

THE CULTIVATION OF MEDICINAL PLANTS.*

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A brief historical review of the subject of drug cultivation in the United States reveals the fact that the subject is not a new one. It is only the revival of an old topic under modern ideas and more attractive possibilities. Concerning the introduction of this work in America, we would doubtless be safe in saying that the first medicinal plants to be cultivated were the so-called "kitchen herbs" in the gardens of the earliest settlers. As early as 1735 Collinson obtained over fifty kinds of "curious seeds" from the Chelsea Physic Garden of England, and Marshall, 1781, was one of the first to attempt the cultivation of the opium poppy in this country. Small gardens containing miscellaneous collections of plants, some of which might be classed as medicinal, were started in different localities only to be abandoned after a few years. Most of these were established for educational purposes and some are still in existence. In these, however, medicinal plants did not predominate, but were only supplementary to certain other families or groups of plants.

Not until the early part of the nineteenth century did medicinal plant-growing appear to have attracted sufficient attention to be considered as a commercial enterprise. The American Garden Calendar enumerates a large number of plants which could be grown in temperate climates and gives general directions for collecting and drying herbs, roots, seeds, etc. In this connection some of our present investigators of medicinal plants seem to be following this early example of McMahan in his Garden Calendar in still enumerating long tedious lists of what they call important medicinal plants and which they emphatically claim could be cultivated successfully in this country upon a commercial scale.

The most extensive operations ever carried on with drug producing plants in this country, were those of the Shakers. They began the work as early as 1800 at the original settlement at Mount Lebanon, New York. It seems they soon established quite a business in medicinal preparations from their cultivated drugs and the work was subsequently taken up by other Shaker colonies, particularly at Union Village, Ohio. Some idea of the amount of drugs produced by the Shakers as compared with the present demands may be gained from the statement that they produced at Lebanon as much as forty or fifty thousand pounds annually. This amount would about equal the average weekly demands of any one of the larger manufacturing concerns of today. While this movement spread somewhat in the Shaker community it never became very general. The Tilden Company, of the same locality, are said to have had as much as forty acres planted to medicinal plants. We find, however, that the work of Tilden & Co. was discontinued about 1880, and the operations of the Shakers gradually diminished until they finally attracted no more attention.

*A lecture delivered to the Purdue Pharmaceutical Society at Lafayette and to the School of Pharmacy at Valparaiso University.

In times past the United States has shown itself capable of supplying materials, not otherwise produced here, which have been cut off by conditions of war. This has been true of opium, which was produced in considerable quantities during the Revolutionary War, the war of 1812 and the Civil War.

At the present time we are feeling the strain of similar conditions and find many of the most important European vegetable drugs not only cut off from the regular channels of trade, but also declared contraband of war. The list of drugs of strictly European origin which might be successfully cultivated in this country is not a large one, especially when we consider only those which are actually essential to the modern practice of medicine and those which from the nature of the plant we might reasonably expect could be grown and cultivated with some degree of certainty. In this list we have such drugs as aconite, belladonna, colchicum, convallaria, digitalis, gentian, henbane, opium, stramonium and valerian. Before seriously considering the cultivation of any of these, they must be studied carefully for peculiarities which may make it impossible to grow them successfully upon a commercial scale. The first thing to consider before deciding what forms one would attempt to grow is a reliable seed supply. This question apparently does not worry the prospective drug grower until he is actually ready to begin, and some have been known to purchase land, erect drying shed, etc., before really knowing what they would grow, or where they could obtain seed of plants of the various medicinal forms.

In the above list, take for instance, aconite. Seeds of *Aconitum napellus*, the official species, may be obtained from several reliable seed firms of the United States. However, with good seed once in hand, we find that all difficulties are not immediately solved. The question at once arises as to how these should be sown. The average farmer or layman knows and considers but one method of seeding for commercial operations. This is the open field method and unless it can be practiced successfully there is little chance of rapid progress. Aconite is usually considered a tuberous rooted plant with the tubers constituting the part used in medicine, the leaves being little used. These tubers do not reach maturity before the end of the second or third season so that when successfully seeded the plants must be grown through two or more successive years before a crop could be harvested. As to seeding we find that aconite is not easy to germinate even under the most accurately controlled conditions of a greenhouse. This eliminates field sowing and greatly increases the cost of production to say nothing of experienced labor and unusual equipment, such as greenhouses and hot beds. Aconite is often grown as a garden form, where its tall, stately stems, surmounted by the spikes of dark blue flowers are both beautiful and interesting. This is no argument, however, that aconite would be an easy crop under field conditions. In this respect we find too many mistakes have already been made with medicinal plants. Many medicinal plants or their varieties have long been used as garden or decorative forms and upon this fact alone, sweeping statements have been made that they could be easily and economically produced upon a commercial scale. Even some college authorities who have strongly advocated drug cultivation have been accused of committing this error.

Whatever the sources of error, however, it is time for their correction as well as time for the adoption of more conservatism in the statements of those not in-

fomed upon the difficulties of commercial drug growing. To cite an example, a well-known writer in pharmaceutical circles, in giving directions for growing henbane, states in extremely brief language that "culturally it could be associated with stramonium, cannabis indica, tobacco and belladonna." The absurdity of the association of such a group of plants from the standpoint of production is self-evident. A biennial, if we are to consider the pharmacopœial species of henbane which reproduces from seed with much uncertainty, has given repeated crop failures in England and has been so difficult to handle in the United States that at one time the government, as well as some individual workers, had given up their investigations of it, is here classed with a group of plants containing annuals, biennials and perennials, of widely different cultural requirements. Of this group, stramonium and cannabis are annuals of very easy culture, probably no easier one could have been selected than cannabis, and the difference between its cultural requirements and those of henbane could hardly be greater. In the case of tobacco we have a plant, old in cultivation, where all details of propagation, cultivation and improvement have been highly perfected, as contrasted with henbane upon which practically nothing has been accomplished. Belladonna, the last named of the group with which henbane is associated, is a strict perennial of decidedly different requirements. It might be grown either as an annual, harvesting both leaves and roots at the end of each season, or left on the ground for three or four years, harvesting only the leaves annually. It requires a calcareous soil, and takes from four to six weeks for seed germination. We do not know the soil requirements of henbane and good seeds germinate in from six to eight days. As to the actual details of planting, cultivating, harvesting and curing, all of the above forms differ widely and no two of them could be handled by exactly the same method.

Returning to the list of plants under discussion we find that colchicum would give difficulties very similar to those of aconite. The parts used consist of the seed and the underground portion in the form of a corm. Seed may be obtained from manufacturers and crude drug dealers as well as from some European seed firms, but they appear to be very difficult to germinate. I have tried many samples from the colchicum seed of the drug markets and one sample from Haag and Schmidt which was supposed to represent fresh seed, but so far have failed to germinate any of them. The seed has a very hard resistant seed-coat and it is possible that some special treatment may be necessary to facilitate more ready and uniform germination. This difficulty alone is sufficient reason for discouraging any attempt at commercial production without some investigations.

Convallaria, another one of the drugs mentioned, presents a different story. The rhizome is most commonly used and there is probably sufficient of the plant already under cultivation in this country to meet the usual demands for some time. Supplies of stock plants can easily be obtained and propagation from root cuttings offers no serious difficulties. Convallaria would be one of the easier medicinal forms to grow should such procedure become necessary.

In belladonna we find one of the most important of the group of vegetable drugs. The commercial supply of the crude drug has come almost entirely from central Europe. This source of supply is now completely shut off by existing conditions and previous crops have largely passed into the hands of manufac-

turers. As to the near future, the prospects of the drug being collected and marketed are extremely poor. Thus belladonna is one of the most promising medicinal plants from the standpoint of commercial supply and demand. To correct a common and rather widespread idea that this plant might be collected from the wild source in the United States, it should be clearly understood that belladonna (*Atropa belladonna*) does not occur in the wild state in this country in sufficient abundance for collection. The belladonna of the United States is nothing more than the little nightshade, *Solanum nigrum*, of common occurrence and which could in no manner serve as a substitute for the true European belladonna.

During the past ten years considerable knowledge has been gained on the cultivation of belladonna in the United States. The investigations of the Bureau of Plant Industry of the United States Department of Agriculture have furnished some valuable information upon the behavior of the alkaloids in the belladonna plant. In California the cultivation of belladonna has been fairly well established in certain localities, but the amount of marketable drug produced there has so far not been sufficient to decrease the annual demands for the foreign drug. The development of this industry has been slow and expensive and many times so discouraging as to almost cause its complete failure and subsequent abandonment. However, the present opportunity promises to be a great stimulus to these efforts and should go far toward seeing belladonna culture in this country, placed upon a sound commercial basis.

Viable seeds of the true pharmacopœial species of belladonna may now be obtained from several reliable sources in the United States in sufficient quantity for both experimental and commercial plantings. One of the most discouraging features of the cultivation of belladonna is the long period required for seed germination. This difficulty places the production of the plant outside of the class of regular farm operations and compels the grower to adopt methods with which he is not ordinarily familiar. When we consider that the seed requires from four to six weeks to germinate, even when under the influence of greenhouse conditions, the difficulties of field sowing are at once apparent. In the central states where weed growth on cultivated land is so luxuriant that almost constant cultivation is required, beginning a few days after the crop is sown, there would not even be a "struggle for existence" in the case of belladonna, for the simple reason that it would rarely come into existence in competition with our rapidly growing weeds. In some of the southern states where growing weather extends through from eight to ten months of the year and where the fall growth of weeds is not a serious factor, field sowings of the seed might be practiced with some degree of success. In our locality, however, experiments extending over several years have demonstrated that the only sure method of obtaining a good stand is by forced propagation and final transplanting to the open field. As to the rate at which plants may be handled by this method we find that an experienced man will move from the seed pans to plant flats or pots, from fifteen hundred to two thousand seedlings per day. This is when the man is working alone and doing all the preliminary work such as soil mixing, filling flats, and other details necessary to such operations. Transplanting to the open field is usually performed at the rate of one thousand to fifteen hundred plants per day. A good man with two helpers to space and drop the plants will work somewhat

faster but his average will not greatly exceed fifteen hundred. Spacing the plants three by three feet in the field will require approximately forty-seven hundred plants per acre. Only rough calculations are necessary to demonstrate the need of cheap but efficient labor in handling a crop of this kind. A mechanical device has been constructed, however, which by the use of three men, not necessarily experienced in handling plants, and a two horse team, will transplant at the rate of from three to five acres per day, at the same time watering each plant and putting on an application of commercial fertilizer.

Everything is not accomplished, however, when the plants are successfully established in the field. In fact the work has only commenced. Subsequent cultivation for belladonna may be about the same as for corn until the plants begin to branch when some forms of single plow must be adopted. In the meantime the crop must be protected from insects and other plant diseases. In this respect the problems involved are somewhat different from those of regular farm crops. In this particular instance both the leaves and roots of the plant are used. This means that any arsenical insecticide applied to the plant, must be used with great caution, or the arsenic, held mechanically upon the surface of the leaves and stems will eventually find its way into some finished product. However, if persistent efforts are made during the earliest stages of growth, the common potato beetle, which is probably the worst insect to contend with, can be eliminated for the entire season. Thus, by the time the plants have reached a size sufficiently large for collecting, the first leaves of the young plants which may have received an application of insecticide have dropped from the stems. The safety of this procedure is evidenced by the free use of arsenicals on cabbage and other garden forms during the early stages of growth. Plant lice have also given serious trouble on belladonna but these can be controlled with any effective nicotine solution. The volatile nature of this substance makes it a perfectly harmless insecticide which may be freely used.

Having protected the plants from insects by some method and carried them safely through the growing season, the approach of harvest brings forth another series of problems. The first to suggest itself will have reference to the time of collection. When the final product is placed on the market its percentage of total alkaloids will be one of the important determining factors in judging the quality, and whether it is belladonna or some other form there will be some definite stage in the development of the plant when the yield of alkaloids or other active principles will be greatest. This condition should determine the time of collection and it can only be ascertained by the collection and testing of many series of samples.

Other questions which the grower would be compelled to answer would be the method of collection for both leaves and roots and the manner of curing these when once they were successfully harvested.

To continue with the list of European drugs we find that it is the opinion of many practitioners that really active digitalis comes only from England, Germany, or some other source, known only to the man who compiles the information on the label. There is in Oregon and Washington an abundant growth of good digitalis which shows an equal value with either the German or English drug. This source of supply could easily take care of the entire demands of the United States. With this abundance of material within easy access it would not be

necessary or wise to attempt the commercial cultivation of digitalis. Those wishing to do so may easily obtain seed of *Digitalis purpurea* from any reliable seed firm. It cannot be sown in the open field, as several writers have stated, but must be propagated about the same as belladonna. It is a hardier plant, however, and may be carried through the seedling stage at a somewhat lower temperature. It flourishes in the ordinary cold frames and may be placed in these with perfect safety as early as March 1st. Only the leaves of this plant are used. The present pharmacopœia requires that these be collected from flowering plants. It is possible, however, that the revision committee will respond to the influence of recent research upon this subject and eliminate that part of the requirement which refers to the flowering plants. *Digitalis* being a biennial, the present pharmacopœial requirement makes it impossible to even think of growing the drug at a profit. Indeed it is doubtful whether it could be cultivated and harvested at the end of the first year with any hope of financial returns.

Gentian was another of the drugs mentioned and is one which holds a rather important place in medicine. It would be a promising drug plant to have established in this country, but we must begin at the beginning. Let us not prepare to grow gentian until we at least have gentian to grow. As in many other instances we find that we cannot obtain good seed of *Gentiana lutea*. I have had seed of this species from Erfurt, Germany, but it failed to germinate. Looking a little further into the history of the plant we find it to be a perennial of which only the roots are used. If we had an abundant supply of good seed with which to begin tomorrow, we could not under these conditions expect to harvest a crop at the end of the present season.

Concerning henbane it is only to be regretted that the United States is not now prepared to produce its own supply of this valuable drug. It is not, however, and the few individuals who have been attempting to grow it should not be discouraged when the government which is at present leading the movement in drug plant cultivation, has almost failed in its attempt to grow the plant. Good seed of henbane is difficult to obtain and I would not advise any one to depend upon those which have not first been thoroughly tested. I have isolated an annual strain, the seed of which germinates quickly and uniformly. Several hundred plants of this strain will be grown this year. This should be a sufficiently large number of plants to test the strain for commercial purposes. The official biennial species has been hard to grow to maturity. Once this is accomplished and a good supply of fresh seed obtained the work on this form should progress more rapidly. One of the worst things to contend with in growing henbane, even on a small experimental scale, is the ravage of the potato beetle. It has been almost impossible to protect the plants from this insect even by the use of the most effective poison.

Concluding with stramonium we find that what was said of digitalis will apply in some degree to this form. With the wild plant growing abundantly in the United States, there is some question of the advisability of attempting its cultivation. It is usually supposed that stramonium will grow in spite of itself, but such is not the case and good results could only be expected on rich soil and by the practice of clean cultivation.

This leads us into a discussion of the problems of drug cultivation from a dif-

ferent viewpoint. We have too often heard of the fortunes to be derived from weeds, of the statements that this or that plant will grow and flourish anywhere and we as often wonder upon what type of reasoning such statements are founded. We know that history records but very, very few fortunes as having originated from weeds except probably through their elimination. It is also evident that all plants now known to man, do possess selective properties which enable them to reach their maximum developments only under environmental conditions which are within certain definite limits. The mere fact that a form has been observed growing as a weed is not good evidence that it will behave in a similar manner when introduced into cultivation. In fact, this is not what we desire. If we merely wish to grow them as weeds and thereby realize an abundant profit we had better stop where we are now, for we would likely derive neither weeds nor profit. What is most desired is to grow medicinal plants not as weeds, but as cultivated plants, improved, perfected and developed in the same manner and to the same degree of perfection as already obtains in the case of other economic forms. To merely grow medicinal plants upon a commercial scale is not sufficient. In fact it is very doubtful whether or not most of them can be produced economically unless some form of improvement is followed. We cannot compete with European producers upon a mere basis of equality. We may be able to compete with them, however, by increasing the quality and yield of the drugs through improvement. This can only be brought about through careful breeding and selection.

The field of research in this respect is almost unlimited and practically untouched. There is hardly a vegetable drug of any importance that does not suggest opportunity and the possibilities for improvement in this line of work. We only need turn to a careful consideration of existing conditions with reference to such drugs as henbane, belladonna, digitalis, stramonium, cannabis, and others for these suggestions. Henbane of disgraceful appearance and low in alkaloidal value is admitted to the United States in order to meet the constant demand for this drug. We have an official description of this drug and a species requirement, but who knows or is able to determine what species are actually included in the crude drug of European origin. From the appearances of many shipments it seems that every species, both plant and animal, which might inhabit the average barnyard has been included in the make-up of this drug. Here is abundant evidence of much needed improvement and it can best be accomplished by the introduction of this plant into cultivation and its subsequent improvement by breeding and selection. The testing of other species of *Hyoscyamus* may lead to the discovery of a more valuable form, and while Schneider says that the annual form of henbane is not desired medicinally, let us not despair since we find that this annual form has really never been tested thoroughly for its alkaloidal and therapeutic value.

Belladonna is in the same class with henbane, and while the range of species is not so large, still there is the variety *lutea*, which has so far never been tested. Seeds of this variety were brought to this country by Professor Henry Kraemer and through his kindness we now have this form growing in our experimental grounds. It offers an opportunity for hybridization with the official species *Atropa belladonna*. Sievers, of the Bureau of Plant Industry, has already shown

what may be expected from consistent selection with the official belladonna. Further work of this nature, but leading to increased yield, together with a better understanding of soil and climatic condition is highly desirable. A similar series of investigations is suggested by the genus *Datura*. Here, however, the range of species is much greater and the variation in the nature of the alkaloids in the various species is such as to present problems of a different character, and which should lead to the use of some of these species for different specific purposes. The species *Datura tatula* has recently been shown to be equal to or better than *Datura stramonium* in the percentage of alkaloids. Both of these species have yielded to selection and hybridization in such a manner as to promise the early development of a much-improved strain. Turning to *digitalis*, we find a host of species and horticultural varieties of unknown therapeutic value which should furnish an abundance of material for the investigator. Many of these have been found to be extremely toxic, both in the flowering and nonflowering stages.

And so the discussion might be continued in detail for *cannabis*, *conium*, *colchicum* and any others that might be grown within the United States. Sufficient has been said, however, to draw attention to the many difficulties that may be encountered in attempting to grow medicinal plants upon a commercial scale, and of the opportunity and desirability for improvement. The beginner in this work should be advised to commence upon a small, experimental scale with a few of the most valuable drug-producing plants and enlarge his operations as results might indicate. The value of the work cannot be questioned, and while it is vitally important that medicinal plants be grown with the same care and consideration as in the case of corn, wheat or other economic forms, still the step from the wild plant to the highly developed variety of known constitution is a long one and cannot be accomplished in a few days.

It is hoped that nothing has been said which will tend to discourage the present widespread movement in drug cultivation. Rather, we would wish to encourage it but in such a manner as to lead to a fair understanding of the true state of affairs and to dispel the idea that large profits may be expected.

BOTANICAL DEPARTMENT, ELI LILLY & COMPANY, Indianapolis, April 8, 1915.

THREE INTERESTING INCOMPATIBILITIES.*

WILBUR L. SCOVILLE.

The first deals with the action of light and heat on the organic acid salts of the cinchona alkaloids.

In 1853, Pasteur found that on heating acid sulphate of cinchonine to 130° C. for several hours, a poisonous compound was formed which was isomeric with cinchonine. This for many years was regarded as one of the curiosities of cinchonine, possessing no practical interest, because in the use of cinchonine it never became necessary to heat it in this way, and consequently no change was expected. Hesse

* Presented to the Detroit Branch, A. Ph. A., Feb. 19, 1915.