Contributed and Selected

COMPARATIVE ALKALOIDAL STRENGTH OF HYDRASTIS ROOTLETS AND RHIZOME.*

CHARLES H. LA WALL.

Some time ago a client called me up on the telephone and asked which contained the greatest amount of alkaloids, the rhizome or rootlets of hydrastis. I told him that I did not know but would try and find out. I could find neither any reference in literature bearing on the subject nor could I find anybody else who could answer the question among about a dozen chemists whom I consulted.

My client then submitted samples and data which form the basis for this short contribution.

A lot of hydrastis weighing 98 pounds net was seen to consist of such a large proportion of rhizomes that it was deemed advisable to make a complete separation and separate assays for guidance in future purchases. Upon cleaning the drug and separating the rootlets from the rhizomes the following fractions were obtained:

Rhizomes	45 1/2 lbs.
Rootlets	48 lbs.
Dirt and dust	3 5/16 lbs.
Loss in cleaning (unaccounted for)	1 3/16 lbs.
Total	98 lbs.

Of the 93½ pounds of hydrastis 48.66% was rhizomes and 51.34% was rootlets. Upon assaying these separately the rhizomes were found to assay 2.48%, while the rootlets were found to assay only 1.38% of hydrastine. The total assay of the mixed drug in its original condition, from these figures, must have been 1.92%, which is slightly lower than the U. S. P. standard drug.

The answer to the original question, however, is that hydrastis rhizomes are between 1.5 and 2 times as rich in alkaloids as the rootlets.

A NEW AND RELIABLE METHOD FOR THE PRESERVATION OF ERGOT PREPARATIONS.*

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The deterioration of ergot preparations has for several years occupied the attention of various investigators, but until the present no one has succeeded in devising a method by which these preparations can be put on the market in a form

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which will remain stable for a considerable length of time. So serious a problem had the deterioration of these products become, that it was deemed advisable that the actual date of test be made to appear on all ergot preparations in order that pharmacists and physicians might be enabled to use their expert judgment as to whether or not any particular product should be employed.

Without question, heat and access of oxygen of the air are the most potent factors in facilitating the deterioration of ergot, but the continued examination of many samples led us to believe the access of air to be the most important cause of deterioration. It has been known for some time that well filled, tightly stoppered containers of fluidextract of ergot will retain their activity for a much longer period of time than containers which are opened from time to time.

Accordingly, on May 2, 1911, the following experiments with fluidextract of ergot were undertaken to determine the value of complete exclusion of air.

A fluidextract was taken which, when intravenously injected in doses of 0.08 cc. per kilo weight gave the following result in changing blood-pressure:

Table No. 1.

	Dog No. 1.			Dog No. 2.		
Injection.	No. 1.	No. 2.	No. 3	No. 4.	No. 5.	Average.
	m.m.	m.m.	m.m.	m.m.	m.m.	m.m
Immediate rise	48	44	28	68	36	48.8
Fall	10	30	46	4	24	22.8
Rise after 5 Min.	38	22	30	38	8	25.2
Rise after 10 Min.	34	20	18	30	8	22.0
Rise after 15 Min.	31	20	14	26	4	19.0

When assayed for total alkaloids by the process of Keller, on May 26, 1911, 0.163% was obtained.

This fluid extract was then divided into four portions which were kept for one year in the laboratory in the following manner:

A—The first portion was put up in vacuum tubes specially designed and made for this purpose.

B—The second portion was filled into bottles which were tightly corked and allowed to remain for one year, unopened.

C—The third portion was filled into bottles which were kept loosely corked for one year, this being obtained by boring a small hole in the cork.

D—The fourth portion was tightly corked but opened occasionally throughout the year.

After three months a test was made of part of the fourth portion (D) which showed a deterioration of 33.3% as shown by Table No. 2.

Injection.	0.08 cc. per kilo.
Immediate rise	30 m.m.
Fall	24 m.m.
Fall after 5 min.	—10 m.m.
Fall after 10 min.	—13 m.m.

A second test was made of this portion at the end of nine months, when it was found to possess only 44 2/6% of the original activity or to show a deterioration of 55½%, as shown by Table 3:

Injection.	No. 1.	No. 2.	Average.
Immediate rise	20 m.m.	20 m.m.	20 m.m.
Fall	34 m.m.	30 m.m	32 m.m.
Fall after 5 min	—16 m.m.	—13 m.m.	—14.5 m.m.
Fall after 10 min	—12 m.m.	—12 m.m.	—12 m.m.
Fall after 15 min	—8 m.m.	—10 m.m.	—9 m.m.

At the end of a year all four portions were tested with the following results:

Table No. 4.

A—First portion put up in vacuum tubes.

	Dog No. 1			Dog No. 2		Dog No. 3	Dog No. 4	Dog No. 5	Dog No. 6	
Injection	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	No. 9	Aver.
	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.
Immediate rise	44	52	40	54	52	44	44	58	54	49.1
Fall	7	18	12	30	12	0	0	0	0	8.7
Rise after 5 min	5	32	20		2	19	0	24	16	13.8
Rise or fall after 10 min.	—2	18		—5	2	4	—3	18	3	4.4
Rise or fall after 15 min.	—2	18		2	1	4	—6	12	—4	3.1

When assayed for total alkaloid by the process of Keller, on May 6, 1912—0.168% was obtained.

Table No. 5.

B—Second portion, tightly corked, unopened.

	Dog No. 1		Dog. No. 2	Dog. No. 3		
Injection	No. 1	No. 2	No. 3	No. 4	No. 5	Average
	m.m.	m.m.	m.m.	m.m.	m.m.	m.m.
Immediate rise	44	28	26	28	23	29.8
Fall	32	22	0	0	6	12.0
Rise after 5 min	0	2	7	10	2	4.2
Rise after 10 min	14	0	1.5	4	0	3.9
Rise or fall after 15 min	14	0	—1.	2.	0	3.0

Table No. 6.

C—Third portion loosely corked.

	Dog No. 1		Dog No. 2		
Injection	No. 1	No. 2	No. 3	No. 4	Average
	m.m.	m.m.	m.m.	m.m.	m.m.
Immediate rise	24	18	6	18	16.5
Fall	38	52	24	24	34.5
Rise or fall after 5 min	2	—8	—4	—8	—4.5
Rise or fall after 10 min	3	—4	—3	—4	—2.0
Rise or fall after 15 min	7	—1	—2	—4	0.0

Table No. 7.

D—Fourth portion, tightly corked, opened occasionally.

Injection	Dog No. 1 No. 1 m.m.	Dog No. 2 No. 2 m.m.	Dog No. 2 No. 3 m.m.	Average m.m.
Immediate rise	12.	10.	23.	15.
Fall	54.	40.	26.	40.
Fall after 5 min	—4.	0.	—18.	—7.3
Fall after 10 min	—6.	—1.	0	—2.3
Fall after 15 min	—6.	—2.	0	—2.7

When assayed for total alkaloid by the process of Keller, on May 6, 1912—0.076% was obtained.

SUMMARY.

Table No. 8

How Kept	Date tested	No. of injections	Aver. rise of blood-pressure	Chemical assay for total alkaloid
Original sample	5-26-11	5	44.8 m.m.	0.163%
D—Tightly corked (3 months), opened occasionally	8-24-11	1	30.0 m.m.	
D—Tightly corked (9 months), opened occasionally	2-29-12	2	20.0 m.m.	
A—In *vacuum* (1 year old)	5- 9-12	9	49.1 m.m.	0.168%
B—Tightly corked (1 year old)	5- 9-12	5	29.8 m.m	
C—Loosely corked (1 year old)	5- 9-12	4	16.5 m.m.	
D—Tightly corked (1 year old), opened occasionally	5- 9-12	3	15.0 m.m.	0.076%

The apparent extreme variations in the rises recorded in the different animals are due to both the difference in the susceptibility of the dogs and to the difference in the order of injection of samples. In order to obtain the true relative strengths of the preparations the order of injection was reversed in succeeding animals until each preparation had been given to each of several dogs and the results based on the analysis of the several injections.

It may thus be seen that by adopting the *vacuum* method of putting up ergot the rate of deterioration can be so retarded as to make this product one of stable quality for a considerable length of time.

We have already taken steps to apply the same method of preservation to the preparation of other drugs somewhat prone to deterioration, such as digitalis and strophanthus.

PHYSIOLOGICAL LABORATORY OF H. K. MULFORD COMPANY.

THE REVISION OF THE UNITED STATES PHARMACOPOEIA.*

JOSEPH P. REMINGTON, CHAIRMAN.

The work of preparing the Ninth Revision is proceeding rapidly. The new plan, which differs essentially from all previous methods, while involving more

*Read before the Section on Pharmacology and Therapeutics of the American Medical Association.