

DRUG EXTRACTION. X. THE SWELLING OF POWDERED DRUGS IN LIQUIDS.^{1, 2}

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As a part of a general study of the fundamental principles of drug extraction, swelling tests have been carried out on eighteen drugs in a series of hydro-alcoholic liquids. The purpose of the study was to secure definite swelling data on a variety of drugs, and to seek any correlations that would assist in the scientific selection of menstrua.

In previous papers of this series, the literature has been reviewed and methods have been developed for the determination of the swelling of drugs in the form of blocks, strips and powders (1), (2), (3). Likewise an apparatus has been developed for measuring the pressure which a drug exerts as a result of swelling in a percolator (4).

EXPERIMENTAL DATA.

It was decided to use the drugs as coarsely ground for percolation, as this would give results applicable to large scale work. The centrifuge method for determining the percentage swelling of powdered drugs in menstrua as developed by Husa and Magid (1) was modified so as to give more accurate results in case of powdered drugs containing coarse particles as well as fine particles; this was accomplished by using larger quantities of the drugs in larger centrifuge tubes.

In each case 5.0 Gm. of the drug was placed in a 50-cc. graduated centrifuge tube, centrifuged for ten minutes and the volume of the drug noted. Thirty cubic centimeters of the liquid were added, the mixture stirred, allowed to stand for ten minutes and then centrifuged for ten minutes. The volume of the drug layer was recorded, the mixture stirred and allowed to stand for a definite period, after which it was centrifuged for ten minutes and the volume again recorded. This procedure was continued until data were secured for several time intervals.

The swelling data observed on a series of drugs are presented in Table I. The results have been recalculated on a percentage basis, the volume of the swollen drug being expressed on the basis of the original volume of dry drug taken as 100. Each value is based on the average of two or more tests; in those cases in which blank spaces occur in the tables, it was impossible to secure an accurate reading because the drug did not settle well enough.

TABLE I.—SWELLING OF DRUGS IN HYDRO-ALCOHOLIC LIQUIDS.

(Volume of Drug Expressed on Basis: Dry Drug = 100.)

Percentage Alcohol (by Vol.).	Digitalis.						Uva Ursi.					
	0.	Time Intervals (in Minutes).					0.	Time Intervals (in Minutes).				
	10.	40.	70.	180.	300.		10.	40.	70.	180.	300.	
95.0	100	111	113	117	120	123	100	108	112	114	115	115
86.5	100	117	127	132	142	144	100	112	115	115	115	119
72.8	100	117	122	126	128	128	100	115	115	119	122	123
49.0	100	121	129	132	136	136	100	115	115	123	123	127
24.0	100	126	126	129	138	138	100	...	123	123	123	127
0 (Water)	100	179	179	186	100	...	131	131	131	131

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		Castanea.					Belladonna Leaves.					
95.0	100	108	108	104	105	101	100	109	109	109	109	109
86.5	100	98	101	102	105	105	100	103	106	107	111	111
72.8	100	103	103	103	112	114	100	86	86	84	84	88
49.0	100	111	111	111	121	126	100	81	81	81	83	86
24.0	100	109	109	109	109	114	100	94	94	95	100	100
0 (Water)	100	...	119	119	119	124	100	...	122	122	122	122
		Buchu.					Gentian.					
95.0	100	111	109	111	111	111	100	110	110	110	110	110
86.5	100	113	116	117	117	117	100	110	112	115	118	118
72.8	100	123	123	123	125	125	100	114	119	124	124	124
49.0	100	121	125	121	121	125	100	130	140	140	148	150
24.0	100	157	157	167	176	181	100	170	170	170	170	165
0 (Water)	100	...	200	200	209	218	100	206	206	206
		Glycyrrhiza.					Cimicifuga.					
95.0	100	117	124	124	120	128	100	114	121	121	129	129
86.5	100	115	120	125	128	130	100	121	121	127	127	129
72.8	100	124	126	128	128	128	100	127	133	140	147	149
49.0	100	130	130	130	130	135	100	127	141	148	155	158
24.0	100	139	139	142	142	142	100	147	153	160	171	173
0 (Water)	100	130	135	135	140	140	100	186	194	205	205	208
		Nux Vomica.					Celery Fruit.					
95.0	100	115	120	117	118	118	100	100	100	100	100	100
86.5	100	117	121	122	122	122	100	111	114	114	118	118
72.8	100	130	137	143	143	145	100	119	125	125	125	125
49.0	100	135	138	149	160	163	100	136	138	139	139	139
24.0	100	151	155	165	167	167	100	136	140	140	147	147
0 (Water)	100	169	175	178	178	188	100	153	156	156	164	164
		Juniper Berry.					Rhus Glabra.					
95.0	100	110	110	110	110	109	100	117	118	121	118	123
86.5	100	108	108	110	113	113	100	118	127	132	139	141
72.8	100	110	110	110	115	115	100	125	140	151	163	168
49.0	100	123	127	127	129	129	100	133	167	178	189	194
24.0	100	140	140	100	175	200	219	231	232
0 (Water)	100	100	200	228	228	239	239
		Cinchona.					Cascara Sagrada.					
95.0	100	114	123	123	123	123	100	108	108	108	115	115
86.5	100	120	128	131	139	144	100	115	121	123	123	123
72.8	100	122	130	140	140	143	100	127	125	125	130	132
49.0	100	133	147	156	158	161	100	129	133	133	133	133
24.0	100	142	150	153	161	164	100	144	144	144	144	144
0 (Water)	100	139	144	150	156	156	100	164	165	168	173	173
		Cocillana.					Euonymus.					
95.0	100	113	118	119	120	124	100	108	115	115	116	117
86.5	100	116	118	118	119	120	100	109	118	119	119	119
72.8	100	118	119	122	124	124	100	108	115	115	122	122
49.0	100	113	119	122	122	124	100	108	108	113	117	117
24.0	100	119	119	120	124	125	100	117	117	117	125	125
0 (Water)	100	...	119	120	122	126	100	157	157	159

	Colchicum Corm.						Aconite.					
95.0	100	112	112	112	112	112	100	113	115	115	115	115
86.5	100	113	113	115	115	119	100	115	115	118	118	122
72.8	100	124	128	128	132	132	100	118	124	124	129	129
49.0	100	125	125	125	125	125	100	133	153	160	160	160
24.0	100	129	129	127	129	129	100	144	153	163	165	173
0 (Water)	100	138	140	138	140	144	100	194	199	199	203	205

DISCUSSION OF RESULTS.

Procter (5) long ago attempted to classify drugs into groups according to the type of menstruum used. The official type processes for fluidextracts in effect classify drugs according to the process used. On the other hand there is considerable doubt as to whether the place of any given drug in such classifications can be predicted or whether it can only be determined experimentally. For more than a hundred years the statement has been repeatedly made by authorities on drug extraction that each drug is a problem in itself and must be studied individually to determine the best menstruum and best method of extraction. If this be true, then, any general rules must necessarily be of limited and conditional application.

In the present investigation, it was observed that all the drugs studied, except celery fruit, swelled in alcohol, the average swelling in alcohol being 12 per cent in 10 minutes. However, celery fruit swelled in a mixture of alcohol 9 volumes—water 1 volume. It is interesting to note that the N. F. V menstruum for fluidextract of celery fruit was alcohol, in which the celery fruit does not swell, but that the N. F. VI changed the menstruum to alcohol 9 volumes—water 1 volume, in which celery fruit swells. The change in the N. F. was made independently of the present investigation.

The table indicates that swelling usually increased with time, although the greatest swelling occurred in the first 10 minutes. Swelling usually increased with increasing concentration of water; however, there were two exceptions: *i. e.*, belladonna leaves and castanea. In the case of belladonna leaves there was a shrinkage in intermediate concentrations of water, with swelling in higher and lower concentrations. The swelling of castanea did not change regularly with changing concentration of water.

Apparently there is no correlation between the part of the plant used and the percentage swelling, *e. g.*, the swelling of different leaf drugs varied considerably. Likewise there is no correlation between the percentage swelling and the type of constituents present in the drug; this conclusion is in accord with the results of Husa and Magid (1), who found that the soluble constituents of chestnut wood did not affect the swelling.

A check of the official menstrea for fluidextracts likewise showed no correlation between the composition of the menstrea and the part of the plant used. Similarly no definite correlation between the official menstrea and the type of constituents present in the drug could be observed.

The results of the present investigation tend to confirm the idea that each drug is a problem in itself and must be studied individually to determine the best menstruum and best method of extraction.

SUMMARY.

The centrifuge method for determining the percentage swelling of powdered drugs in liquids was modified so as to give more accurate results in case of drugs coarsely ground for percolation.

Swelling tests were carried out on eighteen drugs in a series of hydro-alcoholic liquids. All drugs except celery fruit swelled in alcohol, the average swelling in alcohol being 12 per cent in 10 minutes. Swelling usually increased with time, although the greatest swelling occurred in the first 10 minutes. Swelling usually increased with increasing concentration of water, except in the case of belladonna leaves and castanea. With belladonna leaves there was a shrinkage in intermediate concentrations of water, while castanea showed some irregularities.

The results tend to confirm the idea that each drug must be studied individually to determine the best menstruum and best method of extraction.

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- (4) Husa, W. J., and Magid, L., *Ibid.*, 25, 10 (1936).
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THE BIOASSAY OF STROPHANTHUS PREPARATIONS.*¹

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The abundant literature dealing with the methods of assaying *Strophanthus* preparations (cited and reviewed in the original thesis) leaves one in considerable doubt concerning the answer to the following questions:

1. Do the several more widely accepted methods of assay furnish a reliable estimation of the clinical activity of *Strophanthus* preparations?
2. Do the various methods measure the same or different types of activity in the preparations?
3. If the various methods yield significantly different results, which method is the more reliable in insuring clinical efficiency?
4. If the various methods yield results which are not significantly different from one another, which method affords the greater precision and dependability in routinely standardizing *strophanthus* preparations?

In order to assist in answering the above questions, four tinctures were prepared by the U. S. P. X Method from as many different lots of *strophanthus*. The four specimens of the drug were selected from a number of recent importations. From the standpoint of physical characteristics, all appeared to be of better than average quality. These tinctures were carefully assayed periodically over a period of over a year by the methods indicated below.

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