

Contributed and Selected

THE POTENCY OF FIRST-YEAR CULTIVATED DIGITALIS LEAVES AS INDICATED BY PHYSIOLOGICAL ASSAY.*

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The supply of many valuable medicinal plants once so abundant from natural sources is rapidly becoming or is entirely exhausted. This has been brought about by the destruction of the forests; the devotion of more and more of the waste lands to agriculture, and the destructive methods of harvesting without any thought or care to preservation. The supply was ample and little effort was made toward cultivation. Where attempts were made to introduce medicinal plants into other countries, soil and climatic conditions were often unfavorable. Many plant forms mature very slowly and several years must pass before the drug can be marketed. Possibly from this arose the belief that cultivated plants were less valuable than wild ones. The small returns to be had and the limited demand for the product has been responsible for the undevelopment of this form of industry.

In view of the advance now being made in plant culture and improvement, it is entirely within the realm of possibility that the desired constituents of drug plants can be increased and undesirable ones decreased or eliminated as is being done with many cultivated forms. In the case of some drugs, the active principles of which can be more or less closely paralleled by synthetic preparations it may be questionable as to the advisability of expending much energy upon their cultivation. The forms which contain neutral principles, glucosides, etc., cannot be so closely paralleled. In this class digitalis easily stands first. One of the factors in the way of its successful cultivation has been the belief that wild plants were more potent and this has been furthered by the Pharmacopœias of various countries. Some of these Pharmacopœias now admit cultivated leaves, but all require the second-year leaves at the time of flowering. This requirement appears to be founded more upon tradition than as a result of scientific investigation. This is a question of considerable economic importance. A larger quantity of leaves can be obtained from first-year plants, and if it can be conclusively proven that first-year leaves are as therapeutically active as the second, it will greatly shorten the period and the cost of production.

From a review of the literature, it appears that very little work has been done to determine the relative potency of first and second-year leaves.

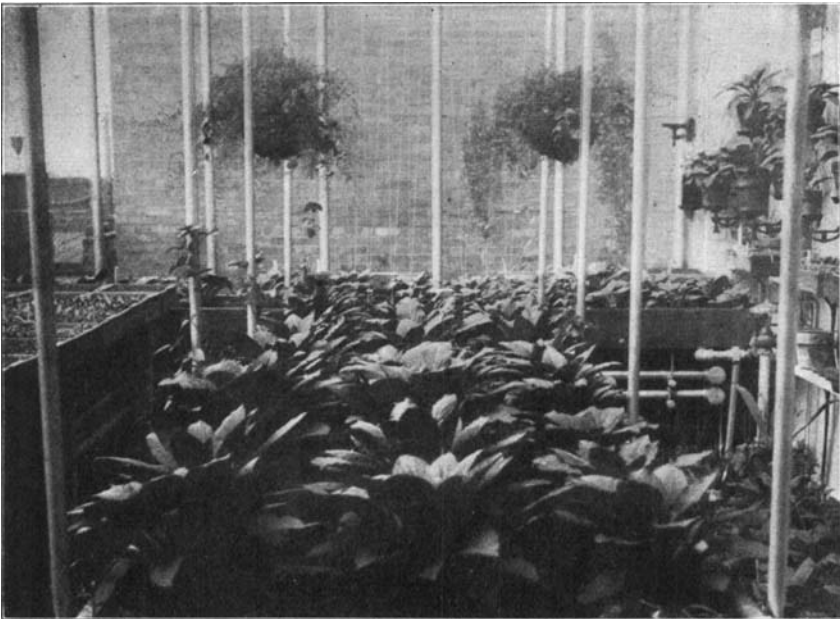
Duffield(1) in 1869 using chemical methods found American leaves superior to English and these in turn superior to German. Edmunds(2) assayed biologically, three U. S. P. tinctures made from English leaves and three from German

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leaves and found them to give values of 8-18-25 and 11-20-29, respectively. Ott(6) pointed out that Bohemian leaves were much more toxic than others.

Focke(3) found cultivated leaves to be 50% less active than leaves from wild plants. Allen's English leaves are garden grown and are recognized as quite active.

Hart(5) found first-year leaves to be 20% more toxic than second-year. Hale(4) reports some assays of first-year garden-grown leaves, one sample grown at Arlington, Va., in 1907, a second in 1909, and a third sample grown at Madison, Wis., in 1908. Each lot of leaves was reduced to a No. 60 powder and made into tincture according to the U. S. P. VIII. The M. L. D. per gram body weight by the one hour frog heart method, for Arlington, 1907, was 0.0050 cc.; for the 1909, 0.0050 cc., and for the Wisconsin, 1908, 0.0055 cc. These were

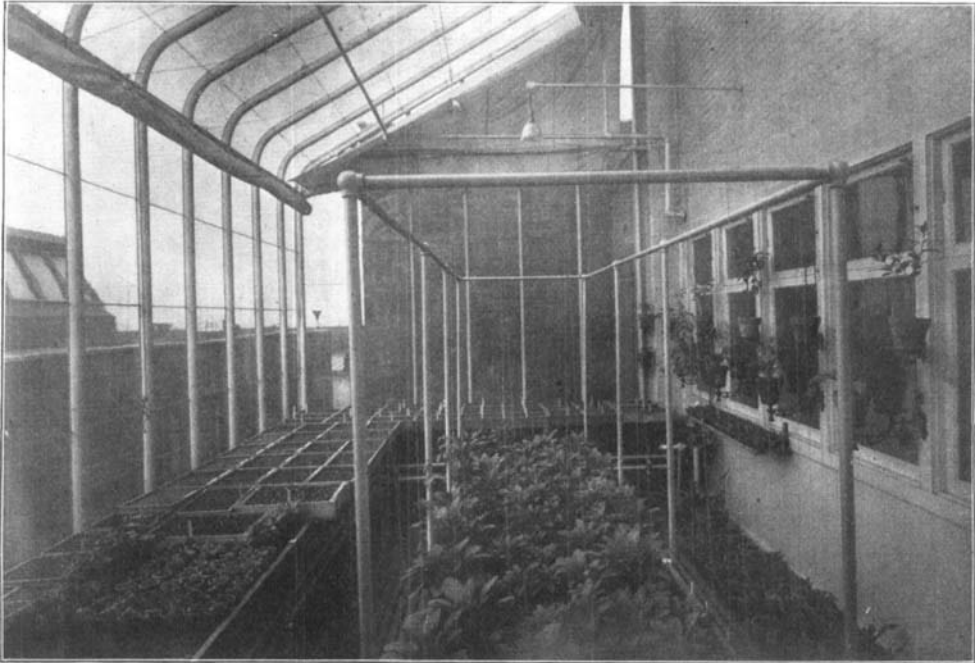


Digitalis Growing in Conservatory.

compared with a tincture made at same time from selected English leaves of second-year's growth. The M. L. D. for this was 0.0070 cc. He further reports a comparison of a sample of first year garden-grown with a sample of wild-growing second-year leaves from Seattle, Wash. The first-year leaves assayed 0.0060 and the second-year leaves 0.0085.

In view of these statements and of the approaching pharmacopoeial revision it has been deemed advisable to publish the results of some assays of samples of first-year cultivated leaves and compare them with samples of selected commercial leaves. The samples tested were taken from plants grown from seed purchased of Henry A. Dreer, of Philadelphia. The botanical source is *Digitalis gloxineaeflora* mixed. It is a well known fact that this form is a cultivated and improved gloxinia like strain of the official *Digitalis purpurea* L. It is probably

one of the oldest of the cultivated varieties of the genus *Digitalis* and for this reason should represent the average conditions which are to be expected in cultivated forms of this group. The seeds were planted June 10, 1911, and soon after germination were transplanted to two-inch flower pots. They were retained in these until the latter part of August of the same year when they were transplanted to a bed in the conservatory maintained at this laboratory. The bed was filled with a mixture of equal parts of clay loam and decayed vegetable substance with an admixture of a small amount of sand. The plants were grown continuously in this situation without the addition of any plant food until the second of February, 1912, when the leaves were collected for testing. The plants at this time appeared as large rosettes of luxuriant leaves. They were in perfect



Tested *Digitalis* Plants Growing in Center Bed.

condition and represented a considerable range in leaf variations as noted in about fifty plants. These plants including the three tested have been under observation and continuous cultivation throughout their entire existence and have responded perfectly to regular methods of cultivation. The leaves which were collected for testing consisted of about an equal mixture of fully developed and half-grown leaves. These when collected were designated as samples, B-994, B-995, and B-996. They were placed in a drying oven and the temperature slowly raised to 100° C. Drying was considered complete at the end of twenty-four hours. During an interval of twelve hours the temperature was lowered to 60° C. The leaves after being dried were reduced to No. 60 powder and exhausted with 75% alcohol. At same time and by same method tinctures were made from samples of commercial leaves designated as No. 1, 2 (cultivated), and 3. The alcoholic

strength was reduced to 25% before testing. Ten cc. of these tinctures represented 1 gm. of drug. The samples were all assayed at same time by the one-hour frog heart method at 20° C.

The results were as follows:

Sample	M. L. D. per gm. body weight
B-994	0.0050 cc.
B-995	0.0040 cc.
B-996	0.0030 cc.
No. 1	0.0040 cc.
No. 2 (cultivated)	0.0030 cc.
No. 3	0.0025 cc.
Ouabain 1:10000	0.00000045 gm.

These results, although not conclusive, indicate that leaves from horticultural varieties are by no means inactive; that leaves collected prior to the flowering period may be nearly or quite as active as second-year leaves from the wild plants and that conservatory conditions do not materially lessen the activity. There also appears to be a marked variation in the activity of the individual plants. This condition if existent in commercial digitalis leaves may account in part at least for the variation that has been found to exist, both in the crude drug and its preparations. Whatever influence this individual variation may have upon the character and quality of the drug or whether it may ever be utilized in bringing about greater uniformity are matters of conjecture. This condition of variation, however, suggests a broad field for further investigations in the improvement of medicinal plants. If the active constituents of digitalis were found to be of an inherent nature a practical application of the methods of plant selection and breeding would be possible for the purpose of improvement. In this connection, it would be of great importance if the leaves of first-year plants of cultivated varieties could be utilized. These forms have already passed through the experimental stage which is always necessary to the successful introduction of any plant forms and would thus respond more readily to methods of breeding. The preliminary nature of this work, however, will not permit of a full discussion of the possibilities in drug plant improvement. It is sufficient to say that work of this nature has been undertaken in connection with the further testing of the many different species and varieties of digitalis. Seeds of these forms have been obtained not only from all the prominent sources of this country, but also from those of England, Germany and Japan. Individual plants of the various forms from these sources will be tested at different periods of growth and at different seasons. The three plants herein considered will be continued under cultivation and again tested at the time of flowering. At this time, these plants will be inbred and the seeds collected separately. The following year the progeny will be grown and tested separately for relative values and uniformity.

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