

## EMPIRE PRODUCTION OF DRUGS

## III—EPHEDRINE\*

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Probably because of advertisements of proprietary articles, the drug ephedrine has aroused a good deal of interest in the public mind. When experiments were first started on the growing of various species of *Ephedra* they received too much advertisement. An article in the London *Times* spoke of these experiments as being well under way before we had succeeded in getting a single plant established. Such premature advertisement is liable to lead to disappointment, but it must be stated that most of those who collaborated have maintained their interest remarkably well.

The genus *Ephedra* contains a fairly large number of species which vary in size from dwarf shrubs to a small tree. In all species the leaves have degenerated to mere scales, the work of photosynthesis being undertaken by the stems, which are green; the plants thus resemble the "horsetails". All species are dioecious; that is, there are male and female plants.

One species, *Ephedra sinica*, has been employed in Chinese medicine for many centuries under the name of Ma-huang. Although the alkaloid responsible for the therapeutic effects was isolated as early as 1887, it is only within the last ten to fifteen years that the drug has been employed in European medicine, but the extent of its use has increased immensely.

The alkaloidal content of the various species of *Ephedra* varies from none, or mere traces only, in the North American species, to between 1 and 2 per cent in some of the Old World species. From a therapeutic aspect the most important species are *E. sinica* and *E. equisetina*, *E. distachya*, *E. gerardiana* and *E. intermedia*. The main sources of supply are China and Spain, and a fair quantity too comes from India. As a result of the wars in China and Spain supplies decreased heavily, so when in 1937 Mr. Lyne Watt, Senior Agricultural Officer, suggested that it be tried here, steps were taken to obtain material. The Director of the Royal Botanical Gardens, Kew, has been indefatigable in obtaining and supplying cuttings and seed of many species, and to him

the Department of Agriculture is deeply indebted.

In March, 1938, a number of cuttings of *E. equisetina* and *E. distachya* arrived from Kew. Most of the former had broken up into short lengths at the nodes; a few, however, remained in fair condition. The *E. distachya* cuttings did not break up to the same extent. All that could be were planted in a sand-box, but gradually one after the other died; a few did show signs of callusing, and were the last survivors.

In October, 1938, one of the collectors of Kew was able to obtain seed of *E. sinica* in the neighbourhood of the Great Wall of China. This was sent us. Some was sent to people who desired to collaborate, but they all reported that the seed failed to germinate. No difficulty was experienced here; perhaps the collaborators, not without reason, had failed to recognize the seedlings. Trouble was, however, experienced with damping-off, so as soon as possible the seedlings were pricked out into banana pots and, as they developed, distributed. Further lots of seed were received in January, 1939, and at the end of April, 1939. No difficulty was experienced with seedlings raised from both these lots. On account of the expense of banana pots, seedlings were pricked out into seed-boxes and no trouble at all resulted.

Reports received from collaborators under all sorts of climatic conditions regarding growth of these plants were most disappointing. Growth was very little or none; in many cases the plants languished and died.

Later, seed of *E. sinica* was obtained from South Dakota. Plants raised from this appeared to do rather better in the early stages, but here too growth has been most disappointing.

At the end of November, 1939, seed of *E. intermedia* was received, and in December seed of *E. gerardiana*. Right from the early stages of growth these two species showed great promise. In March, 1940, seed of *E. intermedia* var. *tibetica* and of *E. nebrodensis* var. *procera*, a Baluchistan species, arrived

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from Kew. Germination was very good, but during the heavy rains of April the seedlings damped off heavily. On removal to the Laboratory verandas, where the seed-boxes could dry out, damping-off ceased, but, unfortunately, most of the plants had been lost.

As most of the *Ephedras* of value as sources of the drug ephedrine are natives of comparatively dry countries having a marked summer and winter, it was believed that the areas in Kenya that would be most suited to the growing of *Ephedra* would be some of our cooler, fairly dry zones, such as Timau and Thomson's Falls. However, in order to obtain the fullest possible information, distribution was wide and covered all the cool zones. Recently, however, a very much warmer zone has been put under trial; reports from here are not yet available. About thirty-five people collaborated in these experiments, but owing to war conditions it has not been possible to obtain reports from all; nevertheless, a sufficient number have been received to enable us to reach some conclusion.

#### THE WESTERN MAU ZONE

Climatic conditions cool to cold, humid.

*E. sinica*.—In most cases died, probably due to long-continued wet conditions.

*E. intermedia*.—Very poor growth everywhere, plants unhealthy and dying. One report stated that plants not yet planted out looked very well in the boxes.

*E. gerardiana*.—At one station, probably the driest in the series, very fair growth was recorded and the plants have seeded. At another, in a wetter zone, all the plants died.

#### FORT TERNAN

Climatic conditions fairly warm; not so humid as previous zone.

*E. sinica*.—Fair but straggly growth.

*E. intermedia*.—Very fair growth.

#### NAKURU DISTRICT

Climatic conditions variable; under Laikipia Escarpment fairly warm with cool to cold nights, comparatively humid, changing to comparatively dry under the Mau Escarpment.

*E. sinica*.—A failure; one report stated that the only growth occurred during dry weather.

*E. intermedia*.—Not healthy; straggly growth and suffered from much dying back.

*E. gerardiana*.—Fair growth, plants bushing out, no signs of flowering.

*E. nebrodensis* var. *procera*.—Growth not so good as that of *E. gerardiana*.

#### GILGIL-THOMSON'S FALLS

Climate variable; generally fairly cool; rather humid at high altitudes, but fairly dry at Thomson's Falls.

*E. sinica*.—Generally very poor or no growth. Many plants died. One report was unusual, stating that the plants tended to die back in dry weather.

At Thomson's Falls there was very fair growth, but this was straggly.

*E. intermedia*.—A repetition of *E. sinica*, with the exception of Thomson's Falls, where there was good growth, the plants bushing well.

*E. gerardiana*.—Only two stations received plants, but at the more humid there was very slight growth with a tendency to die back and form weak new growth. At Thomson's Falls this species developed very bushy growth and is flowering.

#### KINANGOP PLATEAU

Climatic conditions variable; fairly dry at the edge of the plateau to humid under the mountains.

*E. sinica*.—In no case was good growth reported. Plants died out in the wetter zones. From the drier part there were two reports of flowering. There is a possibility that stray plants of another species may have been included.<sup>1</sup>

*E. intermedia*.—In the wetter zones very little growth; from the drier zones it is reported that the plants are flourishing and bushing out well.

*E. gerardiana*.—Only one station in the drier zone received plants, where they are doing really well.

#### LIMURU

Climatic conditions cool and moist, with dry periods.

Both *E. sinica* and *E. intermedia* failed.

<sup>1</sup> That it was probable that a plant of another species was present is borne out by the fact that in the boxes of transplants of a single species sometimes there would be one or two plants of a very different habit, e.g. in a box of *E. sinica* a typical plant of *E. intermedia* would appear. Possibly in the collection of the seed from wild plants, seeds of an occasional plant of another species may have been reaped.

## NGOBIT

The station where these experiments were conducted has a fairly moist cool climate.

All species failed; *E. gerardiana* did best, but produced very spindly weak growth.

## TIMAU

A dry cool zone. Owing to war conditions reports were received from one station only.

*E. sinica*.—All varieties died out.

*E. intermedia*.—Good growth.

*E. gerardiana*.—Doing very well, much better growth than *E. intermedia*.

## TRANS NZOIA

Climate variable, warm to hot near Kitale; Cherangani, warm to cool; Elgon, cool. Rainfall, greater part of the year, well distributed; marked dry period.

*E. sinica*.—Failed in every part.

*E. intermedia*.—Good growth at Kitale and Cherangani, bushing out. Poor growth on Elgon.

*E. gerardiana*.—Very good growth in all parts, beginning to flower at Kitale.

SCOTT AGRICULTURAL LABORATORIES,  
KABETE

Climatic conditions warm to cool; rainfall not well distributed; two marked dry periods.

*E. sinica*.—Very little growth and straggly; does not like wet.

*E. intermedia*.—Most satisfactory, about 18 inches high, branching well and beginning to sucker. Does not like wet.

*E. gerardiana*.—Growth not so tall as *E. intermedia*, but more bushy; commenced to flower beginning of December, 1940, and seeded. Flowering, however, uneven, so many female plants not fertilized.

*E. intermedia* var. *tibetica*.—Good growth, showing signs of being very satisfactory.

*E. nebrodensis* var. *procera*.—Slower than previous species.

## CONCLUSIONS

The results accruing from these experiments enable the following conclusions to be drawn:

- (1) Climatic conditions in Kenya are unsuitable to the growth of *E. sinica*.
- (2) *E. intermedia* and *E. gerardiana* will thrive under many conditions in the Kenya highlands.
- (3) None of the species so far tried will tolerate wet or humid conditions.

It is not yet possible to do more than indicate what parts of the Colony are most suitable for the growing of *Ephedra* on a commercial scale.

As the value of the plant depends upon its alkaloidal content, assays have been made of material produced at the Scott Agricultural Laboratories. It is stated that the alkaloidal content is highest in the autumn after the seeds have ripened, and that this increases with the age of the stem. Kenya, of course, has no autumn, and at present all of our material is only one year old. Well-grown stems of *E. intermedia* and *E. gerardiana* were cut from the plots here, dried at a temperature of 50° C. and assayed for total alkaloids. The results are as follows:—

	<i>E. gerardiana</i>		<i>E. intermedia</i>	
Date of cutting ..	4-2-41	27-3-41	4-2-41	27-3-41
Dry matter ..	30.8%	29.6%	35.5%	27.7%
Total alkaloids in				
dry matter ..	1.66%	1.69%	1.54%	1.60%

These figures are most satisfactory, especially when one takes into consideration the fact that both plots are well under one year old.

Not all the alkaloids are of physiological value. Read and Feng<sup>1</sup> give the following proportions of ephedrine in the total alkaloids:—

<i>E. gerardiana</i> ..	70-80 per cent
<i>E. intermedia</i> ..	30-40 per cent

It is indeed fortunate that *E. gerardiana* is the most promising. Since it is seeding and beginning to sucker, it should not be difficult in the course of the next year to work up a large amount of planting material.

Experiments are being undertaken on vegetative propagation so as to speed up multiplication if possible.

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<sup>1</sup> Read & Feng, *J. Am. Pharm. Ass.*, 1928, 17, 1189, quoted in *Textbook of Pharmacognosy* by G. E. Tracey.