

THE IMPROVEMENT OF MEDICINAL PLANTS.

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The principles of plant breeding have as yet hardly been brought to bear upon the improvement of medicinal plants. The necessity of improvement and the possibilities of the application of modern methods of breeding to this group of plants has led the writer to undertake a series of investigations upon this subject. A discussion of the results and progress of these investigations is the object of the present paper.

The broadening influence of plant breeding is gradually bringing under control members from all groups of the plant kingdom, and it is only fitting that this very important group of plants should be made to yield the best of nature's possibilities. That the group contains many plastic forms which will yield readily to modern methods of breeding is evidenced by the fact that some of the most potent medicinal forms appear in families from which have been obtained many valuable horticultural varieties. The Solonaceæ for example, with the genera *Atropa*, *Hyoscyamus*, *Datura*, *Solanum* and *Capsicum*, and the no less important Scrophulariaceæ containing the now widely known genus *Digitalis*, which is found to be equally as variable both in chemical and physical characteristics as the common garden forms derived from the same and related genera, will serve to illustrate this point.

A review of the literature on drug plant improvement reveals but few attempts at systematic investigation by the employment of standard methods of breeding. On the other hand much has been written and no little accomplished upon the introduction and cultivation of medicinal plants. Introduction and cultivation with no improvement has been the order of procedure. It is quite true that some improvement has resulted from a changed environment and a reduced struggle for existence, but not through the intensive application of particular methods. Improvement by means of seed and plant selection, the isolation and testing of favorable varieties, the study of soil and climatic conditions, trials in hybridization, grafting, or other methods which might prove applicable, have not been tried except in comparatively few instances. Had the government made

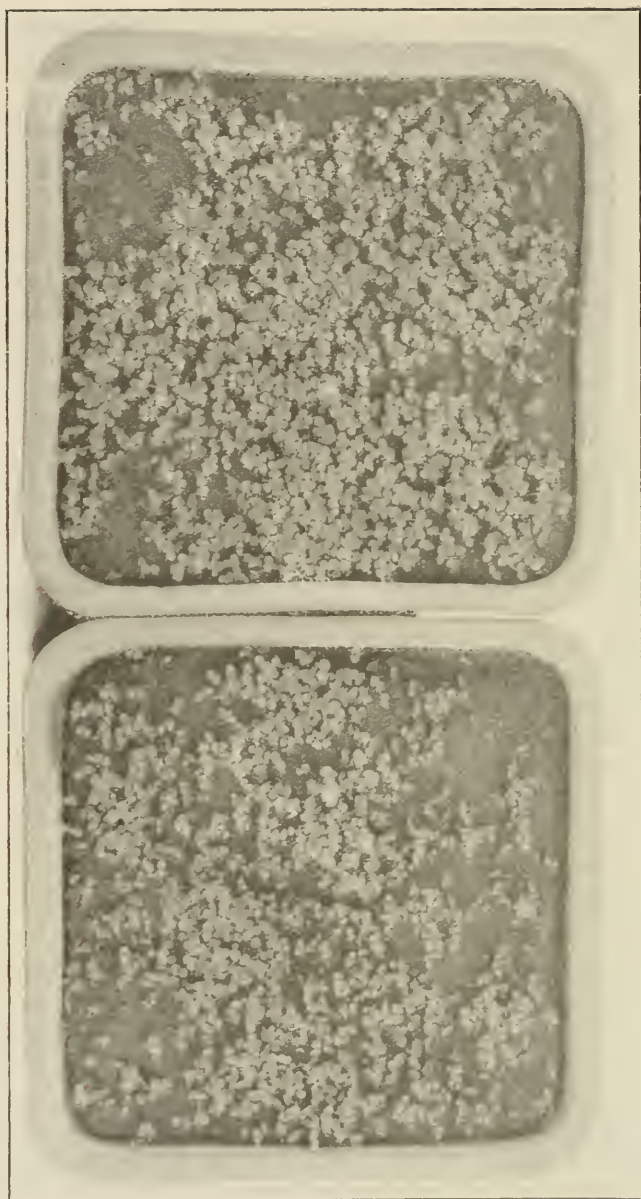
selections of hydrastis (*Hydrastis canadensis* L.) ten years ago upon a basis of alkaloidal percentage, their plantings made at that time might now be yielding interesting and valuable data upon the behavior of this plant under cultivation. Problems relating to propagation, cultivation, collecting and curing have been solved, but the cause of the wide range in the percentage of alkaloids in this drug remains an unknown factor. From January 6, 1909 to November 8, 1911, this range in the percentage of alkaloids was found to be from 2.79 to 7.60.

Another illustration of cultivation without improvement which will at the same time serve to demonstrate the practical value of the application of a single standard method is the growing of the drug burdock. This drug consists of the root of *Arcium lappa* L. collected from plants of the first year's growth. For the past fifteen years this plant has been grown under cultivation on a commercial scale near Indianapolis for the production of the first year's roots in the recent condition. The superior quality of the resulting product over that obtained from wild plants was early recognized. The drug was more uniform in every respect, almost free from fibrous tissue and is believed to produce a more active preparation. With this favorable beginning it is surprising, indeed, to learn that the final results of fifteen or more years of continuous cultivation have failed to advance this plant beyond the point reached at the end of the first year. Upon seeking an explanation of this fact it was found that from one year to the next the total seed supply came from wild plants found growing by the roadside. This plant being a biennial and the crop being harvested at the end of the first year's growth has left the farmer at the end of each season to search for a new seed supply. When interviewed as to why seed plants were not selected upon a basis of green weight of root produced, the answer has been that it would not pay. That seed and plant selection could be made to pay can be demonstrated upon a basis of original investigation and reliable data. A study of the results obtained in the Division of Botany of the United States Department of Agriculture upon "the Superior Value of Large, Heavy Seed," indicates an increase in the weight of the plant which is in direct proportion to the weight of the seed employed. To obtain data for calculations upon such a basis, burdock seeds were taken from a lot collected miscellaneously from wild plants and separated into light and heavy portions. The separation was accomplished by the use of an apparatus designed after one

used for the separation of tobacco seeds, in the experiments on tobacco breeding performed at the Connecticut State Experiment Station. This apparatus is described in the Yearbook of the Department of Agriculture for 1904. Slight modifications were found necessary to adapt it to this type of seed. A number of seeds from both the heavy and light portions were accurately weighed. The average of the light seeds was 0.0035 grams and of the heavy 0.0084, a ratio of 1:2.40. The variation in the heavy seeds was from 0.0077 to 0.0091 grams and in the light from 0.0017 to 0.0046. The greater variation in the light seeds was found to be due to the force of the air current employed in the separation. That a separation into light, medium and heavy can be made just as readily as into light and heavy will be shown in connection with another form.

A planting of three acres of burdock of the present year has been chosen as a type upon which to calculate the increase in yield which might have been obtained by means of seed selection. This planting was made upon a deep mellow loam and the total yield of 33,890 pounds is rather unusual. Assuming that the seed supply used on this planting consisted of light and heavy seeds in the determined proportion of 1:2.0, the total yield can be theoretically divided into two portions of 6,778 and 27,112 pounds, respectively produced by the light and heavy seed. Had the light seed used been equal in weight to the heavy seed they would have produced twice as much as they theoretically did, which would have been 13,556 pounds. This would make a total yield of 40,668 pounds instead of 33,890, an increase of 20 per cent.

Even of greater importance, however, to the medical and pharmaceutical professions is the improvement of henbane and digitalis, representing as they do two valuable drugs of the United States Pharmacopœia. By their being more amenable to chemical and physiological methods of standardization, the investigator is furnished with additional means of following the progress of various methods of improvement. Official henbane is supposed to consist of the dried leaves and flowering tops of *Hyoscyamus niger* L. collected from plants of the second year's growth and yielding not less than 0.08 per cent. of mydriatic alkaloids. That the above chemical and botanical conditions of this drug rarely obtain has been clearly demonstrated. An average of a large number of samples examined from August 25, 1908, to September 23, 1911, indicates that only 13 per cent. conformed to the requirements of the United States Pharma-



DIGITALIS PURPUREA L.

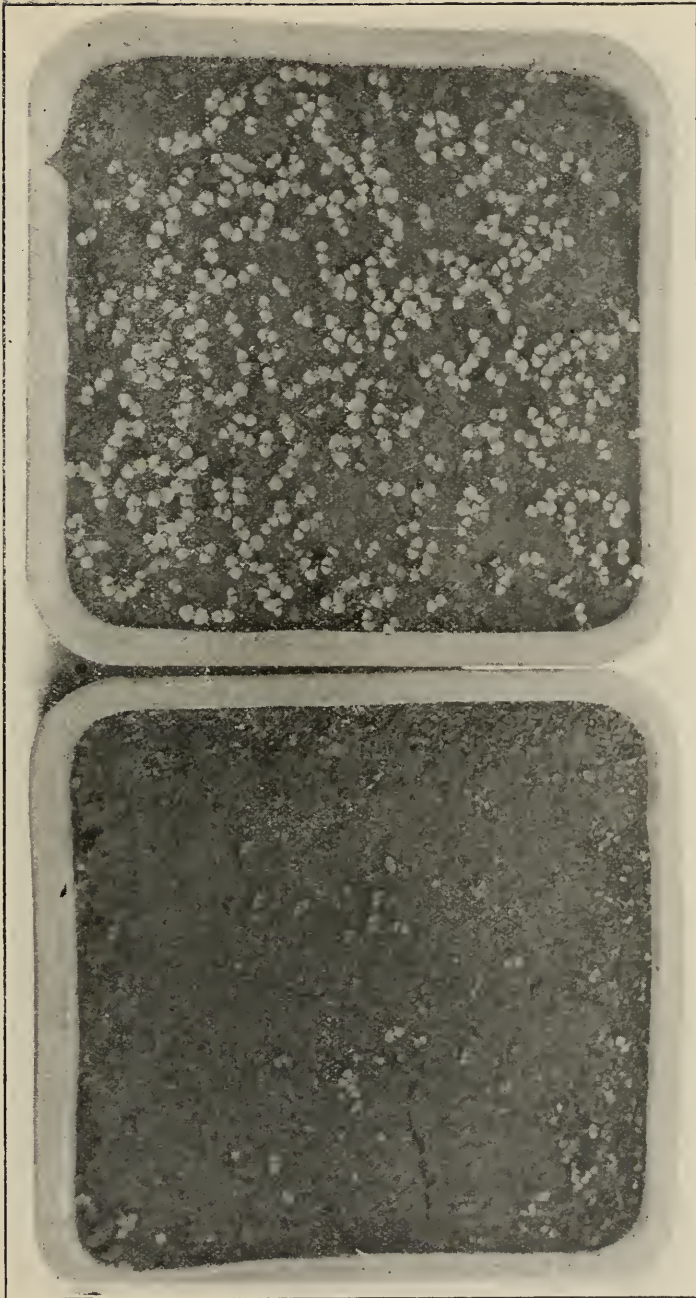
Result of equal volumes of selected and non-selected seed. Upper seed pan sown with selected heavy seed. Lower seed pan sown with non-selected seed.

copœia from a chemical standpoint. The average alkaloidal percentage of all samples for the same period was 0.0340 and the range of variation in individual samples was from 0.018 to 0.125 per cent.

The botanical characteristics approach the official requirements with no greater degree of certainty. The crude drug varies from fragmentary specimens of unevenly cured leaves and stems containing an admixture of grass, straw and other plant parts, as well as the refuse of chicken and barn lots, to pure, bright, clean, evenly cured leaves, compressed in such a manner that the entire leaf is available for inspection. The botanical source of the drug is also questionable, as evidenced by numerous seed tests from samples and lots from which viable seeds could be obtained. These tests have shown this drug to consist of a mixture of two distinct forms. The so-called annual variety, which is not included in the pharmacopœial description, appeared regularly in these tests. Specimens of this form have been grown to maturity in the writer's garden and close observation has failed to substantiate the statements that it is identical with *Hyoscyamus niger* L. Seedling plants from both forms are now under observation and will be studied both botanically and chemically through succeeding generations. To determine the possibility of obtaining a uniform henbane, seeds were purchased from August and George Fischer of London, which were found to possess a high percentage germination. Plants from these seeds differed greatly in size and vigor in the early seedling stages, and a selection from approximately two thousand seedlings was necessary in order to obtain one hundred and forty plants of uniform character. The great variation noted in the seedling stages of these plants led to a second application of the seed separator. The seeds of this form being quite small, several portions of two hundred seeds each, were taken from light, medium and heavy separations. The respective weights of these were 0.0705, 0.945 and 0.125 grams. Plantings from these different weight seeds have not progressed sufficiently at the present time to justify a discussion of the merits of the method. Open field experiments with this drug have demonstrated that seed germination is uncertain, that the plants are subject to the attacks of many insects and that the seedlings transplant with considerable difficulty. No conclusions can be drawn from these facts, however, since the seeds employed in all outdoor tests were imported and but very few lots of such seeds have given satisfactory results. The two forms of henbane mentioned, i. e., annual

and biennial do not represent the limit of possibilities in this genus. According to Engler and Prantl the genus consists of eight species widely distributed throughout temperate and subtropical regions. In the subtropical is found the very promising form, *Hyoscyamus muticus* L., yielding over one per cent. of alkaloids, while the remainder are found in the temperate regions. Of these, some have passed through periods of prominence in different countries, as *Hyoscyamus albus* in France, the annual form in parts of Germany and the biennial form in England, all of which suggest the possibilities within the entire genus.

In this group of plants the necessity of systematic efforts leading to the development of pure-bred strains of promising species, and to an increase in the percentage of alkaloids is indicated by the above data. The famous corn-breeding experiment at the Illinois State Experiment Station, the records of which now cover thirteen generations, indicates what may be done through selection. That the efforts to increase and decrease the protein and oil have met with great response is shown by the fact that two strains of corn have been produced out of a single variety, one of which contains more than half again as much protein as the other. The effect upon the oil content is even more striking, since from this same variety two other strains have been produced, one of which contains practically three times as much oil as the other. The sugar beet industry of this and other countries is illustrative of the necessity of the intensive breeding, essential to the production of high yielding plants. The gain of 22.2 per cent. in the total sugar beet output of Germany for 1910-11 with an increased acreage of only 3.6 per cent. was due to three factors, one of which was the higher sugar content of the beets. Experiments have shown a variation of seven per cent. in sugar content in beets of the same parentage grown in different localities, a fact which is suggestive of the necessity of a careful choice of localities for drug plant investigation. The introduction of various species of *Cinchona* into India by the British Government over fifty years ago has long passed the experimental stage, but the records of the difficulties overcome stand as convincing evidence of what may be accomplished in the introduction and improvement of arborescent forms. Many of these forms were long grown and propagated under glass until individuals could be isolated which would endure the new environment and be made to serve as starting points for future generations. The work of the Department of Agriculture on capsic-



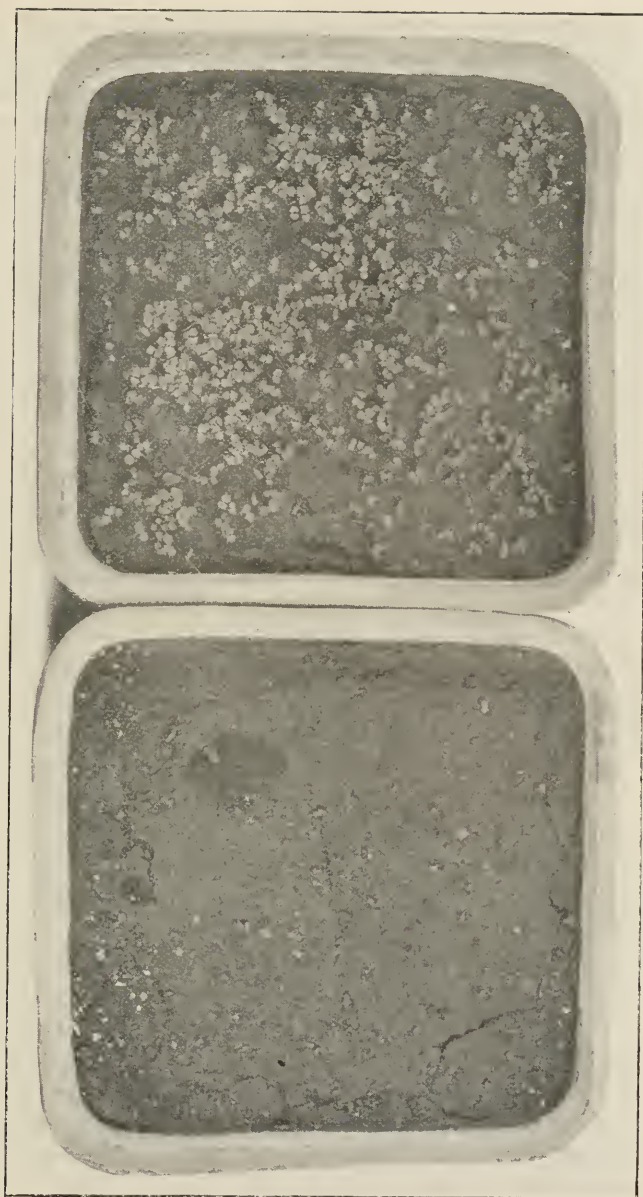
DIGITALIS MONSTROSA.

Upper seed pan sown with heavy seed. Lower seed pan sown with light seed. Equal volumes of seeds were used.

cum, camphor, tea, tobacco and a host of other forms bears out the evidence of the foregoing, and furnishes the worker with a wealth of data applicable in many ways to drug plant improvement.

The drug digitalis, consisting of the dried leaves of *Digitalis purpurea* L. collected from the second year's growth at the commencement of flowering, is equally in need of improvement. Physiological tests have shown a variation in the toxicity of preparations made from drugs representing different geographical sources. Differences of opinion also exist as to the relative medicinal value of first and second year leaves, of those from wild and cultivated plants and of those from plants of different species and varieties, as well as to the effects of different periods of collecting and methods of curing, packing and storing of the crude drug and to the relative value of preparations made from fresh and dry leaves. A botanical examination of the genus reveals conditions which will probably account, in part at least, for the above differences of opinion.

The genus is a large one, consisting of twenty-one widely distributed species, a fact which alone increases the possibilities of an admixture of leaves from several species or from the same species growing under different climatic conditions. This possibility is also increased by the numerous varieties originated by florists and gardeners who have not been slow in recognizing the aesthetic value of the genus. Their catalogues now contain many standard varieties which are noted for their attractive nature and ease of culture. The official species *Digitalis purpurea* L. has figured largely in this production, having given rise to no less than half a dozen distinct forms which are now listed as hardy perennials. Other species have been active in this respect but have not produced such a diversity of forms. This property of a genus to yield multiple forms is strongly suggestive of a wide range of variations in the corresponding percentage of active principles. The botanical inspection of the crude drug is in no degree indicative of this percentage of active principle, but that such an indication is possible is suggested by recent investigations of Gregory upon the association of transmissible characters in *Primula sinensis*, where it has been shown that some characters are always found to accompany others with recurring regularity. But until such a convenient relation is found to exist between active principle and specific morphological characters, the botanical examination can only point to the possible source and not to the comparative medicinal value of the drug.



DIGITALIS PURPUREA L.

Upper seed pan sown with heavy seed. Lower seed pan sown with light seed. Equal volumes of seeds were used.

Observations now being made upon several species and varieties of digitalis have revealed variations which would prove of considerable commercial value if found associated with a correspondingly high percentage of active principle. A dissimilarity of leaf forms has been obtained in plants grown from seed which offer valuable material for selection as to form, size, color, and arrangement, relative number per plant, length of petiole, texture and curing properties. Differences have also been noted as to rate and percentage of seed germination, flowering period, production of suckers, hardiness, and ease of propagation and cultivation.

In the course of an investigation upon a form of digitalis found growing adventively in parts of Oregon, an excellent example has been obtained of the uncertainty of the botanical origin of commercial digitalis and the difficulty of the separation of distinct forms upon a basis of leaf characters. One hundred and forty plants said to represent the first year's growth were obtained from this source. These plants were collected in the open and represented a locality from which commercial digitalis leaves had been marketed. These plants arrived in excellent condition and were transplanted in the open near Indianapolis in early spring. They were closely observed throughout the season and during this time but few plants flowered, all of these, however, coming true to the description of *Digitalis purpurea* L. and were quite uniform as to leaf characters. The plants made excellent growth during the summer and went into the winter as large, strong healthful plants in fit condition for experimental purposes. To test this form for hardiness in this latitude these plants were left in an exposed locality in an unprotected condition throughout the year. Forty-three per cent. withstood the severe winter of 1910-11 and flowered, but very irregularly, during the ensuing summer. The effects of the exposure were manifested by a much lower production of leaves than that attained during the first year's growth. Among the sixty plants which survived the winter there was one which produced racemes of pure white flowers instead of the characteristic purple flowers of *Digitalis purpurea* L. The presence of this form among a comparatively small number of plants indicates the admixture of a varietal form, the medicinal properties of which are not known. The other individuals which flowered were fairly uniform in all visible characters except as to variations in flower arrangement, some bearing upright instead of drooping flowers, an arrangement which gave the plants a striking appearance. Seed selec-

tions were made from these forms and a further study will be made of them both for hardiness and as to fitness for medicinal use.

Preliminary work has been done on seed selection with several forms of *Digitalis*. Seed tests of light and heavy seeds obtained by means of the apparatus previously mentioned have given striking results in the early stages of seedling growth as shown by the accompanying photographs. The following data will indicate the accuracy of this method of seed selection and the uniformity in the seeds separated. It also demonstrates the practical value of the method if applied to the commercial production of *digitalis* leaves. Seeds collected from the foregoing plants of *Digitalis purpurea* L. were separated into light, medium and heavy. The extreme smallness of these seeds made it necessary to use five hundred seeds from each separation for weighings. Seeds of *Digitalis grandiflora* Lam. obtained from Henry A. Dreer of Philadelphia were also separated, weighed and tested. These were heavy enough to be weighed in one hundred lots and were of such uniformity that they were only separated into light and heavy portions.

The following table includes the results of these separations and weighings:

Digitalis purpurea.

Light.	Medium.	Heavy.
500 seeds	500 seeds	500 seeds
0.0217 gm.	0.0253 gm.	0.0341 gm.

Digitalis grandiflora.

Light.		Heavy.	
100 seeds.....	0.0168 gm.	100 seeds.....	0.0215 gm.
100 seeds.....	0.0167 gm.	100 seeds.....	0.0223 gm.
100 seeds.....	0.0161 gm.	100 seeds.....	0.0223 gm.
100 seeds.....	0.0161 gm.	100 seeds.....	0.0215 gm.
100 seeds.....	0.0164 gm.	100 seeds.....	0.0217 gm.
Total		Total	
0.0821 gm.		0.1093 gm.	

In conclusion it is only necessary to say that the application of these methods of breeding and the possibilities in drug plant improvement herein suggested should be extended until they include such valuable forms as

cannabis indica, belladonna, buchu, and others. Hardy productive varieties of these forms must be discovered or produced, and these brought under the influence of modern agriculture where they may be utilized to meet the conditions of growing scarcity, advancing prices and the demand for better products.

*Botanical Department, Eli Lilly & Company,
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