With both stop-cocks closed, the flask is removed from the trough and placed in its normal position. Through the vertical stop-cock, to which a funnel has been attached, is introduced a freshly prepared solution (3) of 50 Gm. of sodium hydrosulfite in 250 cc. of distilled water to which have been added 40 cc. of a solution of 500 Gm. of potassium hydroxide in 700 cc. of water. The oxygen absorption commences with the introduction of the first few drops of the solution and the entire volume of the hydrosulfite solution can be drawn into the flask, aided by occasional shaking, within a few minutes. With both stop-cocks closed, the flask is shaken vigorously for five minutes. Distilled water is then

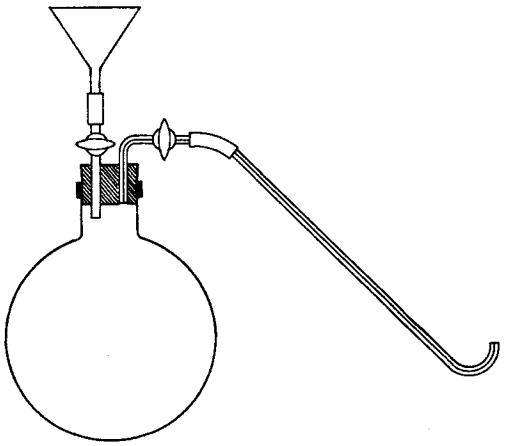

Fig. 1.—Flask and Attachments.

allowed to flow into the flask through the vertical stop-cock until atmospheric pressure is restored therein.

The residual gas volume of approximately 75 cc. is then transferred to a 100-cc. volumetric flask which has been filled with water and inverted over a pneumatic trough. To the capillary stop-cock is attached a delivery tube of capillary tubing for the transfer of the gas to the volumetric flask and the distilled water is introduced through the other stop-cock to displace the residual gas from the balloon flask. After complete transfer of the gas to the volumetric flask the balance of the water therein is completely displaced by nitrogen and the flask is then stoppered. Throughout the procedure, care should be taken to avoid the introduction of air into the gas sample.

A sample of carbon monoxide-free oxygen is carried through the same procedure and we then have two 100-cc. volumetric flasks corresponding, respectively, to the test gas and to the carbon monoxide-free oxygen.

To each of the flasks are added 2 cc. of a freshly prepared aqueous solution of 1 cc. of blood diluted to 20 cc. The flasks are immediately restoppered and, during a period of fifteen minutes, are rotated from time to time to facilitate maximum contact between the blood solution and the gas.

The blood solutions are then treated by the standard pyrotannic method in which one cc. of a fresh solution containing 1 Gm. of pyrogallic acid and 1 Gm. of tannic acid in 50 cc. of distilled water is added to each flask. After thorough mixing the flasks are allowed to stand in subdued light for 15 minutes after which time the contents of the flasks are transferred to small similar test-tubes for comparison. If the test gas contains 5 parts per million of carbon monoxide, the contents of the corresponding tube will show a pinkish tint in contrast to the brown color of that of the carbon monoxide-free sample.

SUMMARY

1. A method for the detection of carbon monoxide in medicinal oxygen has been described.

2. The method which involves a very simple procedure is considerably more rapid than the methods hitherto available and is sensitive to approximately 5 parts per million of carbon monoxide.

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A Study of the Extraction of Astringent Drugs*

By H. F. Lefevre† and C. O. Lee‡

Methods of drug extraction have been the subject of much pharmaceutical research. Recent work upon the problem has involved drugs containing alkaloids or other constituents which are rather easily assayed. The astringent drugs and their preparations are not easily standardized because their astringency is attributed to their tannin content for which there is no satisfactory assay.

This study was undertaken for the purpose of applying some of the more recently acquired knowledge of the subject of drug extraction to the preparation of astringent fluidextracts and to establish the following objectives:

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1. To determine the method, apparatus and menstruum best suited for the extraction of tannins from the astringent drugs.

2. To study the possibility of preparing full-strength astringent fluidextracts without the collection of weak percolates.

3. To show the proportion of tannin lost in the astringent galenicals over stated periods of time.

Most of the experimental work embodied in this investigation has been performed on powdered krameria root since this drug was suggested as representative of the astringent group.

EXPERIMENTAL

Assay Methods.—Inasmuch as the preparations studied depended upon the presence of tannins for their astringency, it was necessary to adopt a method of tannin assay. A modified Loewenthal-Proctor method (1) was accordingly investigated and found to be the one most suitable for this purpose and has been used exclusively in this study.

For the determination of total extractives the method used by Arnett and Lee (2) in their study of the astringent galenicals was adopted. The procedure was as follows: 10 ml. of the galenical were pipetted into a tared 2-inch porcelain evaporating dish. The dish was then placed in an electric oven and the contents dried to constant weight at 105°. The weight of the residue, multiplied by ten, gave the percentage of total extractive, weight/volume.

Menstruum Variations in the Manufacture of Fluidextract of Krameria.—Some doubt has been cast upon the value of glycerin in drug extraction. Scoville (3) expressed the opinion that although glycerin is valuable for the prevention of precipitation in fluidextracts, it has been largely overrated for that purpose. However, it appeared from his investigations that glycerin was of value in the extraction of the astringent drugs. Husa and Magid (4) found that glycerin retarded extraction in the case of belladonna root.

Table I.—Results of Tannin Assays

No.	Alcohol	Glycerin	Water	Percentage of Tannin N. F. VI Process	First 500 Ml.
1	9	1	.	18.96	16.5
2	8	2	.	19.5	16.0
3	9	.	1	19.97	17.2
4	6	.	4	18.95	15.5
5	2	.	8	17.0	14.7

Fluidextracts were prepared from a number 20 powder of krameria root, using cylindrical Pyrex glass tubes 150 cm. long and 51 mm. uniform inside diameter as the percolators. The National Formulary VI menstruum I for the preparation of Fluidextract of Krameria was varied by changes in alcohol, glycerin or water content. The results of the tannin assays made upon the fluidextracts so prepared are shown in Table I.

Comments: The substitution of water for the one part of glycerin increased the amount of tannin in the fluidextract prepared by the National Formulary VI procedure. It also increased the amount of tannin present in the first 500 ml. of fluidextract. Increasing the glycerin content of menstruum I also increased the amount of tannin found in the finished product, but the preparation was somewhat more viscous than the official fluidextract. The substitution of 8 parts of water and 2 parts of alcohol in place of the official menstruum I yielded less tannin. A heavy precipitate also occurred in these fluidextracts, indicating that highly aqueous menstruums are undesirable for the extraction of krameria.

The Use of Cylindrical and Conical Percolators in the Preparation of Fluidextract of Krameria.—Many workers, including Rosenwasser (5), Kelly and Krantz (6) and Breddin (7), have expressed the belief that long narrow percolators are to be preferred over broad conical percolators in the preparation of fluidextracts. Husa and Huyck (8) compared the efficiency of the Oldberg percolator, funnel, and tube of uniform diameter and found that the Oldberg percolator and the funnel gave better yields of alkaloids, whereas uniform glass tubes were somewhat more efficient for total extractive. The same workers later (9), working with a modified repetition diacolation process, found that the use of cylindrical tubes apparently had no advantages over the Oldberg percolators.

Three groups of fluidextracts were prepared from a number 20 powdered krameria root, one group in cylindrical tubes of uniform diameter, another in conical percolators and the third in cylindrical percolators, but omitting the collection and evaporation of weak percolates. The dimensions of the percolators were as follows:

1. Cylindrical (uniform diameter)
   - Length of tube 150 cm.
   - Inside diameter 49 mm.
   - Outside diameter 51 mm.
   - Length of drug column 80 cm.
   - Ratio, diameter: length drug column 1:16

2. Conical (slightly tapering)
   - Length 37 cm.
   - Diameter at top 12.5 cm.
   - Diameter at base 8.0 cm.
   - Diameter at top of drug column 11.5 cm.
   - Length of drug column 22.0 cm.
   - Ratio, diameter: length drug column 1:2

The fluidextracts were assayed for tannin content and total extractive directly after completion. The results of the assays are shown in Table II.

Table II.—Results of Tannin and Total Extractive Assays

No.	Type of Percolator	Method of Extraction	Per Cent Tannin	Per Cent Total Extractive
A_1	Conical	N. F. VI	12.10	26.02
A_2	Conical	N. F. VI	12.41	26.07
A_3	Conical	N. F. VI	12.98	26.04
B_1	Cylindrical	N. F. VI	14.15	29.88
B_2	Cylindrical	N. F. VI	13.20	28.70
B_3	Cylindrical	N. F. VI	13.90	28.72
C_1	Cylindrical	Modified[a]	9.77	20.38
C_2	Cylindrical	Modified[a]	9.78	20.26
C_3	Cylindrical	Modified[a]	10.25	20.72

[a] Prepared without the collection and evaporation of weak percolates.

Comments: The results indicate that it is possible to extract somewhat more of the tannin from krameria if long cylindrical tubes are used rather than conical percolators. The fluidextracts of Group *C*, those prepared without the collection of weak percolates, showed that even with the advantage of a longer column of drug it was not possible to extract more than approximately 80% of the tannin obtained by the National Formulary VI method using conical percolators.

The Preparation of Fluidextract of Krameria by a Modified Diacolation Process.—The process of diacolation was devised by Breddin (10) and has undergone numerous modifications, including those made by the originator himself (11). This method of drug extraction has been investigated by Gstirner (12), Keller (13), Husa and Huyck (14) and others, most of whom have reported favorable results in its application.

The apparatus used in the experimental work of this study was similar to that of Breddin, as modified by Husa and Huyck (14). It consisted of a series of seven Pyrex glass tubes of 22 mm. outside diameter and 70 cm. length, connected by Pyrex glass U-tubes of the same diameter. The connections between straight sections and U-tubes were made with short lengths of three-quarter inch rubber tubing, three-quarter inch garden-hose clamps serving to tighten all such connections. Menstruum, contained in an air-tight tank, was forced through the drug, contained in the seven tubes, by means of compressed air obtained from the laboratory air jets. A fairly constant pressure of 9–13 pounds per square inch was available at all times.

Details concerning the apparatus are as follows:

Inside diameter of tubes	19 mm.
Outside diameter of tubes	22 mm.
Length of straight tubes	70 cm.
Length of U-tubes	22–24 cm.
Total length of drug column	700 cm.
Volume of packed drug	1915 ml.
Ratio, inside diameter:length drug column	1:368

Fluidextract of Krameria was prepared, in duplicate, by the modified diacolation process from 1000 Gm. of a number 20 powdered krameria root, 1000 ml. of finished fluidextract was collected, as were five additional fractions of 200 ml. each of the weak percolate. The various fractions of each fluidextract were assayed for tannin content and total extractive directly after they were collected. The results of the assays are shown in Tables III and IV.

Table III.—Results of Tannin Assays of Fractions of Percolate

Fraction	Per Cent Tannin Extracted Trial 1	Trial 2
First 1000 ml.	12.81	12.14
Weak percolates:		
First 200 ml.	0.79	0.78
Second 200 ml.	0.25	0.43
Third 200 ml.	0.16	0.43
Fourth 200 ml.	0.0	0.26
Fifth 200 ml.	0.0	0.0
Total	14.01	14.04

Table IV.—Results of Total Extractive Assays of Fractions of Percolate

Fraction	Per Cent Total Extractive Trial 1	Trial 2
First 1000 ml.	38.26	34.62
Weak percolates:		
First 200 ml.	2.87	4.24
Second 200 ml.	1.73	2.24
Third 200 ml.	1.17	1.67
Fourth 200 ml.	0.82	1.18
Fifth 200 ml.	0.88	0.92
Total	45.73	44.87

Comments: Most of the tannin was present in the first 1000 ml. of percolate. The small amount remaining in the drug was removed in subsequent weak percolates. The amount of tannin extracted

Table V.—Comparable Results of Different Methods of Extraction

No.	Percolator	Process	Per Cent Tannin Extracted	Per Cent Tannin Available	Efficiency[a]
A_1	Conical	N. F. VI	12.10	14.01[b]	86.3%
A_2	Conical	N. F. VI	11.40	14.01	81.4%
B_1	Cylinder	N. F. VI	13.05	14.01	93.0%
B_2	Cylinder	N. F. VI	12.95	14.01	92.4%
C_1	Cylinder	Modified	10.12	14.01	72.2%
C_2	Cylinder	Modified	10.09	14.01	72.0%
D_1	Diacolation		12.81	14.01	91.9%
D_2	Diacolation		12.14	14.01	86.9%

[a] A process which yielded a fluidextract containing 14.01% tannin would be 100% efficient.
[b] This figure was obtained from Table III and represents the amount of tannin present in the sample of krameria from which these products were prepared.

in the first 1000 ml. of percolate represented, in trial 1, 91.9% and in trial 2, 86.9% of all the tannin available in the drug. Variations in the two trials may be attributed to differences in time required for the menstruum to pass through the drug, probably caused by different pressures being exerted in packing the drug in the tubes.

Modified Diacolation Compared.—Fluidextracts of Krameria were prepared in conical and cylindrical percolators, the dimensions of which have already been outlined, by the National Formulary VI procedure, and by a modified process in which no weak percolates were collected. These were assayed and compared with the fluidextracts made by modified diacolation. The results are shown in Table V.

Comments: The results would indicate that modified diacolation has no advantage over the official process in which a long cylindrical tube is used as the percolator except, perhaps, economy of alcohol. The process does show advantages, however, over the National Formulary VI process conducted in a conical percolator.

Loss of Tannin in Fluidextract of Krameria.—All of the fluidextracts prepared in this study were assayed for tannin after they had aged for known periods of time. It was found that, in general, the amount of tannin lost in Fluidextracts of Krameria became greater with increased aging time. Although the fluidextracts prepared by modified diacolation were not allowed to age as long as the others, results showed that they exhibited approximately the same degree of instability.

SUMMARY AND CONCLUSIONS

1. It is not possible to extract the tannin from krameria completely and efficiently by ordinary percolation methods without the collection of weak percolates.

2. Increasing the length of the drug column seems to increase the efficiency of extraction when the National Formulary VI process of percolation is employed.

3. It is possible to remove approximately 90% of the tannin from krameria without the collection and evaporation of weak percolates by employing a modified diacolation procedure.

4. Modified diacolation seems to be preferable to the National Formulary VI process in which a conical percolator is employed for the preparation of Fluidextract of Krameria, but it apparently possesses no advantages over the same process using a long cylindrical tube as the percolator.

5. Losses of tannin in Fluidextracts of Krameria were studied. As high as 12.5% of the original tannin was lost over a period of four and one-half months.

6. As far as they were observed, Fluidextracts of Krameria prepared by a modified diacolation process lost their tannin at about the same rate as did those prepared by other methods.

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A Study of Hydrophile Ointment Bases*

By G. W. Johnston† and C. O. Lee‡

The so-called "Absorption Bases" are relatively new products. The word absorption is used to denote their hydrophile or water-holding property and not to describe their action when applied to the skin. However, claims are made for the absorption of many of these preparations which are being marketed under a variety of names.

These bases have found a definite place in pharmacy and cosmetology because of their special properties. Due to the interest and attention that they have been receiving it was felt that it would be worth while to attempt to produce a similar preparation from official substances.

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