

SCIENTIFIC SECTION

THE DETERIORATION OF "U. S. P." AND "FAT-FREE" TINCTURES OF DIGITALIS.*

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Many papers have been published on the subject of digitalis, in which practically all of the authors conclude that the galenical preparations of digitalis deteriorate quite rapidly.

The laboratories connected with the larger pharmaceutical manufacturing houses, although using many different methods of assay, all found that these preparations deteriorated so rapidly that they deemed it necessary to warn their customers of this fact by placing small labels upon the containers reading as follows:

"Owing to the rapid deterioration of preparations of digitalis, they should only be purchased in quantities sufficient to meet immediate demands."

The more ethical manufacturers also state upon the label the date of manufacture in order that the druggist or physician may know the age of the particular preparation he is dispensing or administering.

Dr. George B. Roth, Government Pharmacologist, states in the conclusion of his paper entitled "Digitalis Standardization"[†] "in view of the fact that deterioration of digitalis occurs so rapidly it is advisable that, if such preparations are to be marketed, the date of their manufacture should be stated, so that physicians may know the age of the preparations and may not be misguided into purchasing worthless preparations."

Hatcher,¹ however, in an article entitled "Observations on the Keeping Properties of Digitalis and Some of Its Preparations" gives the results of many tests made upon old samples of the drug, and arrived at the conclusion that preparations of digitalis do not deteriorate. He found that in many cases samples from two to twenty years old were as active, and in some cases more active, than the freshly prepared samples and therefore concluded that digitalis preparations do not deteriorate.

As the investigations of Fränkel,² Edmonds and Hale,³ Hale,⁴ Pittenger,⁵ and others show that the digitalis preparations upon the market vary hundreds of percent, there is every reason to believe that the preparations which showed standard activity after several years may have originally been six or eight times standard strength.

It is the authors opinion that the only way in which any definite information can be obtained as to the rate of deterioration of a particular drug is to prepare:

* Read before Scientific Section, A. Ph. A., Indianapolis meeting, 1917.

† Roth, *Hygienic Laboratory Bulletin*, No. 102, 1916.

¹ Hatcher, *Druggists' Circular*, June 1913, page 325.

² Fränkel, *Charite-Ann.*, Berlin, 1881, VI, page 207.

³ Edmonds and Hale, *Hygienic Lab. Bulletin*, No. 48, 1909.

⁴ Hale, *Hygienic Lab. Bull.*, No. 74, 1911.

⁵ Pittenger, Text-Book "Biochemic Drug Assay Methods," 1914, page 6.

a fresh tincture or fluid extract of the same, test it immediately after it is prepared and then retest the *same preparation* at intervals of a few months. In this way absolute scientific information can be obtained.

Roth, in the paper referred to, shows that "fat-free" tinctures of digitalis show a marked deterioration after five to seven months. At several of the medical societies, which the authors have attended during the past year, the remark has been made during the discussion of papers that the so-called "fat-free" or "defatted" tinctures of digitalis deteriorate more rapidly than the U. S. P. tinctures. These remarks, however, were made without the support of experimental data. In order to prove, therefore, whether or not tinctures of digitalis deteriorate, and if so, whether the "fat-free" preparations deteriorate more or less rapidly than the regular U. S. P. tinctures, we carried out the following experiments:

A sample of digitalis drug was obtained from different sources, namely, H. K. Mulford Co., P. E. Anderson, Werner & Gerathy, McKesson & Robbins and the National Aniline & Chemical Company. Each lot of drug was divided into three parts, "A," "B," and "C."

"A" was percolated with fifty percent alcohol and made into the regular U. S. P. VIII tincture.

"B" was percolated with benzine until a small quantity of the percolate evaporated to dryness on a watch crystal left no trace of fat, thus proving that the fat had been entirely removed from the drug. The drug was then spread out on paper until the benzine evaporated. The drug was then moistened, repacked in the percolator, macerated, and percolated with fifty percent alcohol to tincture strength.

"C" was "defatted" the same as given under "B," but was macerated and percolated with eighty percent alcohol instead of fifty percent alcohol.

Each of the fifteen samples were assayed immediately after they were prepared, re-assayed after four or five months had elapsed and again after seven or eight months.

As there is no satisfactory chemical method for assaying digitalis, the above preparations were tested by the Reed and Vanderkleed Guinea-Pig Method, which consists in determining the minimum dose per two hundred and fifty gramme body-weight of animal necessary to cause the death of the animal within twenty-four hours, when the preparation is subcutaneously injected. The standard for tincture of digitalis is 1.0 mil (Cc.) per two hundred and fifty gramme body-weight of animal.

The following tables show the detailed results of these experiments:

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 1 A. H. K. M. Co. drug, U. S. P. VIII. Menstruum 50 percent. Date of test, 6-28-16	0.4	285	0.45	Recovered
	0.6	215	0.51	Recovered
	0.6	225	0.54	Recovered
	0.7	250	0.7	Recovered
	0.8 ¹	345	1.1	Recovered
	0.8 ¹	260	0.83	Died
	0.8 ¹	185	0.95	Died
	0.9	250	0.9	Died
	1.0	210	0.84	Died
	1.0	245	0.98	Died

¹ M. L. D. = 0.8 = 125.0%.

JOURNAL OF THE

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 1 A. Same drug. Second test. After 5 months. Date of test, 11-29-16	1.2	310	1.48	Recovered
	1.3	350	1.82	Recovered
	1.3	385	2.0	Recovered
	1.4	390	2.18	Recovered
	1.6	435	2.78	Recovered
	1.6	335	2.14	Recovered
	1.6	350	2.24	Recovered
	1.8 ¹	485	3.49	Died
	1.8 ¹	340	2.44	Died
	2.0	250	2.0	Died

¹ M. L. D. = 1.8 = 55.5%.

No. 1 A. Third test after eight months. Date of test, 2-1-17	1.8	405	2.91	Recovered
	2.0	400	3.2	Recovered
	2.2	420	3.69	Recovered
	2.5	345	3.45	Recovered
	2.6	405	4.21	Recovered
	2.6	395	4.1	Recovered
	2.6	420	4.36	Recovered
	2.7 ¹	410	4.42	Died
	2.7 ¹	360	3.88	Died
	2.7 ¹	435	4.69	Died
	2.8	395	4.42	Died
	2.8	425	4.76	Died
	2.8	395	4.42	Died
3.0	395	4.74	Died	

¹ M. L. D. = 2.7 = 37.0%.

No. 1 B. Same drug as No. 1 A. "Defatted" U. S. P. VIII. Menstruum, 50 per- cent. Date of test, 6-28-16	0.8	230	0.73	Recovered
	1.0	220	0.88	Recovered
	1.0	225	0.9	Recovered
	1.0	235	0.94	Recovered
	1.0	245	1.01	Died
	1.1	245	1.07	Recovered
	1.1	280	1.23	Recovered
	1.2	190	0.91	Recovered
	1.2	325	1.6	Recovered
	1.3	270	1.4	Recovered
	1.3	225	1.17	Died
	1.4 ¹	270	1.5	Died
	1.4 ¹	190	1.06	Died
1.5	250	1.5	Died	

¹ M. L. D. = 1.4 = 71.5%.

No. 1 B. Second test after 5 months. Date of test, 11-29-16.	1.2	425	2.04	Recovered
	1.4	335	1.87	Recovered
	1.4	440	2.46	Recovered
	1.6 ¹	390	2.49	Died
	1.6 ¹	355	2.27	Died
	1.8	420	3.02	Died

¹ M. L. D. = 1.6 = 62.6%.

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 1 B. Third test after 8 months. Date of test, 2-1-17	1.4	410	2.29	Recovered
	1.6	405	2.59	Recovered
	1.8	405	2.91	Recovered
	1.8	405	2.91	Recovered
	2.0	350	2.8	Recovered
	2.0	330	2.64	Recovered
	2.2	405	3.56	Recovered
	2.3	370	3.4	Recovered
	2.3	410	3.77	Recovered
	2.4 ¹	305	2.92	Died
	2.4 ¹	385	3.61	Died
	2.5	405	4.05	Died
¹ M. L. D. = 2.4 = 41.7%.				
No. 1 C. Same drug as No. 1 A and No. 1 B. "De-fatted" 80 percent alcohol menstruum. Date of test, 6-28-16	0.5	225	0.45	Recovered
	0.6	250	0.6	Recovered
	0.6	240	0.57	Recovered
	0.6	270	0.64	Died
	0.7	205	0.57	Recovered
	0.7	245	0.68	Recovered
	0.8 ¹	285	0.91	Died
	0.8 ¹	335	1.07	Died
	0.8 ¹	205	0.65	Died
	0.0	250	1.0	Died
¹ M. L. D. = 0.8 = 125.0%.				
No. 1 C. Second test after 5 months. Date of test, 11-29-16	0.6	390	0.93	Recovered
	0.8	370	1.18	Recovered
	0.9	420	1.51	Died
	0.9	405	1.45	Recovered
	0.9	395	1.42	Recovered
	0.9	250	0.9	Recovered
	1.0	450	1.8	Died
	1.0	410	1.04	Recovered
	1.0	460	1.84	Recovered
	1.1	250	1.1	Recovered
	1.2 ¹	375	1.8	Died
	1.2 ¹	395	1.89	Died
1.3	500	2.6	Died	
1.3	250	1.3	Died	
¹ M. L. D. = 1.2 = 83.3%.				
No. 1 C. Third test after 8 months. Date of test, 2-1-17	1.1	400	1.76	Recovered
	1.1	370	1.62	Recovered
	1.2	400	1.92	Recovered
	1.2	370	1.77	Died
	1.2	335	1.6	Recovered
	1.3 ¹	300	1.56	Died
	1.3 ¹	380	1.97	Died
	1.3 ¹	360	1.87	Died
	1.4	375	2.1	Died
	1.4	270	1.51	Died
	1.4	355	1.98	Died
	1.5	455	2.73	Died
1.6	455	2.91	Died	
1.8	415	2.98	Died	
¹ M. L. D. = 1.3 = 76.1%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 2 A. Drug from P. E. Anderson, U. S. P. VIII. Menstruum, 50 percent. First test, 7-6-16	0.4	235	0.37	Recovered
	0.6	195	0.47	Recovered
	0.6	295	0.7	Recovered
	0.7	250	0.7	Recovered
	0.8 ¹	200	0.64	Died
	0.8 ¹	185	0.59	Died
	1.0	265	1.06	Died
	1.2	295	1.41	Died
¹ M. L. D. = 0.8 = 125%.				
No. 2 A. Second test after 4 months. Date of test, 11-29-16	0.7	325	0.91	Recovered
	0.8	440	1.4	Recovered
	1.0	435	1.74	Recovered
	1.1	295	1.29	Recovered
	1.2	380	1.82	Recovered
	1.2	375	1.8	Recovered
	1.3	325	1.67	Recovered
	1.3	425	2.21	Recovered
	1.4 ¹	310	1.73	Died
	1.4 ¹	450	2.52	Died
¹ M. L. D. = 1.4 = 71.4%.				
No. 2 A. Third test after 7 months. Date of test, 2-1-17	1.4	355	1.98	Recovered
	1.4	385	2.15	Recovered
	1.5	350	2.1	Died
	1.5	305	1.83	Recovered
	1.5	355	2.13	Recovered
	1.6 ¹	360	2.3	Died
	1.6 ¹	325	2.08	Died
	1.6 ¹	380	2.43	Died
¹ M. L. D. = 1.6 = 62.5%.				
No. 2 B. Same drug as No. 2 A. "Defatted" U. S. P. VIII. Menstruum, 50 per- cent. Date of test, 7-6-16	0.8	330	1.05	Recovered
	0.8	240	0.76	Recovered
	0.9	235	0.75	Recovered
	1.0	245	0.98	Recovered
	1.0	265	1.06	Recovered
	1.0	230	0.92	Recovered
	1.0	265	1.06	Recovered
	1.1 ¹	425	1.87	Died
	1.1 ¹	500	2.2	Died
	1.2	250	1.2	Died
¹ M. L. D. = 1.1 = 90.9%.				
No. 2 B. Second test after 4 months. Date of test, 11-29-16	1.0	465	1.86	Recovered
	1.1	390	1.71	Recovered
	1.2	390	1.87	Recovered
	1.2	375	1.8	Recovered
	1.4 ¹	365	2.04	Died
	1.4 ¹	365	2.04	Died
	1.6	395	2.52	Died
	1.6	355	2.41	Died
¹ M. L. D. = 1.4 = 71.4%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 2 B. Third test after 7 months. Date of test, 2-1-17	1.2	435	2.08	Recovered
	1.3	335	1.76	Recovered
	1.3	250	1.3	Recovered
	1.4 ¹	330	1.84	Died
	1.4 ¹	255	1.42	Died
	1.4 ¹	430	2.4	Died
	1.5	420	2.52	Died
	1.5	320	1.92	Died
	1.6	350	2.24	Died
	1.6	450	2.88	Died
¹ M. L. D. = 1.4 = 71.4%.				
No. 2 A. "Defatted" 80 percent alcohol menstruum. Date of test, 7-6-16	0.2	220	0.176	Recovered
	0.3	260	0.31	Recovered
	0.4	185	0.29	Recovered
	0.4	260	0.41	Recovered
	0.4	215	0.34	Recovered
	0.5 ¹	270	0.54	Died
	0.5 ¹	310	0.62	Died
	0.6	310	0.74	Died
	0.6	215	0.51	Died
	0.7	250	0.7	Died
¹ M. L. D. = 0.5 = 200%.				
No. 2 C. Second test after 4 months. Date of test, 11-29-16	0.4	365	0.58	Recovered
	0.5	485	0.97	Recovered
	0.5	385	0.77	Recovered
	0.6 ¹	340	0.81	Died
	0.6	335	0.8	Recovered
	0.6 ¹	415	0.99	Died
	0.6 ¹	395	0.94	Died
	0.7	250	0.7	Died
¹ M. L. D. = 0.6 = 133%.				
No. 2 C. Third test after 7 months. Date of test, 2-1-17	0.6	390	0.93	Recovered
	0.6	395	0.94	Recovered
	0.7	500	1.4	Recovered
	0.7	400	1.12	Recovered
	0.7	305	1.13	Recovered
	0.8 ¹	250	0.8	Died
	0.8 ¹	450	1.44	Died
	0.8	410	1.31	Died
	0.9	250	0.9	Died
	0.9	500	1.8	Died
¹ M. L. D. = 0.8 = 125%.				
No. 3 A. Drug from Werner & Gerathy, U. S. P. VIII. Menstruum, 50 percent. Date of test, 7-6-16	1.0	305	1.22	Recovered
	1.0	305	1.22	Recovered
	1.1	235	1.03	Recovered
	1.1	250	1.1	Recovered
	1.2 ¹	275	1.32	Died
	1.2 ¹	335	1.6	Died
	1.2 ¹	245	1.1	Died
	1.3	250	1.3	Died
	1.3	500	2.6	Died
	1.4	245	1.37	Died
¹ M. L. D. = 1.2 = 83.3%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 3 A. Second test after 4 months. Date of test, 11-29-16	1.2	350	1.61	Recovered
	1.4	245	1.37	Recovered
	1.4	400	2.24	Recovered
	1.6 ¹	390	2.49	Died
	1.6	245	1.56	Died
	1.7	365	2.48	Died
¹ M. L. D. = 1.6 = 62.5%.				
No. 3 A. Third test after 7 months. Date of test, 2-1-17	1.4	345	1.93	Recovered
	1.4	405	2.26	Recovered
	1.4	305	1.7	Recovered
	1.4	335	1.87	Died
	1.5 ¹	300	1.8	Died
	1.5 ¹	415	2.49	Died
	1.5 ¹	345	2.07	Died
	1.6	415	2.65	Died
	1.6	425	2.72	Died
1.6	475	3.04	Died	
¹ M. L. D. = 1.5 = 62.0%.				
No. 3 B. Same drug as No. 3 A. "Defatted" U. S. P. VIII. Menstruum, 50 per- cent. Date of test, 7-6-16	0.6	195	0.46	Recovered
	0.6	225	0.54	Recovered
	0.8	295	0.94	Recovered
	0.8	285	0.91	Recovered
	1.0	230	0.92	Recovered
	1.2	220	1.05	Recovered
	1.4	230	1.28	Recovered
	1.4	260	1.45	Recovered
	1.5	250	1.5	Recovered
	1.6 ¹	285	2.8	Died
1.6 ¹	305	1.95	Died	
1.8	250	1.8	Died	
¹ M. L. D. = 1.6 = 62.5%.				
No. 3 B. Second test after 4 months. Date of test, 11-29-16	1.4	330	1.84	Recovered
	1.4	375	2.1	Recovered
	1.6 ¹	445	2.84	Died
	1.6 ¹	375	2.4	Died
	1.8	285	2.05	Died
	1.8	360	2.59	Died
¹ M. L. D. = 1.6 = 62.5%.				
No. 3 B. Third test after 7 months. Date of test, 2-1-17	1.4	355	1.98	Recovered
	1.4	350	1.96	Recovered
	1.4	340	1.9	Recovered
	1.5	435	2.61	Recovered
	1.5	375	2.25	Died
	1.5	345	2.07	Recovered
	1.5	250	1.5	Recovered
	1.6 ¹	405	2.59	Died
	1.6 ¹	390	2.49	Died
1.7	250	1.7	Died	
¹ M. L. D. = 1.6 = 62.5%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 3 C. Same drug as No. 3 A. "Defatted" 80 percent alcohol menstruum. Date of test, 7-6-16	0.4	205	0.32	Recovered
	0.4	240	0.38	Recovered
	0.5	250	0.5	Recovered
	0.6 ¹	180	0.43	Died
	0.6 ¹	230	0.55	Died
	0.8	290	0.92	Died
¹ M. L. D. = 0.6 = 166%.				
No. 3 C. Second test after 4 months. Date of test, 11-29-16	0.6	465	1.11	Recovered
	0.6	410	0.98	Recovered
	0.8 ¹	335	1.07	Died
	0.8 ¹	380	1.21	Died
	1.0	365	1.46	Died
	1.0	4.10	1.64	Died
¹ M. L. D. = 0.8 = 150%.				
No. 3 C. Third test after 7 months. Date of test, 2-1-17	0.6	385	0.92	Recovered
	0.6	395	0.94	Recovered
	0.7 ¹	365	1.02	Died
	0.7	390	1.09	Recovered
	0.7 ¹	420	1.17	Died
	0.7 ¹	310	0.86	Died
	0.7 ¹	365	1.02	Died
	0.8	420	1.34	Died
¹ M. L. D. = 0.7 = 143%.				
No. 4 A. Drug from McKesson & Robbins, U. S. P. VIII. Menstruum, 50 percent. Date of test, 7-13-16	0.5	290	0.58	Recovered
	0.6	205	0.49	Recovered
	0.6	190	0.45	Recovered
	0.8	230	0.73	Recovered
	1.0	285	1.14	Recovered
	1.0	190	0.76	Recovered
	1.1	240	1.05	Recovered
	1.1	240	1.05	Died
	1.1	295	1.29	Recovered
	1.1	285	1.25	Recovered
	1.2 ¹	200	0.96	Died
	1.2 ¹	250	1.2	Died
1.2 ¹	375	1.80	Died	
1.3	315	1.63	Died	
1.3	250	1.3	Died	
1.4	195	1.09	Died	
¹ M. L. D. = 1.2 = 83.3%.				
No. 4 A. Second test after 4 months. Date of test, 11-29-16	1.0	465	1.86	Recovered
	1.1	390	1.71	Recovered
	1.2	435	2.08	Recovered
	1.2	375	1.8	Recovered
	1.3	335	1.76	Recovered
	1.4 ¹	365	2.04	Died
	1.4 ¹	330	1.84	Died
	1.4 ¹	365	2.04	Died
	1.6	450	2.88	Died
	1.6	395	2.52	Died
¹ M. L. D. = 1.4 = 71.5%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 4 A. Third test after 7 months. Date of test, 2-1-17	1.5	340	2.04	Recovered
	1.5	435	2.61	Recovered
	1.6	350	2.24	Recovered
	1.6	355	2.27	Recovered
	1.7	325	2.21	Recovered
	1.7	325	2.21	Recovered
	1.8	350	2.52	Recovered
	1.8	420	3.02	Recovered
	1.9	250	1.9	Recovered
	2.0 ¹	485	3.88	Died
	2.0 ¹	440	3.52	Died
2.2	385	3.38	Died	
¹ M. L. D. = 2.0 = 50%.				
No. 4 B. Same drug as No. 4 A. "Defatted" U. S. P. VIII. Menstruum, 50 percent. Date of test, 7-13-16	0.8	270	0.86	Recovered
	0.8	245	0.78	Recovered
	1.0	230	0.92	Recovered
	1.0	285	1.14	Recovered
	1.2	215	1.03	Recovered
	1.2	230	0.92	Recovered
	1.3	210	1.09	Recovered
	1.3	285	1.48	Recovered
	1.5 ¹	255	1.41	Died
1.5 ¹	250	1.5	Died	
¹ M. L. D. = 1.5 = 76.8%.				
No. 4 B. Second test after 4 months. Date of test, 11-29-16	1.1	390	1.71	Recovered
	1.2	375	1.8	Recovered
	1.2	275	1.32	Recovered
	1.3 ¹	345	1.79	Died
	1.3 ¹	285	1.48	Died
	1.4	450	2.52	Died
¹ M. L. D. = 1.3 = 70.7%.				
No. 4 B. Third test after 7 months. Date of test, 2-17	1.0	385	1.54	Recovered
	1.1	250	1.1	Recovered
	1.2	400	1.92	Recovered
	1.2	340	1.63	Recovered
	1.3 ¹	385	2.0	Died
	1.3 ¹	335	1.76	Died
	1.4	425	2.38	Died
1.4	400	2.24	Died	
¹ M. L. D. = 1.3 = 70.7%.				
No. 4 C. Same drug as 4 A. "Defatted" 80 percent alco- hol menstruum. Date of test, 7-13-16	0.7	310	0.86	Recovered
	0.8	235	0.75	Recovered
	0.9	295	1.0	Recovered
	0.9	270	0.97	Recovered
	1.0	235	0.94	Recovered
	1.0	225	0.90	Recovered
	1.1 ¹	275	1.21	Died
	1.1 ¹	175	0.77	Died
	1.2	250	1.2	Died
1.2	340	1.63	Died	
¹ M. L. D. = 1.1 = 90.9%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 4 C. Second test after 4 months. Date of test, 11-29-16	1.9	250	1.9	Recovered
	2.0	375	3.0	Recovered
	2.0	260	2.88	Recovered
	2.1	250	2.1	Recovered
	2.1	500	4.2	Recovered
	2.2 ¹	250	2.2	Died
	2.2 ¹	495	4.35	Died
	2.2 ¹	395	3.47	Died
	2.3	250	2.3	Died
2.3	315	2.89	Died	
¹ M. L. D. = 2.2 = 45.4%.				
No. 4 C. Third test after 7 months. Date of test, 2-1-17	3.0	280	3.3	Recovered
	3.0	280	3.3	Recovered
	4.0	310	4.9	Recovered
	4.0	275	4.4	Recovered
	5.0	330	6.6	Recovered
	5.0	165	3.3	Recovered
	6.0 ¹	340	8.1	Died
	6.0 ¹	300	7.2	Died
	7.0	270	7.5	Died
8.0	370	11.8	Died	
¹ M. L. D. = 6.0 = 16.6%.				
No. 5 A. Drug from National Analine Co., U. S. P. VIII. Menstruum, 50 percent. Date of test, 7-13-16	0.6	285	0.68	Recovered
	0.8	230	0.73	Recovered
	1.0	215	0.86	Recovered
	1.2	235	1.12	Recovered
	1.2	365	1.17	Recovered
	1.3	225	1.17	Recovered
	1.3	250	1.3	Recovered
	1.4 ¹	235	1.31	Died
	1.4 ¹	260	1.45	Died
1.5	250	1.5	Died	
¹ M. L. D. = 1.4 = 71.5%.				
No. 5 A. Second test after 4 months. Date of test, 11-29-16	1.4	385	2.15	Recovered
	1.5	355	2.13	Recovered
	1.6	325	2.08	Recovered
	1.7	355	2.41	Recovered
	1.8	360	2.59	Recovered
	2.0 ¹	365	2.9	Died
	2.0 ¹	410	2.08	Died
	2.2	240	2.1	Died
¹ M. L. D. = 2.0 = 50.0%.				
No. 5 A. Third test after 7 months. Date of test, 2-1-17	2.5	385	3.85	Recovered
	2.5	295	2.95	Recovered
	2.7	415	4.48	Recovered
	2.7	360	3.88	Recovered
	2.9	250	2.9	Recovered
	2.9	250	2.9	Recovered
	3.0 ¹	390	4.68	Died
3.0 ¹	430	5.16	Died	
¹ M. L. D. = 3.0 = 33.3%.				

Sample	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 5 B. Same drug as No. 5 A. "Defatted" U. S. P. VIII. Menstruum, 50 percent. Date of test, 7-13-16	0.8	305	0.97	Recovered
	1.0	250	1.0	Recovered
	1.2	275	1.32	Recovered
	1.4	225	1.26	Recovered
	1.6	275	1.76	Recovered
	1.8	235	1.69	Recovered
	2.0	205	1.64	Recovered
	2.0	250	2.0	Recovered
	2.1	250	2.1	Recovered
	2.2 ¹	265	2.33	Died
2.2 ¹	295	2.59	Died	
2.5	200	2.0	Died	
¹ M. L. D. = 2.2 = 45.4%.				
No. 5 B. Second test after 4 months. Date of test, 11-29-17	3.0	305	3.66	Recovered
	3.2	335	4.28	Recovered
	3.2	440	5.63	Recovered
	3.4	250	3.4	Recovered
	3.5	320	4.48	Recovered
	3.5	415	5.81	Recovered
	3.7 ¹	380	5.62	Died
	3.7 ¹	250	3.7	Died
¹ M. L. D. = 3.7 = 27%.				
No. 5 B. Third test after 7 months. Date of test, 2-1-17	3.0	435	5.22	Recovered
	3.2	335	4.28	Recovered
	3.4	250	3.4	Recovered
	3.5	280	5.32	Recovered
	3.6	500	7.2	Recovered
	3.7 ¹	425	6.29	Died
	3.7 ¹	310	4.58	Died
	4.0	415	6.64	Died
	4.0	250	4.0	Died
	4.2	320	5.37	Died
¹ M. L. D. = 3.7 = 27.0%.				
No. 5 C. Same drug as No. 5 A. "Defatted" 80 percent alcohol menstruum. Date of test, 7-13-16	0.6	285	0.68	Recovered
	0.8	195	0.62	Recovered
	1.0	415	1.66	Recovered
	1.4	410	2.29	Recovered
	1.5 ¹	435	2.61	Died
	1.5 ¹	340	2.04	Died
	1.6	350	2.24	Died
	1.8	285	2.05	Died
	1.8	360	2.59	Died
	2.0	400	3.2	Died
¹ M. L. D. = 1.5 = 66.6%.				
No. 5 C. Second test after 4 months. Date of test, 11-29-16	1.4	425	2.38	Recovered
	1.4	405	2.26	Recovered
	1.6	385	2.46	Recovered
	1.8	420	3.02	Recovered
	2.0 ¹	375	3.0	Died
	2.0 ¹	360	2.88	Died
	2.2	495	4.35	Died
	2.3	315	4.35	Died
¹ M. L. D. = 2.0 = 50%.				

Sample.	Dose per 250 Gm.	Weight of pig. Gm.	Actual dose.	Results.
No. 5 C. Third test after 7 months. Date of test, 2-1-17	1.2	335	1.6	Recovered
	1.3	210	1.09	Recovered
	1.4	270	1.5	Recovered
	1.6	300	2.3	Recovered
	1.8	405	2.91	Recovered
	2.0	350	2.8	Recovered
	2.2 ¹	405	3.56	Died
	2.2 ¹	465	4.13	Died
	2.3	410	3.79	Died
	2.5	345	3.45	Died
	2.7	410	4.42	Died
2.8	395	4.42	Died	

¹ M. L. D = 2.2 = 45.4%.

The summary of the results obtained from the previous experiments is given in the following tables:

SUMMARY OF RESULTS.

Sample.	1st assay.	2nd assay.	3rd assay.	Total deterioration.
No. 1 A. H. K. M. drug, U. S. P. VIII, 50% menstruum	6-28-16	11-29-16	2-1-17	6-28-16 to 2-1-17 68%
	125%	55.5%	37.0%	
No. 1 B. Same drug as No. 1 A. "Defatted" U. S. P. VIII, 50% menstruum	6-28-16	11-29-16	2-1-17	6-28-16 to 2-1-17 33.8%
	71.5%	62.5%	41.7%	
No. 1 C. Same drug as No. 1 A and No. 1 B. "Defatted" 80% alcohol menstruum	6-28-16	11-29-16	2-1-17	6-28-16 to 2-1-17 48.9%
	125%	83.3%	76.1%	
No. 2 A. Drug from P. E. Anderson, U. S. P. VIII, 50% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 62.5%
	125%	71.4%	62.5%	
No. 2 B. Same drug as No. 2 A. "Defatted" U. S. P. VIII, 50% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 19.5%
	90.9%	71.4%	71.4%	
No. 2 C. Same drug as No. 2 A and No. 2 B. "Defatted" 80% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 75.0%
	200%	133%	125%	
No. 3 A. Drug from Werner & Gerathy, U. S. P. VIII, 50% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 21.3%
	83.3%	62.5%	62.0%	
No. 3 B. Same drug as No. 3 A. "Defatted" U. S. P. VIII, 50% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 0.0%
	62.5%	62.5%	62.5%	
No. 3 C. Same drug as No. 3 A and No. 3 B. "Defatted" 80% menstruum	7-6-16	11-29-16	2-1-17	7-6-16 to 2-1-17 23%
	166%	150%	143%	
No. 4 A. McKesson & Robbins drug, U. S. P. VIII, 50% menstruum	7-13-16	11-29-16	2-1-17	7-13-16 to 2-1-17 33%
	83%	71.5%	50.0%	
No. 4 B. Same drug as No. 4 A. "Defatted" U. S. P. VIII, 50% menstruum	7-13-16	11-29-16	2-1-17	7-13-16 to 2-1-17 6.1%
	76.8%	70.7%	70.7%	
No. 4 C. Same drug as No. 4 A and No. 4 B. "Defatted" 80% alcohol menstruum	7-13-16	11-29-16	2-1-17	7-13-16 to 2-1-17 74.3%
	90.9%	45.4%	16.6%	
No. 5 A. Drug from National Aniline Co., U. S. P. VIII, 50% menstruum	7-13-16	11-29-16	2-1-17	7-13-16 to 2-1-17 38.2%
	71.5%	50.0%	33.3%	
No. 5 B. Same drug as No. 5 A. "Defatted" U. S. P. VIII, 50% menstruum	7-13-16	11-29-16	2-1-17	7-13-16 to 2-1-17 18.4%
	45.4%	27.0%	27.0%	

SUMMARY OF RESULTS—Continued.

Sample.	1st assay.	2nd assay.	3rd assay.	Total deterioration.
No. 5 C. Same drug as No. 5 A and No. 5 B. "Defatted" 50% alcohol menstruum	7-13-16 66.6%	11-29-16 50%	2-1-17 45.4%	7-13-16 to 2-1-17 21.2%

It will be noted from the above results that every sample except one, *i. e.*, No. 3 B, showed marked deterioration, some samples deteriorating as much as 75 percent in seven months. These results will, therefore, tend to prove that in most cases tincture of digitalis not only deteriorates but deteriorates very rapidly.

The results also show that the "fat-free" or "defatted" tinctures of digitalis *do not* deteriorate more rapidly than the regular U. S. P. VIII tincture, as the ten "defatted" tinctures only show an average deterioration of 32 percent for the seven months' period of test, whereas the five U. S. P. VIII tinctures show a deterioration of 44.6 percent for the same period of time.

From the results of these experiments we can, therefore, draw the following conclusions:

- (1) Most tinctures of digitalis deteriorate very rapidly.
- (2) "Fat-free" or "defatted" tinctures of digitalis do not deteriorate at a greater rate than the U. S. P. VIII tinctures.

PHARMACODYNAMIC LABORATORY,
H. K. MULFORD COMPANY,
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AN IMPROVED LIME METHOD FOR ASSAYING OPIUM.*

BY WM. MASKE, JR.

This assay method has been the outcome of several which the writer has read and experimented with but the foundation of the assay outlined herein is a somewhat crude process by A. Guerin as given in the *Jahresberichte der Pharmazie*, Vol. 48, Page 45. As this writer collects 52 Cc. filtrate instead of the 50 Cc. as advised in this paper, and the first quantity can not readily be measured accurately, one can just as well collect 50 Cc., an amount which can be accurately measured in a volumetric flask or sucked up in a volumetric pipette, and add the correction factor, which amounts to the same thing as collecting 52 Cc. of filtrate.

The lime method of assaying opium for its morphine content is probably used more than any other method of assaying this drug. The U. S. P. uses a lime process which gives good results in the hands of experienced workers, but which for a beginner is apt to prove cumbersome. Moreover, the method takes more time and work than is necessary. The writer has successfully used the following modification of the lime method, which is simpler, less cumbersome than the U. S. P. method, and gives just as accurate results:

Method: Weigh out 7.5 Gm. of opium and dry at 60° C. Transfer the dried opium to a mortar containing 5 Gm. of fine, clean quartz sand and 3 Gm. of slaked lime. Triturate the three ingredients thoroughly until a finely divided homo-

* Read before Scientific Section A. Ph. A., Indianapolis meeting, 1917.