the second and third time. This second and third peel is said to come from trees that were too small to yield heavy enough bark at previous cuttings. The trees peeled to-day are much smaller in the aggregate than trees peeled twenty or thirty years ago.

One means of lengthening the life of the industry would be to find a satisfactory method using more of the tree.

In view of the fact that the thinner bark yields the highest per cent of constituents, it may be possible and profitable in the future to grind up the smaller twigs and limbs for extraction of the contents. This process would permit of much closer utilization, and should make the growing of the tree on a commercial basis more profitable.

# CHINESE BOTANICAL SOURCES OF EPHEDRINE AND PSEUDOEPHEDRINE.\*

# BY B. E. READ AND J. C. LIU.<sup>1</sup>

After the very illuminating note upon the botanical sources of ephedrine by Holmes (7) it appears quite clear that the European source of these alkaloids is not the same as the Chinese Mahuang as was assumed by Chen and Kao (3). A private communication from Merck's assures us that contrary to recent statements (2) their European supplies are yielding ephedrine and only a small amount of pseudoephedrine. Various publications from these laboratories (4) show that ephedrine and pseudoephedrine (12) occur in Chinese Mahuang. Hence it is plain that there are good sources for these two alkaloids in both Europe and Asia.

The work of Neilsen, *et al.* upon American ephedras confirms our results (14), namely that California ephedra contains no ephedrine nor pseudoephedrine. We found a small amount of a basic substance in the Nevada species which we should like to try out further.

The article published by Neilsen (10) dealing with Chinese species of *Ephedra* shows the great need for definite identification and classification of the Chinese plants. The purpose of this paper is to provide this as adequately as possible.

Material has been sent by us to Dr. O. Stapf, the world's authority upon *Ephedras*. His well-known monograph (16) sets forth the characteristics of the various species quite clearly. It is now definitely known that the material collected and sold as Mahuang consists chiefly of *Ephedra sinica*, Stapf, an entirely new species described by him (17) from incomplete material in the *Kew Bulletin*.

This plant we have made unusual efforts this year to personally collect in numerous out-of-the-way places, and to secure it from remote areas through friends. We have now obtained plenty of complete material providing the male, female and flowering plants, which come from the exact areas where the drug collection is made. This plant grows abundantly in North China particularly on the mountains running up through Shansi, Northern Chihli, and around the edge of the Mongolian plateau down to the sea near Peitaiho. At the latter place Cowdry (5) listed *Ephedra equisetina*, Bunge, in 1922. This species is quite common in

<sup>•</sup> Received for publication December 15, 1927.

<sup>&</sup>lt;sup>1</sup> Department of Pharmacology, Peking Union Medical College, Peking.

## JOURNAL OF THE

Shansi and is known as "Mupen Mahuang," E. sinica being called "Tsaopen Mahuang." A third species collected by Eriksen in Mongolia was sent by us to Stapf, who pronounces it to be another new species. Holmes' (7) assumption that the species sold in Peking is E. intermedia var. Tibetica, Stapf, is not supported by the facts as they are so far known. For the flowering plants sent by us to Stapf are an entirely new species. It is probable that all of the above-mentioned species, not E. intermedia, are sold, and that E. sinica is the commonest in the Peking drug market.

We herewith give a detailed description of the two plants, *Ephedra sinica* and *E. equisetina* both of which grow in great abundance along the T'ai-Hang-

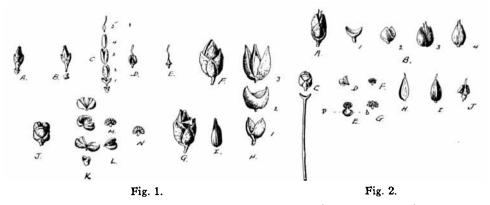


Fig. 1.—Ephedra equisetina, Bge. A-I, female flower or fruit (about natural size); J-N, male flower (about natural size). A-B, female spike with 4 pairs of bracts; C, the same with bracts separated, C-5 flower with exserted micropyle and entire perianth; D, perianth split open; E, ovule with micropyle; F-G, mature fruit; H, the same with bracts separated, showing one seed inside; I, seed with both surfaces convex. J, male spike; K, the same with bracts separated; L, androeccum in perianth; M, stamen with anther-sacs, front view. N, back view of the same.

Fig. 2.—*Ephedra sinica*, Stapf spec. nov. (about natural size). A, female spike; B, the same with bracts separated and showing the 2 flowers or fruits in the last pair of bracts. C, male spike; D, perianth with calyciform bract; E, the same opened—b, the bract, p, the perianth; F, anther-sacs (8) and stamen; G, the same, torn apart; H, seed, showing the flat side; I, seed, showing the triangularly convex side; J, female flower.

Shan mountains, which follow north along the Great Wall of China and south through Shansi, marking the provinces of Chihli, Shansi, Shensi, Kansuh, Jehol, Chahar, Suiyuan, Honan and Hupeh. The area covered is shaped like a letter T and is defined by its terminations in the two Kuans and the two Kous, Shanhai-kuan, Chia-yü-kuan, Chang-chia-kou and Hankow, see Fig. 5.

Both of these plants yield ephedrine and pseudoephedrine (12) (13), and both show great seasonal variation. The best yield is from the green stems of the E. equisetina collected in October which contained 1.75 per cent as compared with 1.32 per cent in E. sinica. The berries (15), roots and woody stalks do not contain ephedrine.

#### EPHEDRA EQUISETINA, BGE.

I. General Characteristics.—Plant 1-2 m. high; stem woody; branches cauline, longitudinally striated; much branched, 2-3 branchlets whorled at node; internodes 1-3 cm. mostly, April 1928

and 4 cm. rarely; in general less than 1 mm. thick; flower sessile or sub-sessile, axial at nodes; female spike solitary, or 2 opposite or decussate; male spikes 3-5 glomerated.

II. Leaf.-Reduced to sheath at nodes; brownish purple; membrano-coriaceous; almost entirely or only slightly fissioned with a ring at base; 2 mm. in length; closely surrounding the branch or branchlet.

III. Male Spike.-Axial, sessile or very slightly sub-sessile; 3-5 flowers glomerated at node; each flower is 2 mm. each way, and consists of 4 pairs of bracts, arranged decussatelythe lowest pair being sterile; each calyciform bract subtends a pair of membranous sheaths, the perianth, in which is enclosed the stamen with 7 or 8 anthers; the perianth is 2 mm. each way;

the anthers are so arranged that the inner surface appears flat, while the outer one is convex; the filament is 0.5 mm. long.

Female Spike.-Axial, sessile or IV. sub-sessile, peduncle when present is 2.5 mm. long; mostly 2 flowers opposite or decussate at node, or merely solitary; the flower is 7 mm. long, and 3 mm. wide; the peduncle is subtended by a pair of bracts or sheaths, united  $\frac{2}{1}$  of the way; above this, there are 3-4 pairs of bracts, arranged decussately, all sterile, except the top pair, which encloses one flower in an entire perianth sheath; each bract is 4.5 x 2-2.5 mm., the lowest pair being slightly smaller; the micropyle is 3 mm. in length, 2 mm. being exserted; the ovule is 0.5 mm., and the pedicel 0.5-1 mm.

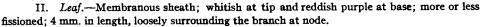
V. Fruit.-When mature, red and fleshy; 9 mm. long, 5 mm. thick with a short pedicel, which is 1.5 mm. or so long; 3 pairs of bracts, the middle one, being the least fissioned: 1 seed is enclosed in the topmost pair of bracts.

VI. Seed .- Coat hard; purplish; ovate, one side more angularly convex than the other; 7 mm. long, 3 mm. wide, and scarcely 2 mm. thick.

#### EPHEDRA SINICA, STAPF, SPEC. NOV.

#### (Mahuang.)

I. General Characteristics.—Plant 30 seed: both surfaces convex. em. high; branches radical and simple, i. e., rarely further branched; somewhat flat and ing spikes terminal, or at upper nodes; surface flat, the other triangularly convex. solitary.



III. Male Spike.-4 x 3 mm.; terminal or at the uppermost 1 or 2 nodes; consisting of 4 or 5 pairs of bracts, the lowest pair always sterile; the bracts are arranged decussately, the 2 middle pairs the largest; each fertile bract subtends a pair of perianth sheaths, in which is enclosed a stamen with 7 or 8 anthers.

IV. Female Spike.-Terminal or at the uppermost 1 or 2 nodes; 3-4 pairs of thick brownish bracts arranged decussately, only the topmost pair, being fertile, encloses 2 flowers.

V. Fruit.-Red and fleshy when mature; 2 seeds are enclosed in the uppermost pair of bracts.

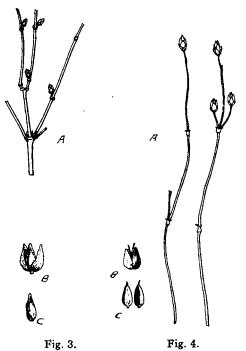


Fig. 3.-Ephedra equisetina, Bge. A, branch, showing axial flowering spikes, smaller leafsheaths, relative shorter internodes and much branched branchlets; B, 1-seed in spike; C,

Fig. 4.-Ephedra sinica, Stapf. A, branch, showing terminal flowering spikes, larger leaflongitudinally striated; internodes 3-5 cm., sheath; longer internodes, and not much rarely below 2 cm.; 1-1.5 mm. thick; flower-branched; B, 2-seeds in spike; C, seed: one VI. Seed.—Coat hard; purplish; one side flat, while the other is triangularly convex;  $5 \times 3 \times 1.5$  mm. for the length, width and thickness of the seed, respectively.

#### COMPARISON OF EPHEDRA EQUISETINA WITH EPHEDRA SINICA.

### Ephedra equisetina.

1. Stem.—1-2 m. high; woody.

2. Branch.—Cauline and much branched; up to 1 mm. thick; round; internodes 1-3 cm.

3. Leaf.—2 mm. long; reddish purple; membrano-coriaceous; closely surrounding the branch at nodes.

4. Spike.—(a.) axial.

(b.) female spike uniflowered.

(c.) male spike 3-5 glomerated.

5. Seed.—1 in the female spike; both sides convex.

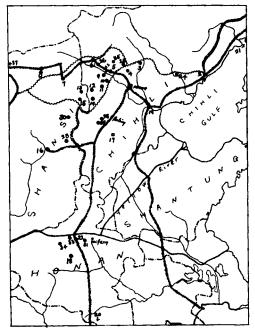


Fig. 5.—Natural Habitat of Ephedra in China. (6), I (The numerals refer to the names of places in the (35). text.) Ephedra sinica.

30 cm. high; herbaceous.

Radical and slightly branched; more than 1 mm. thick; somewhat flat; internodes 3-5 cm.

4 mm. long; whitish membranous above and brownish purple below; loosely surrounding the branch at node.

Terminal or at upper nodes.

Female spike, 2-flowered.

Male spike, solitary.

2 in the female spike; 1 side triangularly convex, the other flat.

THE HABITAT OF EPHEDRA IN CHINA.

(The numerals refer to places in the map.)

I. Ephedra sinica, Stapf, spec. nov. (syn. E. mahuang, Liu) has been collected by us in the following districts in the Chihli province: Kalgan (6), Peitaiho (1), vicinity of Shanhaikwan (2), Huai Lai (5), Fan Shan (10), Ta T'ung (7), Sui Yüan (8), Hsiao Wu T'ai Shan (11), Shuang Shu Tzu (9) and near Hsin Pao An (22).

The same species has been collected and sent to us by drug dealers from Yen Ch'ing Chou (35), Ku Pai K'ou (3), Hsi Feng K'ou (24), Yung Ning (25), and Pao T'ou (27), Hsüan Hua Fu (26) Yü Hsien (12).

II. *E. equisetina*, Bge. has been found by us in T'ai Yüan Fu (16) of Shansi.

The same species has been sent to us through drug dealers from the following districts on the Chihli-Shansi border: Ling Ch'iu Hsien (15), Kuang Ling Hsien (13), Kuang Ch'ang Hsien (14), Yü Hsien (12), another Yü Hsien (23), Ta Wu T'ai Shan (30), Ku Pei K'ou (3), Wan Hsien (28), T'ang Hsien (29), Kalgan (6), Hsuan Hua Fu (26), and Yen Ch'ing Chou (35).

The chief market-places for Mahuang are: Ch'i Chow (17), Tientsin (19), Hankow

(20), Newchuang (21), and Cheng Chow, Honan (32).

In 1885 exported Mahuang amounted to 966 piculs from Newchuang, 213 piculs from Tientsin, 66 piculs from Hankow, and 31 piculs from Ningpo. These figures give some indication of the extent to which Mahuang grows in these or nearby areas.

According to Pen Ts'ao Kang Mu, the Chinese Materia Medica, Mahuang is produced in Chung Mou (31), and Jung Yang (33) in Honan. At present, it is reported that Mahuang is still found in these two places, as well as in Sung Shan (34), and Yü Chow (18), of the same province.

Bretschneider's (12) translation also quotes the occurrence of this plant in Tsingchou, E. Shantung, and in P'eng ch'eng, Kiangsu. Also that the drug from Szechuan is of an inferior quality. An entirely different species is reported from Western China, concerning which we

## April 1928 AMERICAN PHARMACEUTICAL ASSOCIATION

have no chemical or physiological data. Su Kung (7th cent.) said that it grows plentifully in Chengchou (32); Lu t'ai (unknown); Kuan chung, Shensi; Sha yuan, Shensi; on the banks of the Yellow River and sandy islets.

A study of the known geographic distribution of ephedra reveals the fact that heretofore this very important area yielding Mahuang has been entirely overlooked, Fig. 6. It is in no sense a rarity, but owing to its mountainous character

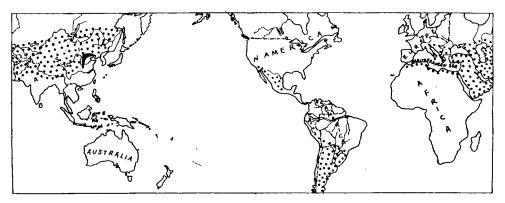


Fig. 6.—Geographical Distribution of Ephedra. (The dots indicate localities where found. The hook mark in Asia indicates a locality not reported before.)

and the lack of good communications in China little has been known about it. Moreover botanical material has only too often been limited to isolated male or female plants, and the tiny bract-like leaves are too insignificant to afford marked distinction between one species and another, without other gross differences.

The general histology of the stem of E. sinica has been described by Liu (8).

The Crude Drug Ma Huang.—Read and Feng (13) have carefully examined the gross material and give the chief points of difference between these two species as far as the weight, length and number of internodes, of the green stems is concerned. The green stems are the only part used in medicine. Old yellow stems are considered worthless.

The woody branches of E. equisetina are useless and make the separation of the stems a troublesome matter. In spite of the fact that this species shows from the green stems a better yield of alkaloid and a larger relative and absolute percentage of ephedrine the difference is not so great as to make it preferable for the Chinese druggist, who can by one blow of an axe sever the green stems of E. sinica from the useless woody parts of the root. It is quite clear that Neilsen has had both of these varieties to deal with.

The roots are useless for making ephedrine. E. equisetina with its excessive wood sometimes shows a large woody root as thick as a man's arm. In both species the roots are very long. This summer many of the small E. sinica dug out from the side of banks were traced for more than a yard. In Chinese Medicine by the bipolar theory, namely that the root has an action opposite to the leaves and branches, Mahuang root is used in the treatment of profuse sweating. Fujii (6) obtained a new base from these roots.

The aroma of fresh Mahuang is quite characteristic. Our experience agrees with Neilsen's report (10), that the penetrating aromatic odor remains during the

# JOURNAL OF THE

entire process of extraction and is quite pronounced in the isolated alkaloid, and its salts. This we have noticed for a very long time and regarded as characteristic of ephedrine compounds, until by exposure to the air for several days we found the aromatic body readily volatilized leaving what is accurately described by the N. N. R. (11) as an *odorless* compound.

Collection of the drug in the autumn before the winter frost, has been shown by us to be essential to a good yield of the alkaloid, there being a difference of 300 per cent between spring and autumn (13).

### SUMMARY.

Mahuang has been identified definitely as Ephedra sinica, Stapf, and Ephedra equisetina, Bunge.

These common species of Ephedra are collected in hitherto botanically unrecognized areas on the Tai-hang-shan mountains from Shanhaikuan in North Chihli, along the Mongolian border and down through Shansi.

Characteristics of both varieties are fully described and illustrated, especially as they relate to the more important uses of the crude drug.

E. equisetina, known as Mupen Mahuang, is very woody and luxurious, and has a high content of ephedrine when collected in the autumn.

E. sinica, known as "Tsaopen Mahuang," is herbaceous and more convenient for collection, and has a good ephedrine content.

## **REFERENCES.**

- (1) J. N. Bretschneider, China Br. Royal Asia. Soc., 29 (1894-95), 180.
- (2) K. K. Chen, JOUR. A. PH. A., 14 (1925), 189.
- (3) K. K. Chen and C. H. Kao, Ibid., 15 (1926), 625.
- (4) T. Q. Chou, J. Biol. Chem., 70 (1926), 109.
- (5) M. H. Cowdry, Proc. Roy. Asia Soc., 53 (1922), 158.
- (6) M. Fujii, J. Oriental Med., 4 (1925), 56.
- (7) E. M. Holmes, Pharm. J., 117 (1926), 643.
- (8) J. C. Liu, China Journal, 7 (1927), 81.
- (9) E. R. Miller, Arch. Pharm., 240 (1902), 481.
- (10) C. Neilsen, et al., JOUR. A. PH. A., 16 (1927), 288.
- (11) N. N. R., J. A. M. A., 88 (1927), 923.
- (12) B. E. Read and C. T. Feng, Chinese J. Physiol., 1 (1927), 235.
- (13) B. E. Read and C. T. Feng, Ibid., 1 (1927), (in press).
- (14) B. E. Read and C. T. Feng, Proc. Soc. Exptl. Biol. Med., 24 (1927), 819.
- (15) B. E. Read and C. T. Feng, Pharm. J. (1927).
- (16) O. Stapf, Deuschr. Akad. Wiss. Wien, math. natw. Kl., 56 (1889), Abt. 2. S. 1-112.
- (17) O. Stapf, Kew Bulletin (1927), p. 133.

### MEDAL TO COMMEMORATE ACHIEVEMENTS OF EDISON.

Proposed legislation authorizing a medal commemorative of the achievements of Thomas A. Edison was approved March 29th, by the House Committee on Coinage, Weights and Measures.

The Committee voted a favorable report on the Perkins resolution (H. J. Res. 243) authorizing the appropriation of \$1000 for a medal to be struck by the Department of the Treasury and providing for duplicate medals to be sold under regulations prescribed by the Secretary of the Treasury.

Information filed with the Committee showed that in the course of his career Mr. Edison has applied for 1328 patents and the monetary value of industries entirely based on the Edison inventions, or which have been materially stimulated by his inventions, was estimated at \$15,599,-000,000.