SCIENTIFIC SECTION

CULTIVATION OF EPHEDRA IN SOUTH DAKOTA.*[1]

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Ephedra sinica seed for trial planting was received from Peking Union Medical College in 1929, and the first planting made in the greenhouse on November 6th of the same year. Germination was excellent by November 20th, and on May 15, 1930, 73 thriving ephedra plants were potted, and on June 30, 1930, these were transplanted into the medicinal plant garden. The following winter the plants were moved into the root cellar for protection and were again set in the garden plots in the spring of 1931. That fall the first cutting of stems was made, and thereafter the roots were allowed to remain in the ground undisturbed during the winters of 1931–1932 and 1932–1933. Such was the status of ephedra in South Dakota at the time the writer became interested in its possibilities as a domestic drug crop.

As proof of the hardiness of the ephedra plants, the writer simply calls to your attention their survival of those memorable years of the "ghastly black blizzard," when the average annual rainfall would not average more than a dozen inches, and the winter of 1935–1936, pronounced the coldest for South Dakota in 50 years. On many occasions the top soil was blown from the plants until they were anchored only by the tip ends of their long sturdy tap roots, but in spite of this they continued to thrive. Small wonder, then, that this plant attracted considerable attention. Furthermore, it is well known that there is no domestic source of supply for this very important crude drug. These considerations prompted the selection of this problem for an original research project, namely, the determination of the possibilities of commercial production of ephedra in South Dakota.

A problem of this sort logically involves two important points, namely, the methods of propagation and cultivation best adapted to handling such a crop, and the methods and proper time of harvesting and the methods of curing which will insure the highest yield possible of the active principle, ephedrine. The fourth season of systematic investigation of these plants is now being completed.

Propagation and cultivation of ephedra appears to be not too difficult a matter, for the plants reproduce from seeds, and also from runners which develop into several sturdy plants that mature rapidly. These new plants transplant very well, by severing them from the old root and allowing them to remain undisturbed for about three weeks before moving them to their new location. This allows ample time for their own root systems to develop and assures greater success in trans-

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planting than when they are moved immediately after cutting the runners. As for the seed, it is best handled by planting it outside in rows where it can be cultivated until the plants are at least two years old, at which time they are well enough developed to transplant into the field at the desired spacing. Ephedra as it matures undisturbed, resembles very much the ordinary alfalfa crop in its growth habits. It roots deeply, and spreads by runners to form a sod which soon eliminates the necessity for cultivation except for hand weeding, all of which makes for easy production of the crude drug.

The soil adaptations of ephedra leaves much to be determined by research into this phase of its cultivation. The plants thrived so well during the drought that it suggested the possibility of their being introduced into the marginal region of the state, particularly of the Bad Lands section. With the limited funds available, however, only one test plot of this type has been established. Stems returned from this plot, which happens to be in the Bad Land region, compared favorably with

Test plots of Ephedra sinica, Division of Pharmacy, Medicinal Plant Garden, South Dakota State College, Brookings.

those produced in eastern South Dakota. They were smaller in size, but the plants were healthy and well established in the light sandy soil. Two-year old stems from this plot assayed 0.347 per cent ephedrine, indicating that ephedra may be suited to a section of the state which is at the present time almost unproductive. The experimental plots in eastern South Dakota are planted in well-drained rich black loam. Hence, even with much left to be done on the soil problem, production of ephedra seems practically assured, leaving the problem of harvesting and curing the herb as the next important step.

The first harvest was used for the determination of the time of year the cuttings should be made, and for the determination of the normal alkaloidal content of the stems. Harvesting was begun on September 13, 1933, and one cutting made each week until six successive cuttings had been completed. By this time heavy frost had checked further development of the plants. These cuttings were oven cured and assayed with the following results:

TABLE I.

1933 Harvest Dates.	Care.	Assay.
1. September 13th	Oven dried	0.0737%
2. September 20th	Oven dried	0.0935%
3. September 27th	Oven dried	0.0977%
4. October 4th	Oven dried	0.0894%
5. October 11th	Oven dried	0.0725%
6. October 18th	Oven dried	0.0792%
7. October 4th[1]	Sun cured	0.126%

A study of the above table revealed three points of particular interest. It showed:

1. The alkaloidal content of the one-year old stems to be exceedingly low.
2. It further suggested that the proper time to cut ephedra was around the latter part of September or the first of October, and also, since the October 4th[1] cutting which was cured on the ground where it fell when cut contained the highest per cent of ephedrine.
3. It suggested that perhaps the proper way to handle ephedra might be to cut and cure it like ordinary hay crops, rather than to oven cure it.

The main concern at this time, however, was over the extremely low ephedrine content.

Further results along the above lines were obtained from the 1934 crop as shown in Table II.

TABLE II.

1934 Harvest Dates.	Care.	Assay.
1. September 27th	Sun cured	0.1501%
2. September 27th	Shade cured	0.1487%
3. September 27th	Oven cured	0.1321%
4. October 11th	Sun cured (frosted)	0.1509%

The above ephedra stems again represented one season's growth for they were all cut back the preceding fall. The findings of this season corroborated those of the year before, mainly:

1. That the alkaloid content was extremely low for single-year stems.
2. That probably the best time to harvest ephedra would be the latter part of September, since there is danger of damaging frosts around the first part of October.
3. That the stems left in the field to cure in the sun contained the highest per cent of ephedrine.

It was evident from the assays figures, that some improvement in quality would have to be made to justify a continuation of the project.

Realizing the futility of attempting to increase the alkaloid content simply by growing and harvesting the stems year after year, the writer became interested in discovering some new procedure which would increase the existent low alkaloidal assay. It was evident, too, that if such could be done, the more natural the process involved, the more valuable it would be, since if ephedra was to become a commercial crop, its production must be as easy as possible. A review of literature disclosed the fact that originally the plants were not cultivated, for the Chinese had long been gathering the drug from its natural habitat in the wild state. It appeared possible, then, that the stems were perennial, and that the ephedrine content of about one per cent had developed gradually in the maturing of the stems for several years.

A careful survey of the garden records for the several years past, showed conclusively that ephedra *roots* were hardy and perennial when left undisturbed, but the records also revealed that the *stems* had never been left uncut for two seasons to determine if they too were perennial in this climate. Accordingly, four test plots were left uncut in the fall of 1934 to determine what the condition of the stems would be in the spring of 1935. These beds contained enough plants so some could be left to mature through their fourth year if it was desired.

The progress of the stems during the winter was carefully noted. They remained upright, and except for developing a slightly black coloration, looked perfectly normal. Their fracture was brittle and green, the color resembling very markedly that of the fresh growing stems in mid-summer. Very early the next spring they regained their normal succulence and green color, and further, there was promise of an increased stem production due to the profuse branching from each node of the old stem. The per acre yield of stems in the fall of 1935 showed that nothing had been lost in crop weight by allowing the stems to mature this extra season, for the branching of the old stems compensated for the lost cutting.

This in itself was particularly gratifying; besides, there was the possibility of an increased seed production to hasten propagation, as well as the possibility that maturing the stems might increase the ephedrine content. By the middle of May, seed production was well advanced, which promised plenty of time for the seeds to mature, where heretofore they had just escaped frost. Seed production from the second-year stems showed an increase of 66 per cent by weight over the best figures ever obtained from stems one season old. This, too, was gratifying, and the question then remained, has the ephedrine content increased, and if so, enough to encourage production?

Cuttings of the two-year old stems were begun on September 23, 1935, followed by three successive harvests at weekly intervals. These were cured and assayed with results shown in Table III.

TABLE III.

1935 Harvest Dates.	Care.	Assay.
1. September 23rd	Sun cured	0.364%
2. September 23rd	Shade cured	0.361%
3. September 30th	Sun cured	0.363%
4. September 30th	Shade cured	0.366%
5. October 5th	Sun cured	0.364%

Cuttings were also made in 1935 from stems that had matured but one season, *i. e.*, they were the stems produced the summer of 1935 from plants harvested in 1934. The results of these harvests are shown in Table IV.

TABLE IV.

1935 Harvest Dates.	Care.	Assay.
1. September 23rd	Sun cured	0.153%
2. September 23rd	Oven cured	0.083%
3. September 30th	Sun cured	0.152%
4. September 30th	Shade cured	0.150%

Table IV substantiates the findings of Tables I and II; that the stems pro-

duced by a single season's growth run extremely low in ephedrine, and further suggests that even moderate heat in oven curing the herb is detrimental to its alkaloidal content.

Table III, however, contained the most promising information of all. By simply allowing the perennial stems to mature this extra season, the ephedrine content increased 144 per cent over the highest figure ever obtained from the single-season stems. Those stems which were left on the ground outside cured so nicely that it assures ease in cutting and caring for the stems.

Aging the ephedra stems an extra season, then, was found to be decidedly encouraging for the following reasons:

1. It increased stem production.
2. Seed production increased 66 per cent.
3. It increased the ephedrine content.

How far the natural phenomena will continue to advance, of course, remains to be determined by continued experimentation. From data thus far obtained it is possible to suggest the following conclusions:

1. *Ephedra sinica* stems and roots are both hardy and perennial in South Dakota.

2. The plants produce viable seeds, assuring rapid propagation both from these, as well as from numerous runners that develop into new plants.

3. The crop may be handled like any ordinary hay crop, by cutting it with mowers, allowing it to cure in the field, and then bale for shipment.

4. The proper time for harvesting favors late September, since damaging frosts are expected by October first.

5. The undisturbed plants spread to form a sod which eliminates cultivation except for hand weeding.

6. Stems produced in a single growing season are small, bear few seeds and run low in ephedrine content.

7. Maturing the stems for a second growing season increased stem production from the nodes of the old stems, stimulated seed production, and increased the ephedrine content.

8. The best assay figure obtained thus far is still considerably below that of the imported drug, but in case of an emergency, ephedra of fair quality could be produced in South Dakota.

THE ASSAY OF MONOETHANOLAMINE IN THE PRESENCE OF THEOPHYLLINE.*

BY ASA N. STEVENS.[1]

The pharmaceutical literature does not appear to provide a method for the determination of monoethanolamine in mixtures containing the various xanthine derivatives. In an effort to develop a satisfactory procedure for the estimation of monoethanolamine in the presence of theophylline the following experiments were made.

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* Scientific Section, A. PH. A., Dallas meeting, 1930.

[1] Control Laboratories, Eli Lilly and Company.