI.

An examination of Table XXV indicates that the official menstruum extracts as much alkaloid in 15 minutes as in 24 hours in a maceration process with the No. 40, 60 and 80 powders, but not with the No. 20 powder, which gives a maximum yield of alkaloids after 1 hour. Similar results have been obtained with a totally different drug, *i. e.*, jalap (14). These results throw considerable doubt on the wisdom of the long periods of maceration specified in many of the pharmacopœias of the world.

Typical results such as those shown in Table XXV*c* indicate that 0.035 Gm. of alkaloids is found in the filtrate while 0.013 Gm. of alkaloids remains in the marc. It is of interest to consider the state of the alkaloids in the marc. Since 0.035 Gm. of alkaloids is dissolved in 74 Gm. of filtrate, a calculation shows that if the 16 Gm. of menstruum remaining in the marc contained the same proportion of dissolved alkaloids, there would be 0.008 Gm. of alkaloids thus existing in the dissolved state in the liquid imbibed in the marc. This would leave 0.005 Gm. of alkaloids remaining in the marc in some other form; this might be present in the undissolved form in the inner recesses of the drug particles or it might be present in a state of adsorption on the surfaces of the drug particles. If the 0.005 Gm. of alkaloids were so situated as to be only slowly accessible to the solvent, it would follow that the amount of alkaloids should gradually increase in the filtrate during the 24 hours, but as a matter of fact the same amount of alkaloids appears in the filtrate in 15 minutes as in 24 hours. From these considerations it appears more likely that this proportion of alkaloids is adsorbed on the drug surfaces. The only other explanation visualized at present is that this proportion of alkaloids is so inaccessible to the solvent that the latter has no effect on it; this explanation seems less likely.

Centrifuge Method.—A technique was devised for determining the rate of extraction of alkaloids and of total extractive on maceration with successive portions of menstruum, as well as the degree of imbibition at different stages of the extraction process. In this method the centrifuge is used for separating the liquid from the drug. In order to facilitate comparisons with the previous maceration experiments, the same quantities of drug and menstruum were employed, *i. e.*, 10.00 Gm. of powdered drug and 90.00 Gm. of menstruum. Into each of four centrifuge tubes of 50 cc. capacity were placed 2.50 Gm. of powdered drug and 22.50 Gm. of menstruum. The contents of each tube were well mixed by means of a glass rod inserted through a cork stopper in the mouth of the tube. The tubes were then placed in a thermostat at 30° C. and allowed to remain there for 15 minutes, being well stirred every five minutes. The tubes were then centrifuged for ten minutes, after which time the clear supernatant liquid was decanted, the liquids from the four tubes being mixed together in a closed container and weighed in order to determine the weight of macerate obtained from 10.00 Gm. of powdered drug and 90.00 Gm. of menstruum. The tubes containing the wet marc were then weighed, and from this weight the amount of liquid imbibed in the marc was calculated. For the next maceration, 22.50 Gm. of menstruum were added to the wet marc in each tube, the mixture stirred well and placed in the thermostat and the same procedure followed as previously described. Thus the amount of liquid imbibed in the marc after each maceration was determined, as well as the amount of macerate in each case. Five macerates were obtained and each was assayed in duplicate for alkaloidal content and total extractive. The total time elapsing from one maceration to the next was 55 minutes, this being kept constant throughout the procedure.

The results shown in the following tables were calculated as in the case of the filtration method, with the exception that the calculations were somewhat simpler due to the fact that corrections for the use of filter paper were eliminated, since filter paper was not used.

TABLE XXVII.—EFFECT OF A MIXTURE OF ALCOHOL 5 VOL.—WATER 1 VOL. ON POWDERED BELLADONNA ROOT OF DIFFERENT DEGREES OF FINENESS ON MACERATION WITH SUCCESSIVE PORTIONS OF SOLVENT.

Maceration.	Weight in Grams of Liquid in Marc.	Dry Marc.	Macerate.	Loss of Menstruum.	Total Extractive.	Alkaloids.
a. Belladonna Root in No. 20 Powder; moisture content = 11.12 per cent.						
1st	19.8	7.70	72.0	0.5	1.19	0.032
2nd	21.0	7.14	89.0	0.3	0.56	0.008
3rd	21.0	6.89	89.9	0.4	0.25	0.003
4th	21.5	6.76	89.4	0.3	0.13	0.001
5th	21.6	6.69	89.5	0.4	0.07	0.001
Marc						0.002
					Total =	0.047
b. Belladonna Root in No. 40 Powder; moisture content = 9.60 per cent.						
1st	17.0	7.62	75.5	0.0	1.42	0.033
2nd	17.9	7.07	89.6	0.1	0.55	0.009
3rd	18.0	6.84	90.3	0.0	0.23	0.002
4th	18.3	6.72	89.9	0.0	0.12	0.000
5th	18.1	6.64	90.5	0.0	0.08	0.000
Marc						0.001
					Total =	0.045

c. Belladonna Root in No. 60 Powder; moisture content = 8.10 per cent.

1st	15.1	7.25	77.7	0.0	1.94	0.038
2nd	15.3	6.62	90.3	0.1	0.63	0.007
3rd	15.7	6.39	89.6	0.2	0.23	0.001
4th	15.8	6.27	89.9	0.1	0.12	0.000
5th	15.7	6.20	90.0	0.2	0.07	0.000
Marc						0.000
					Total =	0.046

d. Belladonna Root in No. 80 Powder; moisture content = 10.35 per cent.

1st	16.1	7.22	76.7	0.1	1.75	0.038
2nd	16.1	6.65	90.6	0.0	0.57	0.008
3rd	16.4	6.44	90.0	0.0	0.21	0.001
4th	16.2	6.34	90.5	0.0	0.10	0.000
5th	16.3	6.28	90.1	0.0	0.06	0.000
Marc						0.000
					Total =	0.047

The technique of maceration with successive portions of solvent throws light on just what is happening during percolation, as the drug repeatedly comes into contact with fresh solvent. The process is, however, broken up into several steps, and it is thus possible to secure data which cannot be conveniently secured in the usual percolation process. The loss of menstruum throughout the procedure is small, being at the greatest only 1.9 Gm. in the handling of 450.0 Gm. of menstruum.

A study of Table XXVII shows that imbibition decreases until No. 80 powder is reached where there is an increase in imbibition. The yield of total extractive increases until No. 80 powder is reached where there is a decrease. These results are in accord with the data shown in Table XXVI.

As the extractive matter is gradually removed there is a corresponding increase in imbibition; this increase from the first to the fifth macerate totals 1.8 Gm. for the No. 20 powder, 1.1 Gm. for the No. 40 powder, 0.6 Gm. for the No. 60 powder and 0.2 Gm. for the No. 80 powder. The increased imbibition may be due largely to the fact that the cell cavities are able to hold more liquid after some of the cell contents have been removed. The larger particles, having a greater proportion of undamaged cells, would be able to hold more solvent in cell cavities. As the fineness of the powder increases, and fewer undamaged cells remain, it would follow that the increase in imbibition on removal of some of the cell contents would become smaller, on the basis that the removal of cell contents from damaged cells would decrease the size of the particles without leaving an enclosed cavity capable of mechanically holding a liquid. The observed results are in accord with this hypothesis.

Calculations indicate that in the No. 20 powder, some of the alkaloids remain undissolved during all five successive macerations; this may be due in part to the fact that for this size of powder the amount of extractive matter removed is the lowest observed in this series of experiments and the extractive remaining in the marc may shield the alkaloid from contact with the solvent; the alternative explanation would be that the constituents having a part in the adsorption of alkaloids by the marc have not been sufficiently removed. With the No. 40 powder,

the rate of extraction is more rapid, but at the end of the fifth maceration a small amount of alkaloids still remains undissolved. With the No. 60 and 80 powders, all of the alkaloids seem to be removed in the first three macerations; in both cases, calculations show that there is some undissolved or adsorbed alkaloids after the first maceration but all the alkaloids are dissolved during the second maceration and finally removed in the third maceration (that is to say, the amount remaining after the third maceration is less than 0.0005 Gm. and hence is neglected).

Certain aspects of the results in Table XXVII are brought out by the calculations presented in the following table.

TABLE XXVIII.—RESULTS ON EXTRACTION OF POWDERED BELLADONNA ROOT WITH SUCCESSIVE PORTIONS OF MIXTURE OF ALCOHOL 5 VOL.—WATER 1 VOL.

Fineness of Powder.	Percentage of Total Alkaloids in First Macerate.	First Two Macerates.	First Three Macerates.
No. 20	68	85	91
No. 40	73	93	98
No. 60	83	98	100
No. 80	81	98	100

Table XXVIII indicates that extraction of alkaloids from powdered belladonna root by maceration was most efficient in the No. 60 and No. 80 powders.

EFFECT OF VARIATION IN SOLVENTS ON EXTRACTION OF BELLADONNA ROOT.

Alcohol-Water Mixtures.—Using belladonna root in No. 40 powder (the fineness of powder specified by the U. S. P. X for the Fluidextract of Belladonna Root), tests were made of the effect of variations in the alcoholic strength of menstrua; this question was studied by the technique of successive macerations with the use of the centrifuge. In each experiment exactly 10.00 Gm. of belladonna root in No. 40 powder (moisture content = 9.60 per cent) were used, while in each maceration 90.00 Gm. of the specified menstruum were employed.

TABLE XXIX.—EFFECT OF VARIOUS ALCOHOLIC MENSTRUA ON POWDERED BELLADONNA ROOT ON MACERATION WITH SUCCESSIVE PORTIONS OF SOLVENT.

Maceration.	Weight in Grams of Liquid in Marc.	Dry Marc.	Macerate.	Loss of Menstruum.	Total Extractive.	Alkaloids.
a. Alcohol.						
1st	15.9	8.52	75.3	0.2	0.52	0.011
2nd	15.9	8.23	90.0	0.3	0.27	0.003
3rd	15.9	8.06	90.0	0.3	0.26	0.001
4th	16.1	7.93	89.7	0.2	0.19	0.000
5th	16.0	7.84	90.0	0.2	0.16	0.000
Marc						0.024
					Total =	0.039
b. Mixture of Alcohol 95 Vol.—Water 5 Vol.						
1st	15.7	8.14	75.9	0.3	0.90	0.022
2nd	16.1	7.71	89.6	0.4	0.43	0.006
3rd	16.3	7.48	89.6	0.4	0.23	0.001
4th	16.4	7.33	89.8	0.2	0.15	0.000
5th	16.6	7.23	90.0	0.0	0.10	0.000
Marc						0.010
					Total =	0.039

c. Mixture of Alcohol 9 Vol.—Water 1 Vol.

1st	16.3	7.93	75.6	0.2	1.11	0.026
2nd	16.9	7.43	89.7	0.2	0.50	0.007
3rd	17.1	7.18	90.0	0.1	0.25	0.001
4th	17.2	7.03	90.0	0.1	0.15	0.000
5th	17.2	6.93	89.9	0.1	0.10	0.000
Marc						0.006
					Total =	0.040

d. Mixture of Alcohol 7 Vol.—Water 1 Vol.

1st	16.6	7.82	75.5	0.1	1.22	0.027
2nd	17.2	7.28	89.8	0.2	0.54	0.007
3rd	17.4	7.03	89.9	0.2	0.25	0.002
4th	17.5	6.90	89.8	0.1	0.13	0.001
5th	17.9	6.82	89.7	0.1	0.08	0.000
Marc						0.002
					Total =	0.039

e. Mixture of Alcohol 5 Vol.—Water 1 Vol.

1st	17.0	7.62	75.5	0.0	1.42	0.033
2nd	17.9	7.07	89.6	0.1	0.55	0.009
3rd	18.0	6.84	90.3	0.0	0.23	0.002
4th	18.3	6.72	89.9	0.0	0.12	0.000
5th	18.1	6.64	90.5	0.0	0.08	0.000
Marc						0.001
					Total =	0.045

f. Mixture of Alcohol 4 Vol.—Water 1 Vol.

1st	17.5	7.47	75.1	0.0	1.57	0.034
2nd	18.3	6.88	89.9	0.0	0.59	0.009
3rd	18.6	6.66	89.9	0.0	0.22	0.001
4th	18.3	6.55	90.5	0.0	0.11	0.000
5th	18.6	6.48	89.9	0.0	0.07	0.000
Marc						0.001
					Total =	0.045

g. Mixture of Alcohol 7 Vol.—Water 3 Vol.

1st	18.3	7.23	74.5	0.0	1.81	0.035
2nd	19.2	6.68	89.7	0.0	0.55	0.007
3rd	19.6	6.50	89.7	0.1	0.18	0.001
4th	19.4	6.42	90.2	0.1	0.08	0.000
5th	19.1	6.38	90.2	0.2	0.04	0.000
Marc						0.001
					Total =	0.044

h. Mixture of Alcohol 1 Vol.—Water 1 Vol.

1st	19.8	7.04	73.1	0.1	2.00	0.034
2nd	20.8	6.52	89.4	0.1	0.52	0.007
3rd	21.2	6.38	89.6	0.1	0.14	0.001
4th	20.8	6.33	90.3	0.2	0.05	0.000
5th	21.0	6.30	89.7	0.2	0.03	0.000
Marc						0.001
					Total =	0.043

i. Mixture of Alcohol 1 Vol.—Water 2 Vol.						
1st	23.2	7.07	69.9	0.0	1.97	0.031
2nd	23.7	6.50	90.2	0.0	0.57	0.008
3rd	23.0	6.34	90.9	0.0	0.16	0.001
4th	23.1	6.28	90.1	0.0	0.06	0.001
5th	22.5	6.24	90.5	0.1	0.04	0.000
Marc						0.002
						Total = 0.043

The results indicate that imbibition increases as the proportion of alcohol in the menstruum decreases. The amount of total extractive obtained likewise increases with a decrease in alcoholic strength of the menstruum. Considering the results of the maceration experiments, it is seen that the four highest alcoholic strengths used do not make good menstrua for belladonna root; however, as the proportion of water increases there is a progressive increase in efficiency of extraction of the alkaloids. The four next proportions, *i. e.*, alcohol 5 vol.—water 1 vol., alcohol 4 vol.—water 1 vol., alcohol 7 vol.—water 3 vol. and alcohol 1 vol.—water 1 vol. have approximately the same efficiency, resulting in extraction of substantially all of the alkaloid. As far as the results go the official menstruum for the U. S. P. X Fluidextract of Belladonna Root appears to be well chosen.

With the higher strengths of alcohol the values for the total alkaloid obtained from the macerates plus the marc were lower than with the more dilute solutions of alcohol. Further tests showed that the U. S. P. X method for determination of alkaloids of belladonna root applied to the marc did not take out all of the alkaloids in cases where the drug had been treated with alcohol of 82.5 per cent by volume or higher. This was shown by exhaustively extracting 10.00 Gm. of powdered belladonna root with alcohol, which yielded 0.039 Gm. of alkaloids, followed by exhaustive extraction with the U. S. P. X menstruum (alcohol 5 vol.—water 1 vol.), which yielded 0.011 Gm. of alkaloids. It thus appears that when the drug has been treated with a strong alcoholic menstruum, neither the menstruum nor the ether-chloroform mixture is capable of extracting all of the alkaloids. But as shown, the official menstruum is capable of removing the remainder of the alkaloids. Possibly the stronger alcoholic menstrua precipitate certain water-soluble constituents which envelop a portion of the alkaloids in such a manner that it cannot be extracted either by the strong alcoholic menstrua or by ether-chloroform mixture. When treated with more aqueous menstrua the precipitated matter might then be dissolved and the alkaloids extracted. 10.00 Gm. of belladonna root in No. 40 powder assayed by the U. S. P. X method yielded 0.045 Gm. of alkaloids, while with alcohol and the official menstruum, 0.050 Gm. of alkaloids was obtained. There is a possibility that the U. S. P. X assay does not extract all of the alkaloids.

Thus it is shown that the discrepancy in total alkaloids is caused by the fact that ether-chloroform mixture does not extract all of the alkaloids when used on a marc which has been treated with strong alcoholic menstrua. In Table XXIX it is thus clear that full reliance may be placed on the analyses of the macerates themselves, but that the analyses of the marcs may best be disregarded. The data on the marcs are not necessary for interpreting the extraction data, the marcs having been analyzed merely as a check on the analyses of the macerates.

Acidic Menstrua.—Since the use of acid in the menstrua for some alkaloidal drugs has been considered advantageous, it was of interest to determine the value of acidic menstrua in the extraction of belladonna root. Using the technique of macerations with successive portions of solvent with the use of the centrifuge as described earlier in the article, tests were made in which hydrochloric acid replaced part of the water used in the official menstruum for the U. S. P. X Fluidextract of Belladonna Root.

TABLE XXX.—EXTRACTION AND IMBIBITION OF BELLADONNA ROOT IN NO. 40 POWDER ON MACERATION WITH SUCCESSIVE PORTIONS OF SOLVENT.

10.00 Gm. of drug of moisture content = 9.60 per cent.
90.00 Gm. in each maceration of a mixture of alcohol 5 vol.—water 0.4 vol.—U. S. P. HCl 0.6 vol.

	Weight in Grams of					
Maceration.	Liquid in Marc.	Dry Marc.	Macerate.	Loss of Menstruum.	Total Extractive.	Alkaloids.
1st	17.2	7.63	75.0	0.2	1.41	0.033
2nd	17.5	7.09	90.0	0.2	0.54	0.008
3rd	17.8	6.84	89.8	0.2	0.25	0.001
4th	18.0	6.70	89.6	0.3	0.14	0.001
5th	17.9	6.59	90.0	0.2	0.11	0.001
Marc						0.001
						Total = 0.045

The results in Table XXX may best be compared with Table XXIX*e*. The rate of extraction of alkaloids and extractive matter by the official menstruum corresponds closely with the rate of extraction using the acidified menstruum. Imbibition of menstruum by the marc is the same in both cases. It is thus seen that the addition of acid was of no benefit in the maceration process used.

SUMMARY.

Methods were developed for determining the swelling effect of solvents on drugs and other vegetable tissues in the form of thin strips, blocks and powders. The rate of penetration of solvents through cells was determined. The solvents studied included various binary and ternary mixtures of water, alcohol and glycerin and some of the newer solvents of the glycol type. Using powdered belladonna root, studies were made of the effect of fineness of powder and variation in solvents on imbibition and extraction in a maceration process.

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A NOTE ON THE ARSENIC TEST FOR REDUCED IRON.*

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INTRODUCTION.

The preparation of the chemicals to be tested for arsenic by the modified Gutzeit's test in many instances is tedious and time-consuming. This is especially true with reduced iron. The residue remaining after the solution of the iron in acid, is oxidized by a chlorate-hydrochloric acid treatment, evaporated, treated with sulphurous acid and again evaporated before subjecting it to the arsenic test.

In an effort to reduce the time and energy expended in this procedure, this experiment was conducted.

EXPERIMENTAL.

Arsenic associated with the iron in reduced iron occurs generally as the acid-insoluble iron arsenide Fe_3As_2. As early as 1839 Wöhler (1) showed that arsenic in this form did not yield arsine when the iron was dissolved in dilute acids. It was further shown by Sautermeister (2) that the literation of arsine could be accomplished by the addition of zinc to the iron before effecting the acid solution. These observations were confirmed by the authors.

Iron arsenide was prepared by the method of A. Brukl (3) which consists of passing arsine into an alcoholic solution of ferrous ammonium sulphate. A trituration of this substance and reduced iron was prepared containing 0.025 per cent of the arsenide. The reduced iron showed no arsenic prior to the incorporation of the arsenide.

The strips in Group I represent the stains obtained when the trituration was subjected to the U. S. P. treatment.

The strips in Group II represent the stains obtained when the trituration was subjected to a modified treatment described in the following paragraph.

The modified procedure employed is as follows: Transfer 0.050 Gm. of Reduced Iron, accurately weighed, to a Gutzeit bottle. Add bromine T.S. (about 6 cc.) in small divided portions until most of the iron dissolves and a slight excess of bromine remains. Heat the mixture on

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