

an outlay of capital. Then, in order to produce enough material to make it worth while, special machinery is necessary both for planting and harvesting. And as drugs are not marketable unless they are of the proper appearance, and of the proper potency, the question of curing is extremely important, and that can only be done successfully in drying houses of proper construction, with proper regulation of heat, and other constant, careful attention until the crop is thoroughly cured.

Then, finally, and one of the most important features of the whole situation, is the control laboratory, because it would be ill-advised from every standpoint to go on the market with a batch of drugs of unknown potency.

There has been much progress made during the last few years in this work. Large pharmaceutical houses in the country have established their own drug growing farms, and they have been successful. The Department of Agriculture established the camphor industry in the south, and it has become an important industry. Hydrastis, which is important in our own materia medica, has been cultivated for a great many years by growers, operating small acreages in parts of the west and northwest. In Washington they have been doing something along that line, and the films which I have brought with me illustrate some of the points that I have tried to bring out in these prefatory remarks. The pictures will take you from the spring when we begin until the present time in our operations; in fact the last picture was taken only a few weeks ago when the thermometer was 124° F. in the sun.

(A series of pictures of the drug growing industry were here shown.)

DRUG PLANT CULTIVATION—DRUG PLANT BREEDING.*

BY F. A. MILLER.¹

I will omit introductory remarks and begin immediately with the slides,² attempting only a brief explanation of the work that we have been doing.

That which we have attempted to do in Drug Plant Cultivation and Drug Plant Breeding has been along the lines of improvement and economic production. I mean by economic production, an attempt to determine the possibilities of growing the more essential medicinal plants upon a basis, that would enable us to grow them as we grow other economic plants. If we set out to grow medicinal plants, regardless of the cost of production, we can probably grow almost any of them, but if we limit ourselves to those which can be produced economically, there are limitations.

(A plot of digitalis in its first year's growth was shown, followed by others of the series.)

During the year that we were working on digitalis, we grew and tested a large number of varieties, in fact all the varieties which could be obtained from this country, England, Germany and Japan, making a special effort to obtain seed of all named varieties and species. *Digitalis purpurea*, being a domesticated form,

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

¹ Biological Department Eli Lilly & Co., Indianapolis.

² As indicated, Mr. Miller spoke while the pictures were being shown on the screen; the subjects related to breeding and cultivation of drug plants.

has been made to produce a large number of varieties, and our aim was to find one that was better in its physiological activities than the official digitalis. It has now been found that digitalis does not need to be grown through the second year to give an active leaf, the first year's growth being fully as active as the flowering plant.

You will notice in this slide a difference in the size of the beds. These are of the nature of test plots, and consist of measured areas. By keeping accurate expense accounts of these test plots, we obtain figures which indicate the possibilities of growing the different species on a larger scale.

The next slide is a view of a selection and breeding plot of all varieties tested. Thirty-two of them were grown and tested physiologically, the results of which were published some two years ago.³ Some of the breeding work that has been done is shown in progress on this slide, the flowers being protected, of course, by ordinary paper bags to prevent cross-pollination.

We have also carried on experimental work in the greenhouse during the winter months, and this is digitalis growing in midwinter. You will notice that some plants are blooming. Digitalis is biennial but it can be brought into bloom by continuous growth without giving it the resting period which it has in its natural state.

Turning now to Cannabis, we have here a very luxuriant growth. This is a strain which we have developed by selection. Animal tests on this drug indicate about 90 to 95% activity when compared with good Indian Cannabis. This slide shows the harvesting of the same field of Cannabis, where you will note the rows to be about three feet apart, the plants being much taller than the average sized man. Some of these plants reach a height of from twelve to fourteen feet. The problems of harvesting are suggested here, where the cutting is being performed by hand. We have attempted to cure Cannabis partially in the field, cutting and binding into bundles and shocking. It is then taken under cover and the curing completed. Later the inflorescence is removed from the stems and separated from the leaves and seed. No effort has been made to eliminate the male plants. That only aids in the reduction of the percentage of seed in the finished product, and we find that we can do that more economically by allowing the plant to produce seed and then remove these at the time of curing.

We have touched lightly upon the question of fertilizers. They are necessary on some types of soil for successful drug cultivation. This slide represents a pot experiment carried out in the greenhouse with various types of fertilizer. We have in the first row, manure and potash; in the second, manure, potash and phosphorus; and in the third, phosphorus and potash. This was an attempt to determine the best fertilizers for Cannabis, and if I remember correctly, the complete fertilizer, potassium, phosphorus and nitrogen gave us the best growth.

Cannabis breeding has occupied some of our time, and we have isolated here a dwarf variety. This individual plant shows short branches and very heavy inflorescence. The inflorescence is heavier, especially on the central stem, than that found on the tall-growing variety.

Unfortunately we do not always find the combinations of characters in plant breeding, that are most desired. In this variety we have obtained a plant of much

³ See JOURNAL A. PH. A., March 1914, pp. 304-314.

better form, but which shows little activity. The variety has been tested for several years, but has never been over 40 percent as active as the Indian drug.

Some work has also been done on *Stramonium*. A large number of species have been under experimentation. This is a plot of mature *stramonium*, showing an attempt to simplify the process of harvesting. This drug has been cut with an ordinary mowing machine, the whole plant being taken in, cured, and the leaves removed after the curing process is completed. This shows the operation of cutting. The poor yield is due to the type of soil. It is not adapted to growing this plant. The ordinary farmer will tell you that *Jimson* will grow anywhere, but we are convinced that it is quite selective in its habitat.

Turning to *Belladonna*, we have here a section of our propagating division in the greenhouse. These are seed flats in which are thousands of seedlings just ready for the first transplanting. This was an experiment upon germination. The right half was planted with seed which had been treated with boiling water.

Here is a section of cold frames where seedlings are handled. These plants are being removed from the greenhouse preparatory to their setting in the cold frame, or transplanting to the open field, as the case may be. Many of our plants are transferred from the greenhouse to cold frames, beginning the first of March. They can be safely transferred at that time and will withstand the usual hardening off process. Transplanting, of course, comes next and we use the machine shown on the screen. Only one man is used on the machine, since it has been found that one experienced man will accomplish as much and do it better than two.

This is a general view of one of our early breeding plots of *belladonna*. To the right you will notice plants with white spots on them. They are paper bags, protecting the flowers from cross-pollination. We are very much delighted with one strain recently isolated. Three years' testing has shown it to possess a very much higher percentage of alkaloid than the average type. Unfortunately, as I stated before, we do not always get the best combination of characters. It grows less vigorously and is more sensitive to soil and weather conditions.

This is a view of the harvesting of a *belladonna* crop. Cutting is done by hand and the entire plant is immediately removed to the drying shed. After partial curing, the leaves and stems are separated. We have grown *belladonna* strictly as an annual, starting about January and completing the harvest at the end of the season, taking out all the roots.

Henbane is probably more important this year than *belladonna*, but more difficult to grow. This is one of our early plantings. This planting was made in 1915 and represents an early stage of growth. Here is a later stage, showing the plants somewhat larger, and still another one where the plants have reached a very luxurious stage of growth. A midsummer shower on this plot, followed by a hot sun, converted the entire plot into one resembling a field treated with hot water, practically every plant in the plot being lost.

This is *Hyoscyamus muticus*. This group of plants, consisting of about two hundred, were transferred to the open ground during the month of May, and were all lost, probably on account of the cold, wet weather which followed. This, of course, is the tropical *hyoscyamus* from which atropine is obtained. It has proved very difficult to grow even under carefully controlled greenhouse conditions. Some few plants have been grown to the flowering stage, but none have so far produced seed. Attempts to cross it with *Hyoscyamus niger* have been unsuccessful.