

to clinical experimentation and then simplified for practical application. Until these matters are solved the modification of milk coagulation will remain as it is on an unscientific and unsatisfactory basis.

In conclusion the writer desires to express his appreciation to Dr. Arthur G. Helmick, of Columbus, Ohio, for many helpful suggestions and information regarding clinical experiences:

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BIBLIOGRAPHY.

1. Bosworth, A. W., and Giblin, L. A., *J. Biol. Chem.*, July 1918, p. 115.
2. Zsigmondy-Spear, "The Chemistry of Colloids," 1917, p. 237.
3. Van Slyke and Bosworth, *J. Biol. Chem.*, 20, 135, 1915.
4. Terry, Rob't W., *Jour. A. Ph. A.*, 8, 538, 1919.
5. Hammarsten, Olaf, "Text Book of Physiological Chemistry," 1910, p. 520.
6. Brennemann, Jos. J., *J. Amer. Med. Assoc.*, 40, 575, 1913.
7. Brennemann, Jos. J., *Archives of Pediatrics*, 34, No. 2, 1917.
8. Terry, Rob't W., *Midl. Drugg. & Pharm. Rev.*, 53, 133, 1919.
9. LaWall, Chas. H., *Amer. J. Pharm.*, 73, 561, 1901.
10. Alleman, O., *Kolloid-Z.*, 24, 27, 1919.
11. Race, Joseph, "The Examination of Milk," 1918, p. 189.
12. Alexander, Jerome, "Colloid Chemistry," 1919, p. 59.
13. Van Slyke and Bosworth, *Tech. Bull. No. 34*, N. Y. Exp. Sta., Geneva.
14. Chesneau-Lincoln, "Theoretical Principles of Analytical Chemistry," 1910, p. 107.
15. Halliburton, "Essentials of Chemical Physiology," 1914, p. 139.
16. Bosworth, A. W., and Bowditch, H. I., *J. Biol. Chem.*, 26, 431, 1916.
17. Southworth, *Archives of Pediatrics*, 1905, p. 131.
18. Chapin and Pesik, "Diseases of Children," 1909, p. 132.
19. Clark, W. M., *J. Med. Research*, 31, 431, 1915.
20. Clarke, T. Wood, *Amer. J. Med. Sciences*, 137, 872, 1909.
21. Hawk, Phillip, "Practical Physiological Chemistry," 1914, p. 124.
22. Terry, Rob't W., and Davy, Edw. D., *Jour. A. Ph. A.*, 9, 148, 1920.
23. Terry, Rob't W., *Ibid.*, 8, 183, 1919.
24. Bastedo, "Materia Medica, Pharmacology and Therapeutics," 1919, p. 96.

THE RELATIVE ACTIVITY OF DIFFERENT PARTS OF THE DIGITALIS PLANT.*

BY GEO. E. ÉWE.

The U. S. P. Ninth requires that official digitalis consist of "the carefully dried leaves of *Digitalis Purpurea* Linné (Fam. Scropulariaceae), without the presence or admixture of more than 2 percent of stems, flowers or other foreign matter. If made into the official tincture and assayed biologically, the minimum lethal dose should not be greater than 0.006 mil of tincture, or the equivalent in tincture of 0.0000005 Gm. of Oubain, for each gramme of body weight of frog."

Determinations of activity have proven that the separate parts of the plant individually answer the U. S. P. requirements for minimum lethal dose.

In order to ascertain the relative proportions of the different parts of the

* I am indebted to Dr. P. S. Pittenger and Arnold Quici for the careful tests of physiologic activity of the various tinctures mentioned in this paper.

digitalis plant and thus determine the increase in yield of drug which was to be expected from gathering the whole plant instead of only leaves, as required by the U. S. P., one hundred freshly harvested, complete, non-flowering digitalis plants grown at Glenolden, Pa., were properly divided into leaves without petioles, petioles and roots and crowns, respectively, the work being performed within twenty-four hours after harvesting.

The results are tabulated herewith:

WEIGHTS OF SEPARATE PARTS OF 100 FRESHLY HARVESTED DIGITALIS PLANTS.

Part of plant.	Weights.	Percentage.
Whole Plant.....	110 ¹ / ₄ lbs.	100.0%
Leaves without Petioles.....	60 lbs.	54.3%
Petioles.....	38 lbs.	34.1%
Roots and Crowns.....	7 ¹ / ₄ lbs.	6.4%
Loss in Handling and as Moisture.....	5 ¹ / ₄ lbs.	5.4%

Since the above figures were based on the fresh, and therefore naturally moist drug, whereas digitalis is purchased on a basis of drug air-dried to a grindable state, the parts of the plants were permitted to air-dry to a grindable state, and were then reweighed. The losses in moisture were 74.8 percent for the leaves without petioles, 83.4 percent for the petioles and 64.7 percent for the roots and crowns.

WEIGHTS OF SEPARATE PARTS OF 100 WHOLE DIGITALIS PLANTS AIR-DRIED TO A GRINDABLE STATE.

Part of plant.	Weights.	Percentage.
Leaves without Petioles.....	15 lbs. 1 ¹ / ₂ oz.	63.0%
Petioles.....	6 lbs. 5 oz.	26.3%
Roots and Crowns.....	2 lbs. 9 oz.	10.7%

Therefore the increase in yield due to collection of the roots and crowns would amount to between 5 and 10 percent, depending upon the moisture content.

On a moisture-free basis the increase in yield due to collection of roots and crowns would be even greater since they contain proportionately less moisture than the other parts of the plant. This is shown by the following table, giving total moisture content of recently harvested drug and drug air-dried to a grindable state (and ground), the determinations being made by drying at 100° C. to constant weight.

Part of plant.	Recently harvested.	dried to grindable state (and ground).
Whole Plant.....	79.6%	6.1%
Leaves without Petioles.....	77.7%	6.6%
Petioles.....	90.1%	7.9%
Roots and Crowns.....	65.3%	4.3%

PHYSIOLOGIC ACTIVITY OF DIFFERENT PARTS OF DIGITALIS PLANT.

The whole plant and the different parts of the plant, air-dried to a grindable state (and ground), were made into tinctures by the U. S. P. process for Tincture Digitalis, and were then assayed physiologically. The results are herewith tabulated:

Part of plant.	Whole plant.	Leaves w/o petioles.	Petioles.	Roots and crowns.
Physiologic Activity (Compared with U. S. P. Standard)	Sample 1—166% Sample 2—166%	Sample 1—250% Sample 2—250%	Sample 1—111% Sample 2—125%	Sample 1—177.6% Sample 2—177%

The results of physiologic assay indicate that the whole plant and each of the different parts of the plant, individually, conform to the U. S. P. standard of activity.

DIGITOXIN CONTENT OF DIFFERENT PARTS OF THE DIGITALIS PLANT.

The tinctures made from the whole plant and different parts of the plant, air-dried to a grindable state (and ground), which were used for the determination of physiologic activity, were assayed for digitoxin with the following results:

Part of plant.	Whole plant.	Leaves w/o petioles.	Petioles.	Roots and crowns.
	Sample 1—	Sample 1—	Sample 1—	Sample 1—
Digitoxin per 100 cc.	0.0145 Gm.	0.0285 Gm.	0.0105 Gm.	0.0068 Gm.
	Sample 2—	Sample 2—	Sample 2—	Sample 2—
	0.0160 Gm.	0.0300 Gm.	0.0125 Gm.	0.0064 Gm.

The arbitrary standard for digitoxin in Tincture of Digitalis is 0.025 Gm. so that only the tincture made from the leaves without petioles is in accordance with this arbitrary standard. This standard is based upon tincture made from the leaf. In view of the high physiologic activity of the petioles and the roots and crowns it is evident that the activity of these portions of the plant is due largely to glucosides other than digitoxin.

TOTAL ASH, ACID INSOLUBLE ASH, EXTRACTIVE CONTENT AND COLOR OF TINCTURES MADE FROM THE DIFFERENT PARTS OF THE DIGITALIS PLANT.

The total and acid insoluble ash of the whole and different parts of the plant and the extractive content and colors of the tincture made from the whole and different parts of the plant are herewith recorded as a matter of interest and as a contribution to this subject:

Part of plant.	Whole plant.	Leaves w/o petioles.	Petioles.	Roots and crowns.
Total Ash Content	32.7%	20.8%	27.7%	14.7- 14.8%
				14.9
Acid Insoluble Ash Content	25.7%	13.6%	19.5%	6.5- 6.6%
				6.7
Extractive Content of Tincture	1.825-1.876%	2.488-2.381%	2.29-2.295%	1.42- 1.435%
	1.928	2.275	2.30	1.45
Color of Tincture	Light greenish brown	Dark greenish brown	Pale brownish green	Pale brown

The total ash and acid insoluble ash determinations were made on samples which were merely vigorously shaken in an effort to deprive them of sandy particles. The roots and crowns were washed and air-dried before the determinations were made. All of the determinations were made on samples air-dried to a grindable state (and ground).

Total and acid insoluble ash determinations made on roots alone, which were washed and then dried at 100° C., showed 13.7 and 13.4%, average 13.55%, of total ash and 8.2 and 8.1%, average 8.15%, acid insoluble ash.

SUMMARY.

Evidence is offered regarding the relative activities of the different parts of the digitalis plant in comparison with the whole plant.

Determinations of physiologic activity, digitoxin content, extractive content and color of tinctures prepared from different parts of the digitalis plant, in com-

parison with the whole plant, are recorded.

The roots and crowns, which are not now official, yield tinctures conforming to the U. S. P. standard of activity when free from excessive soil.

The roots and crowns amount to between 5 and 10% of the crop.

Data are recorded on the relative weights of the separate parts of freshly harvested plants and plants air-dried to a grindable state; the moisture contents of recently harvested plants and their parts and plants and their parts air-dried to a grindable state and total and acid insoluble ash content of the whole plant and its parts.

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THE ASSAY OF MERCURIC SALICYLATE.

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The U. S. P. process for the assay of mercuric salicylate⁷ is faulty in that it does not accomplish what it sets out to do, *viz.*, to produce mercurous chloride and estimate this iodometrically.

The Pharmacopoeia directs that a weighed quantity (about 0.5 Gm.) of mercuric salicylate be heated on a water-bath with a mixture of nitric and sulphuric acids, until dissolved. The solution is never complete, no matter how long the mixture is heated, since the mercuric nitrate produced is not soluble in the acids. What does happen is, the mercuric nitrate remains on the bottom of the container, after the oxides of nitrogen fumes cease to be evolved, and is dissolved immediately on the addition of water. A higher temperature than 100° C. will considerably shorten the process.

Having then a solution of mercuric nitrate, measuring about 150 mls, 30 mls of solution of hydrogen dioxide are added to insure a complete oxidation. To this, the Pharmacopoeia directs that 5 mls of diluted hypophosphorous acid be added, and then 5 Gm. of sodium chloride, dissolved in 20 mls of water. Here the real error occurs in the official process; for when the diluted hypophosphorous acid is added the solution immediately becomes dark, due to the separation of finely divided metallic mercury.

If the sodium chloride solution is quickly added some mercurous chloride may also be precipitated, but the quantity is small. It is true that the metallic mercury, after being collected on a filter and washed, can be estimated iodometrically, but it is taken up so slowly that several hours are required, even if a mechanical shaker be used.

If, however, the order of the addition of the diluted hypophosphorous acid and the sodium chloride solution is reversed, that is, if the sodium chloride is added first and then the reducing agent, a dense white precipitate results, free from metallic mercury. This, when collected and washed, can be estimated immediately with tenth-normal iodine volumetric solution.

The late Dr. Frontis Lentz had occasion to assay some twenty-five samples of mercuric salicylate, produced by several manufacturers, during the period of the war, and found these modifications of the official process to be satisfactory